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ABSTRACTS OPEN

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Poster Session/ Lunch I

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S1. Reactivity to social stress in second-generation Moroccan-Dutch men, a proxy for social defeat

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Background: The increased psychosis risk for ethnic minority groups may be due, at least in part, to the experience of social exclusion. We hypothesized that repeated exposures to social exclusion, through a process of sensitization, may result in larger responses to experiences of social stress. The current study used a within-study cross-paradigm design to test the hypothesis that healthy Moroccan-Dutch men, as a proxy for social defeat, respond stronger to social stress than Dutch controls 1) in daily life, and 2) in an experimental set-up.
Methods: A general population sample of 50 Moroccan-Dutch and 50 Dutch young adult males were tested with 1) the Experience Sampling Method, a structured diary technique, assessing reactivity to social stress in daily life and 2) an experimental exposure to negative social evaluation.
Results: In the course of daily life, no differences were found in affective (B = -0.01, 95% CI -0.08 to 0.06, $P = 0.77$) or psychotic (B = 0.03, 95% CI -0.02 to 0.08, $P = 0.28$) reactivity to social stress between Moroccan-Dutch and Dutch participants. When exposed to a negative social evaluation in a lab environment, a blunted affective (B = -0.31, 95% CI -0.52 to 0.10, $P = 0.004$) response was found in the Moroccan-Dutch group, while the psychotic response (B = -0.16, 95% CI -0.36 to 0.04, $P = 0.11$) did not differ between groups.
Discussion: These findings suggest that healthy Moroccan-Dutch men are not sensitized to social stress. Their blunted affective response to negative social evaluation may signify the occurrence of habituation as a result of repeated exposures to social exclusion instead.

S2. Assessment of cardiac autonomic modulation in antipsychotic-induced akathisia

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Background: Electrophysiologic technology is allowing the acquisition of unprecedented biosignal information related to individuals' subjective well-being as well as the provision of novel methods of psychiatric evaluation. This study aimed to investigate changes in cardiac autonomic modulation preceding antipsychotic-induced akathisia.
Methods: Resting electrocardiograms (ECGs) were recorded from individuals with schizophrenia receiving antipsychotic treatment. Time, frequency and complexity domain parameters of heart rate variability (HRV) were extracted from baseline ECGs, and compared between 14 patients reported antipsychotic-induced akathisia and 14 matched patients without akathisia. Levels of depression, anxiety and subjective well-being were also measured in relation to HRV parameters.
Results: Multivariable analysis of variance suggested a distinctive pattern of cardiac autonomic regulation in association with drug-induced akathisia. Akathisia was associated with a lower high-frequency heart rate power spectrum, a higher ratio of the low- to high-frequency heart rate power spectrum. In addition, lower sample entropy was observed in patients reported akathisia.
Discussion: In addition to low cardiovagal tone, decreased complexity of cardiac autonomic modulation may suggest reduced adaptability of central autonomic network to antipsychotic-induced changes, thereby increasing the risk for akathisia.

S3. Intermediate results of a study about sexual dysfunction in patients with schizophrenic disorders treated with atypical antipsychotics

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Background: Sexual dysfunction is a frequent disorder suffered by patients with schizophrenia, although its aetiology is yet unclear. This problem is documented by schizophrenic patients to be one of the areas of treatment with the most unmet needs. Our objective is to study how the psychopathology, metabolic factors and prolactine levels influence the appearance of sexual dysfunction in patients with schizophrenic disorders treated with different atypical antipsychotics.
Methods: Design: observational, open, transversal with a single visit. Study population: outpatients attended to at Mental Health Centers in the south of Seville (Spain), diagnosed with schizophrenia and schizoaffective disorders (ICD-10 criteria), under treatment for more than 6 months with atypical antipsychotics in monotherapy. Exclusion criteria: severe concomitant somatic pathology; pregnancy and lactation; patients treated in the previous 6 months with antidepressants or moodstabilisers. Psychopathology was evaluated by PANSS and HDRS; metabolic factors by BMI, glycaemia, cholesterol, triglycerides, abdominal circumference and blood pressure; prolactine by plasma levels (basal and 15 minutes after); sexual dysfunction by PRSexDQ-SALSEX.
Our study was financed through an Instituto de Salud Carlos III Grant (PI 11/00569), Ministry of Health, Spanish Government.
Results: To date, 45 patients have been recruited: 32 males, 13 females; mean age 40.1 years (SD = 10.2 years). 31 were single, 7 married and 7 divorced. Only 7 patients were regular drinkers, and 4 consumed cannabis frequently. Mean time since the diagnosis was 13.7 years (SD = 8.8). Only 20% of patients had a normal BMI and 14 of them (31.1%) showed ≥ 2 metabolic syndrome factors. They were treated with: Aripiprazole 7 patients; Clozapine 6; Olanzapine 14; Risperidone / Paliperidone 14; Quetiapine 1. Basal prolactynemia (□ = 20.5 ng/mL) was similar than 15´ prolactynemia (□ = 19.1 ng/mL). Concerning their sexuality, 28 patients (62%) showed drug-induced sexual dysfunction. However, this item was spontaneously communicated only in 22% of them. Sexual relations started at a mean age of 15.9 years.The PRSexDQ-SALSEX total score (mean) was 4.3 (SD = 3.4), which indicates a mild degree of sexual dysfunction among the

subjects of our study. However 55% of them showed moderate or intense quality of dysfunction rated by SALSEX. Respecting HDRS, the total score (mean) was 6.3 (SD = 3.5). Despite this slight degree of depressive symptoms, it significantly associates with sexual dysfunction ($P < 0.01$). Our results are also practically significant about the link between negative and entire schizophrenic symptoms (evaluated by Negative and Total PANSS Subscale) and Sexual Dysfunction ($P < 0.052$).
Discussion: The result of 62% of our patients marking some sexual dysfunction secondary to treatment added to the 55% of them with moderate or intense quality of dysfunction, clearly highlight the presence of this disorder in schizophrenic patients. However, sexual dysfunction in our study only associates significantly with depressive and negative symptoms, not with BMI, prolactynemia, metabolic factors or kind of antipsychotic drug. These findings support a multifactorial aetiology for sexual dysfunction in patients with schizophrenic disorders, which could not only be caused by antipsychotic drugs.

S4. Neurocognitive profile of childhood trauma-related mixed psychopathology phenotype in psychosis

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Background: Earlier studies have shown that psychotic patients exposed to childhood trauma (CT), compared with those without CT, show a mixed phenotype of psychopathology (mp) including affective, anxious, and psychosis symptoms. Cases with CT/mp reported a poorer quality of life and more severe symptoms,than those without CT exposure and/or mp. CT has been found to be associated with poor executive functioning and working memory in schizophrenia. Furthermore, poor cognitive functioning has been linked with poor global outcome and symptom severity, therefore part of the clinical and functional relevance of CT/mp may due to impairments in cognitive functioning. Identifying the cognitive profile of cases with CT/mp may provide indicators for targeted treatment options.
Methods: 532 non-affective psychotic disorder patients were assessed on CT history, symptom profiles (depression, anxiety, psychosis and mania), cognition (verbal learning, attention, working memory), and global functioning (GAF). Subjects were assessed at baseline (T0), 3-year follow-up (T1) and 6-year follow-up (T2). Subjects were divided according to CT history and symptom profiles: no trauma and no or isolated symptoms (CT-/mp-, $n = 272$); no trauma and mixed phenotype (CT-/mp+, $n = 157$); trauma and no or isolated symptoms (CT+/mp-, $n = 49$); and trauma and mixed phenotype (CT+/mp+, $n = 54$). These four groups were compared on all cognitive measures using all three measurements. Furthermore, the relationship between cognitive functioning at baseline and global functional outcome at T2 was assessed.
Results: The CT+/mp+ group showed lower delayed recall than CT-/mp- (B = -0.78, CI95% = -1.49- -0.07, $P < 0.05$) and CT-/mp+ (B = -1.07, CI95% = -1.81- -0.32, $P < 0.01$). CT+/mp+ showed poor immediate recall (B = -1.71, CI95% = -3.35- -0.06, $P < 0.05$) poor retention rate (B = -0.06, CI95% = -0.11- -0.01, $P < 0.05$) than CT-/mp+. CT+/mp+ showed poor working memory than CT-/mp- (B = 0.07, CI95% = 0.006-0.14, $P < 0.05$) and CT+/mp- (B = 0.12, CI95% = 0.04- 0.20, $P < 0.01$). However, most of these contrasts did not survive Bonferroni correction, except for CT+/mp+ vs CT-/mp+ on delayed recall. Poor immediate recall at baseline is linked with more disability at T2 in both the CT+/mp+ (B = 1.52; CI95% = 0.18-2.86; $P = 0.03$) and the CT-/mp- group (B = 0.37; CI95% = 0.02-0.72; $P = 0.03$).
Discussion: Among cases with mp those with CT showed poor delayed recall. Other cognitive domains not distinguish cases with CT+/mp+ from those without CT/mp. Poor cognition predicted poor outcome at follow-up, independent of trauma exposure or symptom profile. Although cognition may be an endophenotypic marker in schizophrenia, further studies are required to clarify the cognitive profile of CT/mp in psychosis.

S5. Impact of different childhood adversities on 1-year outcomes of psychotic disorder in the genetics and psychosis study

Antonella Trotta*[1], Robin Murray[1], Anthony David[1], Anna Kolliakou[1], Jennifer O'Connor[1], Marta Di Forti[2], Paola Dazzan[1], Valeria Mondelli[1], Craig Morgan[1], Helen Fisher[2]

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Background: There is a wealth of evidence suggestive of an association between childhood adversity (eg, physical and sexual abuse, neglect, death of or separation from a parent) and psychosis, reported from both general population and clinical studies. However, little is known about the effect of experiences of adversity during childhood on the course or outcomes of psychosis.
This study aimed to determine the impact of different types of childhood adversity on 1-year outcome across 3 domains (clinical, social, and service use) in a catchment- based sample of individuals presenting to mental health services for the first time with psychotic disorder.
Methods: The sample was drawn from patients who participated in the Genetics and Psychosis Biomedical Research Centre (GAP-BRC) study. The Childhood Experience of Care and Abuse Questionnaire (CECA.Q) was employed at baseline to retrospectively elicit information from participants concerning a range of adverse childhood experiences (physical abuse, sexual abuse, parental separation, parental death, disrupted family arrangements, or being taken into care). Data on illness course, symptom remission, length of psychiatric hospitalization, compliance with medication, employment, and relationship status were extracted from clinical records for the year following first contact with mental health services for psychosis.
Results: Information on childhood adversity was available for 285 first-presentation psychosis patients. Exposure to at least 1 type of childhood adversity was reported by seventy-one percent of patients. No robust associations were found between childhood adversity and illness course or remission. However, childhood physical abuse was associated with almost 3-fold increased odds of not being in a relationship at 1-year follow-up compared to patients who did not report such adverse experiences. There was also evidence of a significant association between parental separation in childhood and longer admissions to psychiatric wards during 1-year follow-up and 2-fold increased odds of non-compliance with medication compared to those not separated from their parents.
Discussion: Given the high prevalence of childhood adversities reported by first-presentation psychosis cases in this sample, routine assessment of adversity history and psychotherapies focused on adverse childhood experiences should be considered by services providing treatment to psychosis patients. Moreover, as shown in this study, without considering past exposure to (at least some) adverse experiences, the efforts to engage and treat psychosis patients may be unsuccessful.

S6. Extrapyramidal symptoms during treatment with quetiapine versus aripiprazole in children and adolescents with psychosis, the TEA trial

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Background: The objective of the Tolerability and Efficacy of Antipsychotics (TEA) trial is to compare the benefits and harms of

quetiapine ER versus (vs) aripiprazole in early onset psychosis (EOP). Compared to adults, children and adolescents treated with antipsychotics are more prone to adverse reactions such as extrapyramidal symptoms (EPS). We hypothesize that EPS is more severe and frequent in patients treated with aripiprazole compared to quetiapine.
Methods: In this Danish investigator-initiated, independently funded, multi-centre, randomised, blinded clinical trial (RCT) patients aged 12-17 years with a first-episode of psychosis were 1:1 randomised to a 12-week, double-blind intervention with quetiapine ER vs aripiprazole. EPS were assessed by the Abnormal Involuntary Movement Scale, the Simpson Angus Scale, the Barnes Akathisia Scale and the UKU (Udvalget for Kliniske Undersøgelser) side effect rating scale at 2, 4, and 12 weeks after randomisation In addition, we registered all between-assessments events of EPS and the use of anticholinergic medication.
Results: A total of $n = 113$ patients (schizophrenia ($n = 75$), schizoaffective disorder ($n = 23$), affective psychosis ($n = 8$) and other psychoses ($n = 7$)) were randomised. Mean age was 15.8 years and 30% were males. We will report the severity and frequency of parkinsonism, akathisia and tardive dyskinesia, and the incidence rates of the use of anticholinergic medication, as well as discontinuations due to EPS.
Discussion: In this first RCT comparing quetiapine and aripiprazole for the treatment of early onset psychosis, we will present data comparing the neuromotor effects during treatment with quetiapine vs aripiprazole in EOP and discuss strengths, limits and future implications.

S7. Violence risk prediction in schizophrenia - a framingham approach?

Seena Fazel*[1], Achim Wolf[1], Susan Mallett[2], Paul Lichtenstein[3], Henrik Larsson[3], Thomas Fanshawe[1]

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Background: Violence risk is high in schizophrenia with absolute and relative risks higher than population controls and other mental illnesses. Current approaches to stratify patients into risk groups have been limited by low to moderate accuracy, inconsistent definitions of risk classifications, and many have considerable resource implications.
Methods: We developed predictive models for violent offending on a total national cohort of individuals aged 15-65 with a diagnosis of severe mental illness (schizophrenia, schizophrenic-spectrum, bipolar disorder, and other psychotic illness) through linkage of population-based registers in Sweden. We identified a cohort of 75 158 individuals with 574 018 recorded patient episodes between January 1, 2001 and December 31, 2008. First, a derivation model was developed to determine strength of pre-specified routinely collected criminal history, socio-demographic and clinical risk factors, and tested them in an external validation. We measured discrimination and calibration for prediction of violent reoffending at 1 year using specified risk cut-offs.
Results: A 16 item model was developed from pre-specified routinely collected criminal history, socio-demographic and clinical risk factors. In an external validation, the model showed good measures of discrimination (c-index 0.89) and calibration. For risk of violent reoffending at 1 year, using a 5% cut off, sensitivity was 64% and specificity was 94%. Positive and negative predictive values were 11% and 99%, respectively. The model was used to generate a simple and freely available web-based risk calculator (OxMIV).
Discussion: We have developed a prediction score in a national cohort of all patients with psychosis that can assist decision-making in clinical practice by identifying those who are at low risk of future violent offending and higher risk individuals who may benefit from additional risk management. Further evaluation in other populations and countries is needed.

S8. Variants in dopamine-related genes are associated to abdominal obesity and metabolic abnormalities caused by antipsychotic treatment

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Background: Obesity and metabolic syndrome frequently occur in patients receiving antipyschotic therapy. Metabolic syndrome (MS) is a major risk factor for cardiovascular and endocrine diseases in schizophrenic patients. All known antipsychotics are dopamine D2 receptor antagonists. It has been, thus, proposed that changes in dopaminergic activity may be associated with these adverse effects. Our aim is to study whether genetic variants, involving dopaminergic activity, influence the development of obesity and metabolic abnormalities in patients treated with antipsychotic drugs during a minimum of three months.
Methods: We included 135 schizophrenic patients (43 women and 92 men). The body mass index (BMI), body fat percentage (BFP), diastolic blood pressure (DBP), serum levels of fasting triglycerides (TG) and high density lipoproteins (HDL) were measured. We used the American Heart Association (ATP-III A) criteria to define MS, and the WHO criteria for obesity. We genotyped the rs4818 polymorphism in the Catechol-O-Methyltransferase (COMT) gene and the VNTR polymorphism in the dopamine transporter gene (DAT). We used Chi square test for association between each allele or genotype frequencies and the presence/absence of altered anthropometric and metabolic parameters. The ANCOVA test, controlling for age and sex, was used to study the association between alleles or genotypes and quantitative values.
Results: We noted that 62% of patients had overweight, 65% abdominal obesity, and 42% MS.
We found an association between COMT rs4818 genotypes and the presence/absence of altered BMI (X2; 6.59 df: 2 $P = 0.0370$), BFP ($X2 = 8.40$, df:2, $P = 0.0150$) and DBP values ($X2 = 8,53$, df:2, $P = 0.0140$). In addition, quantitative analysis shows that individuals heterozygous for the rs 4818 polymorphism had lower levels of BFP and DBP than CC and GG homozygous individuals (BFP: CG 27 ± 10 $n = 60$, CC 33 ± 9, $n = 43$, GG 31 ± 9 $n = 24$, $F = 3.04$, $P = 0.0514$ and DBP (mmHg): CG 74 ± 10 $n = 58$; CC 80 ± 13 $n = 39$; GG 82 ± 8 $n = 24$, $F = 6.48$, $P = 0.0021$). The VNTR DAT genotype was associated with the presence/absence of altered TG values ($X2 = 8.40$, df:1, $P = 0.0150$). Furthermore, patients homozygous for the 9-repeat variant had higher TG and lower HDL levels than 10-repeat carriers (TG (mg/dl): 9-9 genotype 152 ± 46 $n = 19$, 10-repeat carriers 123 ± 77 $n = 99$ $F = 5.72$ $P = 0.0184$ and HDL(mg/dl):9-9 genotype 39 ± 10 $n = 19$, 10-repeat carriers 46 ± 11, $n = 99$, $F = 6.24$, $P = 0.0140$).
Discussion: The observed metabolic abnormalities are similar to those described in other studies. The associations between COMT rs4818 or DAT VNTR polymorphisms and adverse effects of antipsychotic treatment, had not been found in two previous studies. However, different COMT polymorphisms and haplotypes have been found to be associated with BMI, BFP and DBP; and the DAT VNTR polymophism have been associated with different metabolic alterations. The DAT VNTR polymorphism is related with the availability of synaptic dopamine, and the COMT rs4818 polymorphism, located in the gene coding region, may have functional relevance. It is, therefore, possible that the dopaminergic system is involved in some adverse effects produced by antipsychotic treatment.
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S9. Are antipsychotic drugs associated with increased or reduced mortality and serious adverse events? a meta-analysis

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Background: Due to their side-effects antipsychotic drugs are very controversial. An important aspect is the potential mortality associated with these drugs. Antipsychotics could either increase mortality by their side-effects or they could reduce it by the reduction of suicide attempts.
Methods: To better understand this issue, we conduct a meta-analysis of randomised controlled trials that compare the following second-generation antipsychotic drugs and haloperidol with placebo: amisulpride, asenapine, aripiprazole, brexpiprazole, cariprazine, haloperidol, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, sertindole, ziprasidone, zotepine. We include both short-term and long-term RCTs. Data sources will be the Cochrane Schizophrenia Group's specialized register, MEDLINE, EMBASE, CENTRAL, ClinicalTrials.gov and the FDA website, supplemented by requests to study authors. Data extraction is done by two persons independently. All outcomes are dichotomous and will be presented as odds ratios and their 95% confidence intervals.
Results: We expect approximately 200 included studies. Preliminary results will be presented at the conference.
Discussion: Our final results will expand the knowledge on evidence base for the treatment of schizophrenia. In particular, the results will clarify the question whether in randomised controlled trials antipsychotics are associated with increased or decreased mortality compared to placebo. Moreover, rare, but serious adverse events will for the first time be examined in a meta-analysis.

S10. Comparison of 3-monthly versus 1-monthly paliperidone palmitate for time to onset and time to resolution of extrapyramidal symptoms in patients with exacerbated schizophrenia

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Background: This post-hoc analysis was performed to determine if there was a difference in the overall incidence, time of onset and resolution of extrapyramidal symptoms (EPS) related adverse events (AEs) when paliperidone palmitate (PP) was administered as a 3-monthly (PP3M) vs. 1-monthly (PP1M) long-acting injectable in patients with exacerbated schizophrenia.
Methods: Patients with schizophrenia received flexible-doses of PP1M (50, 75, 100, or 150 mg eq.) during open-label (OL) phase (17 weeks), followed by fixed-dose injections of either PP3M (175, 263, 350, or 525 mg eq.) or PP1M (50, 75, 100, or 150 mg eq.) during double-blind (DB) phase (48 weeks) in a randomized, non-inferiority, phase-3 study. Data from this study were used for the post-hoc analysis to compare overall incidence, time-to-onset (TTO) and time-to-resolution (TTR) of EPS-related AEs after treatment with PP1M and PP3M. EPS-related AEs were summarized by grouped terms (Overall and further classified into Dystonia, Dyskinesia, Hyperkinesia, Parkinsonism and Tremor). For any EPS group, TTO is defined as the minimum value of the time to onset for different AEs in that group. TTR of an EPS-related AE is defined as number of days from onset date to resolution date. For patients who had more than one event for a specified EPS-related group, only the event for that specified EPS-related AE with longest time to resolution was included in the TTR analysis. For any AE that did not resolve during a phase, the time to resolution is calculated using the end date of that phase. EPS-related AEs were summarized by EPS groups, study phases, TTO and TTR, and descriptively compared. TTO and TTR for the overall EPS group were further analyzed descriptively by final OL dose (50/75 mg eq., 100 mg eq. and 150 mg eq.) and age (18-25, 26-50 and 50+ years) subgroups.
Results: Overall incidence rate of EPS-related AEs was 12.6% (PP1M) during OL phase, reducing to 8.3% (PP3M) and 7.4% (PP1M) during DB phase. Incidence rates for all categories of EPS symptoms (except for dystonia) were comparable between PP3M and PP1M groups at DB endpoint. Median TTO for all EPS-related AEs was 17 days (range: 1-120) in patients treated with PP1M during OL phase; and 115 days (range: 1-323) and 98.5 days (range: 1-322) after treatment with PP3M and PP1M, respectively during the DB phase. Median TTR of all EPS-related AEs was 36.5 days (range: 1-127) in PP1M group (OL), and was generally similar for PP3M (91 days [range: 1-336]) vs. PP1M (85.5 days [range: 1-337]) during the DB phase. Overall median TTO and TTR values were comparable between the PP3M and PP1M formulations. Furthermore, subgroup analysis revealed no clear dose-response or age-related differences in the TTO and TTR of EPS events for the two formulations.
Discussion: From this post-hoc analysis, the overall incidence of EPS-related AEs, time of onset and resolution of EPS-events were found to be comparable in adult patients with exacerbated schizophrenia receiving either PP3M or PP1M long-acting injectable.

S11. Previous attempts of suicide in first episode of psychosis and premorbid adjustment

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Background: Suicide has been shown to be the single major cause of premature death among patients with schizophrenia spectrum disorders. It has been suggested that history of attempts of suicide are one of the principal predictor of suicidal behavior. This study examined the influence of premorbid adjustment in attempts of suicide occurred before of first episode of psychosis (FEP). Little is known about premorbid functioning like risk factor for suicide attempts. The current study examined the association of premorbid functioning and previous attempts of suicide of FEP.
Methods: Sixty-five first-episode patients participated in this study. Baseline demographic clinical data and information about suicide attempts previous at FEP were collected in the first contact with mental health services. Sociodemographic and clinical data were collected from information provided by the patients and their relatives. We used Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) to screen for psychotic symptoms which were then used for diagnosis. Information about suicide attempts previous at FEP was collected using Schedules for Clinical Assessment in Neuropsychyatry SCAN. This clinical interview contains a question about attempted suicide. Premorbid Adjustment Scale (PAS) comprises 36 items describing levels of functioning before the onset of psychosis during four periods in life: childhood (up to 11 years), early adolescence (12-15 years), late adolescence (16-18 years) and adulthood (19 years and beyond).
Results: Poor premorbid adjustment in early adolescence was significantly associated with prior attempts of suicide at FEP (OR = 1.13, 95% CI = 1.00-1.26). The others premorbid adjustment didn´t predicted attempts of suicide before FEP
Discussion: Few studies have investigated risk factors of priors' attempts of suicide at FEP. The knowledge about those risk factors could help clinicians to identify high-risk patients. In this study poor premorbid adjustment in early adolescence is associated with attempts of suicide previous at FEP. Greater attention to person with poor premorbid adjustment in early adolescence may form the basis for early interventions aimed towards reducing the risk for subsequent suicide attempts.

S12. Benzodiazepines long-term consumption is associated with higher aggressiveness in schizophrenia. Results from the face-sz dataset

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Background: The primary objective of this study was to determine if second generation antipsychotic (SGA) administration was associated with lower aggressiveness scores compared to first generation (FGA) in schizophrenia (SZ). The secondary objective was to determine if antidepressants, mood stabilizers and benzodiazepines administration were respectively associated with lower aggressiveness scores compared to patients who were not administered these medications.
Methods: 331 patients with schizophrenia ($N = 255$) or schizoaffective disorder ($N = 76$) (mean age = 32.5 years, 75.5% male gender) were systematically included in the network of FondaMental Expert Center for Schizophrenia and assessed with the Structured Clinical Interview for DSM-IV Axis I Disorders and validated scales for psychotic symptomatology, insight and compliance. Aggressiveness was measured by the Buss-Perry Aggression Questionnaire (BPAQ) score. Ongoing psychotropic treatment was recorded.
Results: Patients who received SGA had lower BPAQ scores than patients who did not ($P = 0.01$). More specifically, these patients had lower physical and verbal aggression scores. On the contrary, patients who received benzodiazepines had higher BPAQ scores than patients who did not ($P = 0.04$). No significant difference was found between BPAQ scores of patients respectively being administered mood stabilizers (including valproate), antidepressant, and the patients who were not. These results were found independently of sociodemographical variables, psychotic symptomatology, insight, compliance into treatment, daily-administered antipsychotic dose, the way of antipsychotic administration (oral vs long acting), current alcohol disorder and daily cannabis consumption.
Discussion: The results of the present study are in favor of the choice of SGA in SZ patients with aggressiveness, but these results need further investigation in longitudinal studies. Given the potent side effects of benzodiazepines (especially dependency and cognitive impairment) and the results of the present study, their long-term prescription is not recommended in patients with schizophrenia and aggressive behavior.

S13. Treatment with anti-toxoplasmic activity (TATA) for toxoplasma positive patients with bipolar disorders or schizophrenia: a cross-sectional study

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Background: The association between Toxoplasma gondii seropositivity and respectively Bipolar Disorder (BD) and Schizophrenia/Schizoaffective disorder (SZ) is one of the most studied link between one pathogen and psychiatric disorders. The aim of the present study was thus to retrospectively determine if the administration of an antipsychotic and/or a mood stabilizer having known in vitro Anti-Toxoplasmic Activity (TATA+) was associated with a better clinical outcome in a population of 152 BD or 114 SZ patients and seropositive for T. gondii infection compared to patients receiving a treatment without anti-toxoplasmic activity (TATA-).
Methods: This multicenter study was conducted in an academic public hospital during a 3-years period between 2009 and 2011. All consecutive inpatients and outpatients with SZ or BD diagnosis with a stable treatment for more than 4 weeks were recruited. sociodemographic and clinical characteristics measured with validated scales as well as a serological status for toxoplasmic infection were included. Treatments were classified according to their in vitro antitoxoplasmic activity. A multivariate model was used to determine the clinical characteristics that were significantly different between patients receiving a treatment with no antitoxoplasmic activity compared to others.
Results: BD patients with positive serum antibodies against T. gondii presented more lifetime depressive episodes ($P = 0.048$) after adjustment for age, sex and sociodemographic characteristics when treated by drug having no anti-toxo activity, compared to patients having received drugs with anti-toxo activity. A significant difference was not found in BD toxonegative patients and in SZ toxopositive or toxonegative patients.
Discussion: It seems to be of importance to consider prescribing a drug with a clear anti-toxoplasmic activity (TATA+) for BD patients seropositive to T. gondii, in particular valproate that was found as the mood stabilizer with the highest antitoxoplasmic activity. Prospective randomized controlled trials are warranted to confirm this preliminary data.

S14. Lipidomic study of the antipsychotic-induced metabolic syndrome in schizophrenia patients. Towards a lipidic biomarker of metabolic syndrome?

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Background: The development of a metabolic syndrome (MS) in antipsychotic (AP) treated schizophrenia (SCZ) patients is multifactorial. Carbohydrate and lipid abnormalities have been described in patients with MS. Several causes such as disease intrinsic risk, antipsychotic-associated effect, and unhealthy living style have been postulated to promote MS. Nevertheless not all AP-treated patients develop a MS. The purpose of this study was to examine the differences in membrane and plasma lipid profile in SCZ with and without MS.
Methods: Red blood cell (RBC) membrane and plasma lipids have been examined in a population of chronic medicated patients with and without MS (MS+ $n = 8$ and MS- $n = 13$ respectively). Phospholipids (PL) as well as their constitutive fatty-acids (FA), cholesterol and its precursors as well as membrane-intercalated and plasma circulated AP have been identified and measured using mass spectrometry methods. Criteria for metabolic syndrome included waist circumference over 102cm (M) or 88 (F) and any 2 among 4 criteria (blood pressure, HLD, triglyceride, and glucose).
Results: As expected, the plasma TG level was increased in the MS+ population. No differences were observed in PL ratios in neither plasma nor membrane between the two MS subgroups. In contrast, relative to MS- patients, MS+ exhibited a decrease in linoleic acid (C18:2 n-6) in plasma ($P = 0.005$) and RBC membrane ($P = 0.01$). Molecular species of phosphatidylethanolamine (PE) and phosphatidylcholine (PC) significantly differed between the two MS subgroups. An increased level of lathosterol, a cholesterol precursor, was significantly ($P = 0.01$) increased in MS+ patients in plasma and RBC membrane. A membrane concentration of AP above 10% was associated with a significant increase in 7-lathosterol.
Discussion: While some lipid abnormalities found in plasma in MS+ patients are expected and tautological to the MS definition, other can be acknowledged as more specific to the deregulated metabolic pathways associated the AP-induced MS. AP which are known to inhibit some enzymes involved in the metabolic cascade of the cholesterol synthesis seem to exhibit differences in this inhibitory action in patients with and without MS. Furthermore, the lipidic abnormalities observed in MS+ individuals are only in part identical in the plasma and membrane, suggesting both general and compartmentalised lipid deregulation in MS+ relative to MS- individuals.

S15. Molecular prediction of metabolic syndrome in psychosis

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Background: Antipsychotic medications are widely prescribed for the treatment of psychotic disorders. But they carry variable propensities to increase weight. They are therefore important risk factors for diabetes, hypertension and hyperlipidaemia. Such risk factors, (in conjunction with smoking and poor lifestyle habits), are 2 to 5 times more common in psychosis patients than in healthy populations. Thus metabolic dysfunction is the major cause of premature death in psychosis patients. System-based molecular approaches provide scope for tailored interventions and treatment pathways that may avert these risks, depending on the biological make-up of the patient. This study aims to identify predictors of metabolic syndrome amongst medicated psychosis patients in genome-wide expression data.
Methods: The psychosis cohort consists of 100 first-episode (FEP) and 100 chronic cases of psychosis (ICD-10: F20-29 and F30-33) arising from 2 independent studies. Cases are aged 18-65 and both samples ethnically heterogeneous. Participants were recruited from (i) South London and Maudsley, (ii) Oxleas and (iii) Sussex NHS trusts and had been admitted to psychiatric in-patient units. Both projects were approved by the Research Ethics Committee of The Joint South London and Maudsley and The Institute of Psychiatry NHS Research Ethics Committee. All eligible participants gave informed consent and agreed to provide biological samples for biochemical and genetic analysis.
Physical health assessment: A physical health assessment of waist and hip circumference, height, weight, fasting blood glucose, long term blood glucose control (HbA1c), fasting lipids and blood pressure was performed on participants in both studies. For FEP subjects this included baseline, 3 month and 12 month timepoints.
Derivation of gene expression data: RNA samples were collected using PAXgene (FEP) or Tempus (chronics) blood RNA tubes. Blood samples from 200 FEP and chronic psychosis cases were analysed for global gene expression information, using the Illumina HumanHT-12.v4 beadchips. Samples were run at the National Institute for Health Research's (NIHR) Biomedical Research Centre for Mental Health (BRC-MH) at the Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, London. Quality control and preprocessing used a standard pipeline (https://github.com/snewhouse/BRC_MH_Bioinformatics). A total of 4756 probes passed a stringent quality control in all 200 samples.
Identification of gene-expression predictors of metabolic syndrome: Elastic net, a generalisation of ridge regression and the lasso, is a powerful and versatile method for classification and regression that allows feature selection. This statistical learning approach is used to nominate a subset of analytes predictive of metabolic syndrome in first-episode.
Results: Cross validation was used to determine which values of the parameters α and λ minimised the estimated test error in the FEP training dataset. The generalisability of the resulting model was evaluated in the chronic psychosis validation dataset using area-under curve (AUC) metrics.
Discussion: Our results demonstrate the potential tractability of metabolic phenotypes for molecular risk prediction studies

S16. Expression profiles and social function as a predictive biomarker of schizophrenia: a pilot study

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Background: Individuals with schizophrenia or other psychotic disorders experience a prodromal period characterized by non-specific psychiatric symptoms. Several studies reported that the treatment during this prodromal period could result in attenuation, delay or even prevention of the onset of schizophrenia and other psychotic disorders. However, rate of the conversion to psychosis is not 100%, estimated to be 30-40% over 2-3 years. In this study, to identify the biomarker which can distinguish future conversion of schizophrenia, we conducted a transcriptomic study of RNA extracted at a prodromal period and assessed social function, comparing schizophrenia and non-psychosis samples diagnosed after one-year follow-up.
Methods: Subjects comprised six individuals who met criteria by using the comprehensive assessment of the at risk mental state (CAARMS). We evaluated the symptoms of these six individuals for one year and divided them into groups, "schizophrenia" and "non-psychosis" samples. RNA was extracted from whole blood at the first visit. Microarray analysis was performed on the Affymetrix Human Genome U133 Plus 2.0 arrays. We examined cognitive function using the Brief Assessment of Cognition in Schizophrenia in a Japanese-language version (BACS-J) and Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery in a Japanese-language version (MCCB-J). The Japanese version of UCSD Performance-based Skills Assessment Brief (UPSA-B Japanese version) was administered to assess social function.
Results: Expression profiles of three samples from patients with schizophrenia were compared to three samples from patients with non-psychosis. Our data did not detect an association with a genome-wide significance level, although some susceptibility genes were suggested. The top-ranked were the GCLC (glutamate-cysteine ligase, catalytic subunit) gene ($P = 3.7 \times 10(-5)$) in chromosome 6p12, the TMX4 (thioredoxin-related transmembrane protein 4) gene ($P = 3.8 \times 10(-5)$) in chromosome 20p12, and the TRIP11 (thyroid hormone receptor interactor 11) gene ($P = 4.2 \times 10(-5)$) in chromosome 14q31-q32, although none of the genes remained significant after correction of multiple testing. Patients with schizophrenia showed tendency of working memory deficits compared to non-psychotics.
Discussion: The most significant gene were detected around the GCLC gene ($P = 3.7 \times 10(-5)$) in chromosome 6p12, although none of the genes remained significant after correction of multiple testing. Previous studies have implicated that oxidative stress and glutathione (GSH) deficits may be involved in the pathogenesis of schizophrenia and lower GCLC protein expression among schizophrenic patients was reported. The present study provides clues about a predictive biomarker of schizophrenia at a prodromal period. A larger sample should be investigated in further studies.

S17. Childhood inflammatory cytokines as predictors of adult psychosis

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Background: There is accumulating evidence for an inflammatory component to the etiology and pathophysiology of neuropsychiatric brain disorders. Epidemiological, genetic and neuroimaging studies suggest complex interactions between the immune system, systemic inflammation, and the brain, which can lead to changes in mood, cognition and behaviour. Although a possible association between schizophrenia and the immune system was proposed over a century ago and gathering evidence now supports this, the molecular basis and timing of the connection remains unclear. What is clear is that individuals reporting symptoms of psychotic experiences (PEs) in childhood are at a high risk of psychosis in adulthood. We hypothesised that altered levels of inflammatory markers (pro- and anti-inflammatory cytokines) could distinguish those with PEs who transition to psychosis compared to those with PEs who do not.
Methods: We investigated if inflammatory markers could predict the transition from PEs to psychotic disorders in The Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort. PEs and psychotic disorder were assessed by face-to-face semi-structured Psychosis-Like Symptoms interview (PLIKSi) at ages 12 and 18 years. We studied inflammatory markers in childhood (blood sample at age 12) in a cohort of individuals with PEs at age 12, and compared those that transitioned to psychotic disorder at age 18 ($n = 19$) with those who did not transition to psychotic disorder ($n = 19$). Eight cytokines (GM-CSF, IFN-γ, IL-2, IL-4, IL-6, IL-8, IL-10, TNF-α) were quantified in

duplicate in non-fasting blood plasma samples using the Bio-Plex Pro Human Cytokine 8-Plex Panel (Bio-Rad). We performed logistic regression analyses and mixed effects modelling of all cytokines with subject sample as a random effect, adjusting for gender and BMI.
Results: Cytokine mean values were log-transformed. Seven cytokines passed quality control (not IL-4). The risk of psychotic disorder at age 18 years was associated with a change in four pro-inflammatory cytokines: IFN-γ, IL-2, IL-8, TNF-α (all *P*-values < 0.05). Taken together, all cytokines combined are significantly associated with the outcome – transitioning from PE in childhood to psychosis in adulthood (family-wise *P*-value = 0.039)
Discussion: Previous studies have shown the raised markers of inflammation during the prenatal period of life and during childhood are associated with increased risk of future psychotic disorder. Our study extends this literature by showing for the first time that raised markers of inflammation as early as age 12 could predict later psychotic disorder among a cohort of children with PEs. Our findings show that inflammatory markers may form part of predictive models which can aid prediction of young people most at risk of psychosis. Our findings are also of relevance to pathophysiology as our four associated cytokines are known activators of the M1 cytotoxic phenotype of microglia – the brain's immune cells. In the future, processes in the inflammatory pathways may contribute to a diagnostic and therapeutic target for psychotic disorders.

S18. A comprehensive analysis of cortisol secretion in early psychosis

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Background: Schizophrenia is a multifactorial disorder and environmental risk factors for it might contribute to hypothalamo-pituitary-adrenal axis (HPA) dysregulation. While increased cortisol levels have been reported in schizophrenia, the findings in early psychosis are more limited. Here, we report new findings from the first French cohort of young help-seekers (ICAAR) followed by a meta-analysis of all available reports on salivary basal cortisol levels in early psychosis.
Methods: 169 individuals (15-30 years old) had their daily cortisol levels sampled and they were categorized at baseline as either ultra-high risk subjects (UHR), first-episode of psychosis (FEP) and non at-risk help seekers controls (HSC). UHRs who converted to psychosis at the follow up (UHR-P) were compared to non-converters (UHR-NP). Basal cortisol level and daily pattern of secretion were analyzed using classical and innovative statistical analyses (structural equations). We also performed direct and indirect meta-analyses from case-control studies with basal salivary measures of cortisol.
Results: Basal cortisol levels were not significantly different between UHR, FEP, and HSC controls in the ICAAR cohort. Interestingly, initial cortisol levels were correlated with positive symptoms at the one year follow-up in the ICAAR cohort. The meta-analysis revealed a significant elevation of the salivary basal cortisol levels only in UHR individuals compared to controls (8 studies-1060 individuals) but this level was not predictive of the psychotic transition. Many confounding factors should be taking into account. Among them, we identified that cortisol daily pattern could be reflective of nycthemeral phase-offset, a bias not always identified in previous studies.
Discussion: The meta-analysis (including new data) indicates that basal cortisol levels were increased in UHR compared to controls, but FEP levels were not different from UHR or controls. The biological significance of cortisol dysregulation in early psychosis will be discussed.

S19. Neonatal levels of growth factors in non-affective psychosis

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Background: Abnormal levels of certain growth factors critically involved in the development and functioning of the central nervous system have been reported in individuals diagnosed with schizophrenia.
Methods: The purpose of the present study was to measure levels of such growth factors in blood from the neonatal period from 186 individuals (born 1975-1985) with a verified register-based diagnosis of non-affective psychosis and 474 controls matched on age, sex, and hospital of birth. Eleven different growth factors were quantitated in eluates of neonatal dried blood spots by means of a commercially available panel using Luminex technology. All values were adjusted for differences in total protein concentrations in the eluates by means of IR spectroscopy.
Results: Out of the eleven growth factors, five (EGF, HGF, PDGF-BB, SCF and VEGFA) were above the detection limit in $>60\%$ of the samples. Levels of SCF (stem cell factor) in the middle tertile were protective against the later development of psychosis. Levels of the other factors were not associated with psychosis. PDGF-BB levels were associated with neonatal size for gestational age z-scores, an expected association indicating the validity of the growth factor measurement in stored neonatal dried blood spots.
Discussion: Taken together with recent observations of abnormal levels of SCF in adult individuals with schizophrenia, our current observations suggest that such abnormalities can exist already at birth.

S20. Neuroanatomical correlates of stress and inflammatory biomarkers among children at elevated risk for schizophrenia

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Background: Disturbances within the hypothalamic-pituitary-adrenal (HPA) axis and inflammatory system have been observed among patients with schizophrenia and preliminary evidence suggests that these biological systems may be functionally altered prior to illness onset among those at elevated risk for the disorder. These disturbances might contribute to the development of psychosis via the potentially toxic effect of elevated levels of HPA axis and inflammatory biomarkers on the brain. Few studies have examined the relationship between regional brain volumes implicated in schizophrenia and markers of HPA axis and inflammation in those with psychosis; none, to our knowledge, have examined these relationships among children at-risk for the disorder. The aim of the current study was to investigate the extent to which salivary cortisol and C-reactive protein (markers of HPA axis function and inflammation, respectively) were associated with regional brain volumes among medication-naive children at elevated-risk for schizophrenia, who present multiple developmental antecedents of schizophrenia (ASz) or a family history of illness (FHx), and their typically-developing (TD) peers.
Methods: ASz ($n = 30$), FHx ($n = 22$), and TD ($n = 32$) children were identified at age 9-12 years via community screening or as relatives of individuals with schizophrenia. Salivary cortisol, salivary CRP samples, and structural neuroimaging data were obtained at age 11-14 years. Total grey matter (GM) and white matter (WM) volume and total cerebral spinal fluid (CSF) were extracted from structural brain images using SPM5. Regional brain volumes were extracted using FreeSurfer (processing and extraction is continuing); specific regions of interest included the hippocampus, amygdala, and prefrontal cortex. Planned within-group analyses will determine whether salivary cortisol and CRP predict regional brain volumes.
Results: Consistent with findings in larger, overlapping samples, FHx children, but not ASz children, showed a blunted cortisol awakening response compared to TD children ($P = 0.01$), yet neither group were characterised by elevated diurnal cortisol levels or CRP. Among TD children only, higher CRP levels during the day and a higher cortisol awakening response were associated with lower CSF and GM volume, respectively ($P < 0.02$). Associations between these biological markers of stress and inflammation and regional brain volumes will next be tested.
Discussion: Children at elevated risk for schizophrenia already display some disturbances within the HPA axis system. Biological markers of stress and inflammation are not associated with global GM, WM, or

CSF volumes in these at-risk children. Current analyses will determine whether these biological markers predict regional brain volumes in key areas associated with schizophrenia among these youth.

S21. Increased neural noise is associated with the psychosis-like effects of THC

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Background: Neural noise, the randomness of brain activity, is increased in schizophrenia. Furthermore, neural noise has been shown to increase further during periods of symptomatic exacerbation. Increased neural noise may disrupt information processing thus contributing to psychosis. This suggest that neural noise has the potential of being a biomarker of psychosis and, if sensitive enough, a tool to estimate the risk of psychosis in individuals with a predisposition to develop transient (e.g., drug-induced) or persistent psychosis.
Methods: The acute effects of THC on neural noise and the relationship between noise and the psychosis-like effects of THC were studied in the baseline EEG of 24 healthy humans. In addition, the potential of neural noise to be used to estimate the risk of transient robust clinically significant THC-induced psychotic symptoms was explored. Participants completed 3 test days during which they received intravenous THC (placebo,.015 and.03 mg/kg) in a double-blind, randomized, cross-over, and counterbalanced design. Neural noise in the EEG was measured using Lempel-Ziv complexity (LZC), a non-linear index of signal randomness. A 5-factor model of the positive and negative syndrome scale (PANSS) was used to measure psychosis-like effects. A survival analysis was conducted to model the relationship between the risk (probability) of experiencing robust clinically significant (>4 points change in PANSS positive subscale) THC-induced psychotic symptoms and the changes from baseline (pre-THC state) in neural noise (LZC).
Results: THC increased LZC in a dose-dependent manner: the higher dose showed increased LZC compared to both the lower dose and placebo, and the lower dose showed increased LZC compared to placebo (all ps $<$ .001). Analogous dose-related effects of THC were observed on PANSS factors (all ps $<$ .03). The regressions of PANSS factors on LZC revealed a strong positive relationship between LZC and the positive ($\beta = .685$, $P < .001$) and disorganization ($\beta = .754$, $P < .001$) symptoms factors but not between LZC and the negative symptoms factor ($P > .1$). The survival analysis showed that the relationship between risk of robust psychosis-like symptoms and changes in LZC could be fitted with a sigmoid curve with an extremely high goodness of fit (R^2 = 0.98). The distribution of risk values revealed that the probability of experiencing robust psychosis-like symptoms tended to 1 when LZC increases were $\geq$20%, i.e., every subject with an increase in LZC $\geq$20% experienced robust psychosis-like effects.
Discussion: At doses that induced psychosis-like effects, THC increased neural noise (LZC) in the EEG of healthy humans in a dose-dependent manner. Furthermore, neural noise showed a strong positive relationship with positive- and disorganization-like symptoms but not with negative-like symptoms. In addition, the risk of experiencing robust psychosis-like effects augmented with the magnitude of the increases of LZC. Furthermore, psychosis showed to be inevitable after increases in LZC $\geq$ 20%. Taken together, these findings suggest that increases in neural noise may contribute to the psychosis-like effects of THC and that LZC should be explored as a potential biomarker for psychosis. Furthermore, these results raise the intriguing possibility of using a similar approach to model the risk of relapse in established schizophrenia patients (analogous to the risk of robust psychosis-like symptoms under THC) in terms of increases in LZC from baseline (clinically stable periods).

S22. Deficient myelination in treatment resistant schizophrenia: evidence using mcDESPOT imaging

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Background: Schizophrenia has been conceptualised as a disorder of neural connectivity. An underlying deficiency in myelination may cause dysfunctions seen in schizophrenia; however in-vivo evidence is sparse. Moreover, given the large proportion of individuals with treatment resistant schizophrenia (TRS), it is possible that differences in myelination explain illness severity and predict treatment response. Previous connectivity studies have mostly focused on diffusion imaging techniques implemented in patients with SZ as a whole, but have not contrasted TRS with treatment responsive SZ. In addition, despite high sensitivity of diffusion imaging, the specificity in terms of the underlying causes of observed changes is relatively low. In contrast, multicomponent driven equilibrium single pulse observation of T1 and T2 (mcDESPOT) is a new imaging technique which allows for myelin-specific measures to be derived from rapid imaging sequences. We use this technique in order to assess myelin water content in TRS.
Methods: mcDESPOT data were acquired at 3 T for 20 healthy controls (HC), 18 patients with TRS, and 9 treatment responsive patients with a diagnosis of SZ. Myelin water fraction (MWF) maps were derived using published mcDESPOT procedures, and tract-based spatial statistics (TBSS) methods employed in FSL in order to derive a white matter (WM) skeleton from the maps. Skeletonised MWF data were then compared between groups using non-parametric permutation tests and threshold-free cluster enhancement.
Results: HC vs. TRS: The results show widespread MWF reduction in TRS compared to HC throughout the WM skeleton. Affected tracts include the superior longitudinal fasciculus (L), inferior longitudinal fasciculus (bilateral), and inferior frontal-occipital fasciculus (R).
HC vs. treatment responders: No voxels survived thresholding at $p < .05$. At a more lenient threshold of $P < .1$, remitted patients showed minimal MWF reduction in left inferior occipital WM.
TRS vs. responders: The analysis showed no significant differences between TRS and treatment responders, ps $>$ .05.
Discussion: Our findings provide novel evidence of a myelin-specific deficit in TRS. The preliminary results on a small sample of treatment responsive patients with SZ suggest that this deficit may be less pronounced and/or localised in different brain regions in treatment responsive patients with SZ. It is possible that TRS is characterised by distinct neural mechanisms which prohibit an adequate response to antipsychotic treatment. These findings warrant further investigation of changes in myelin content as well as possible underlying causes – such as neuroinflammation – in TRS.

S23. Combinatorial neuroanatomical and cognitive signatures of remission and relapse in schizophrenia

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Background: Schizophrenia is a severe disorder marked by high relapse rates and sudden, unpredictable transition from remission to relapse. The relapses result in increased economic, social and caregiver burden. The early identification of patients with differential relapse and remission outcomes could inform intervention strategies that may delay or reverse the illness trajectories and improve outcomes. Many structural magnetic resonance imaging (MRI) studies of patients with schizophrenia have associated structural abnormalities across distributed regions of the brain with symptomatic worsening. Also, cognitive dysfunction has been associated with poor functional outcomes in schizophrenia. Hence, combinatorial measures of brain anatomy and cognition, on top of clinical measures, could serve as predictive measures of either remission or relapse. This study aims to apply pattern recognition techniques on high dimensional neuroimaging-cognitive data to improve prediction of disease remission and relapse in schizophrenia.

Methods: Measures of 1) subcortical volumes and cortical thickness of whole brain structures, derived from FreeSurfer (version 5.3) automated labeling of preprocessed high-resolution anatomical MRI scans; and 2) several cognitive domains, using the Brief Assessment of Cognition in Schizophrenia, were acquired alongside clinical measures from 92 subjects with a DSM-IV diagnosis of schizophrenia. Disease remission status (38 non-remitted and 54 remitted subjects, age and gender matched) were defined by both symptomatic remission (8 items from the Positive and Negative Symptom Scale proposed by the Remission in Schizophrenia Working Group) and general psychosocial functioning. Relapses (25 non-relapsed and 67 subjects with relapses, age and gender matched) were defined as hospital readmission at 12 months follow-up. We trained and tested a series of predictive models using the Random Forest algorithm on the combinatorial clinical, cognitive and MRI measures, and identified key features which highly correlate with the respective patient outcomes.
Results: Random forest predictive models that achieved a positive predictive value and sensitivity of 0.62 and 0.89 respectively for disease remission were demonstrated, when tested using a 5-fold cross-validation process. On the other hand, predictive models for disease relapse demonstrated positive predictive value and sensitivity of 0.83 and 0.94 respectively. In addition, we have identified and ranked several cognitive features (e.g. generalized cognition) and brain MRI features (e.g. a pattern of prefrontal-limbic measures) which contribute significantly to model performance.
Discussion: We trained and tested a series of accurate machine learning models using the random forest algorithm, on both clinical and brain MRI measures, for predicting disease remission and relapse. Future work on independent longitudinal datasets could verify the prognostic values of these combinatorial neuroanatomical-cognitive-clinical signatures.

S24. Using metabolomics to identify biomarkers of psychotic experiences at age 17 in the AVON longitudinal study of parents and children (ALSPAC) cohort

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Background: The identification of biomarkers of psychotic experiences is of importance because these biomarkers have relevance to the pathophysiology of psychosis and may aid in the prediction of transition to later mental disorders. Metabolomic methods allow the study of small molecules or metabolites within given biosamples. Presently, a relatively small number of investigations have applied metabolomics to identify biomarkers of schizophrenia and first onset psychosis. These studies identified various metabolite signatures and have provided valuable insights in order to understand the mechanism of the disease; however the studies did not focus on biomarkers of the at risk mental state (ARMS). Furthermore, the identification of early biomarkers of psychosis would be important for early disease prognosis. Therefore, the aim of this study was to apply an untargeted metabolomic approach to identify biomarkers of psychotic experiences at age 17.
Methods: A mass-spectrometry based approach was used to identify small molecular weight metabolites in the fasting plasma samples of healthy controls ($n = 117$) and compared with fasting plasma samples of subjects with psychotic experiences ($n = 116$) at age 17 in the ALSPAC cohort. The ALSPAC cohort was set up to examine genetic and environmental determinants of health (including mental health) and development (http://www.bristol.ac.uk/alspac/). Psychotic experiences were defined as those participants who at age 17 had experienced a suspected or definite psychotic experience, which were identified through face-to-face, semi structured Psychosis-Like Symptom Interview (PLIKSi) conducted by trained psychology graduates in assessment clinics.
Censored regression analysis using the Lifereg procedure in SAS was used to identify significantly discriminatory metabolites between the control and psychotic experiences groups. Regression models were adjusted for gender, BMI and depression. Multivariate statistical approaches were also used to identify and evaluate any potential psychotic experiences biomarkers. Such approaches included principal component analysis (PCA) and hierarchical cluster analysis (HCA).
Results: A total of 151 metabolites were identified and quantified in the plasma samples, which included metabolites from the following classes; fatty acids, amino acids, organic acids, sugars, sugar derivatives and alcohols. Censored regression analysis identified 11 significantly altered metabolites between the control and psychotic experiences group (adjusted for BMI, gender and depression), although did not remain significant at false discovery rate (fdr) level; these metabolites included organic acids, an amino acid and 4 unknowns (to be identified). HCA analysis identified 9 clusters of metabolites of which 1 was significantly down-regulated (P 0.016) in the psychotic experiences group. The cluster contained a total of 22 metabolites which included organic acids, an amino acid, sugar derivatives and some unknowns.
Discussion: A panel of 11 potential biomarkers for psychotic experiences were identified in a population based sample of adolescents, although none remained significant at fdr level. However, using a clustering approach, a cluster of metabolites were identified that were significantly discriminatory between the study groups. This cluster contained a number of organic acids including citric acid and lactic acid. Future work will validate this cluster of metabolites and examine their potential as biomarkers.
Study funded by HRB CSA/2012/8 and HRA POR/2013/282.

S25. Studying the influence of clinical and demographic moderators in multivariate modeling of brain function in schizophrenia

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Background: In the last decade there has been a growing interest in the application of Multivariate Pattern Analysis (MVPA) to model group differences in clinical populations. The application of these methods to different data domains and the results raised expectations of producing biomarkers suitable for the clinical practice. The most critical point is the generalizability of the diseases models across populations, hence the characterization and translation of these models to a biological/clinical framework is as important as theirs performance. The aim of this study is to use clinical and demographical moderators to predict the individual probabilities score outputted by a multivariate classification analysis between Schizophrenia patients (SZ) and Healthy Controls (HC) based on functional connectivity as measured by resting state Functional Magnetic Resonance Imaging (RS).
Methods: The RS data from 74 healthy controls (HC, 35.8 (11.5) age, % 19.7 female) and 71 patients with schizophrenia (SZ, 38.1 (13.9) age, 31.1% female), obtained from the COBRE database (http://coins.mrn.org/dx) were used to generate a multivariate predictive model of Schizophrenia (accuracy of 71%). The clinical data of 62 subjects of the SZ population that had a complete clinical dataset were used as features in a nu-Support Vector Regression (SVR) algorithm having as target values the class membership probabilities generated by the predictive model. The SVR process was wrapped in a nested cross validation and a wrapper, greedy forward search, approach with an early-stopping at the 25% of the total number features, selected an optimal subset of features for prediction at each fold.
Results: The SVR model significantly predicted the class membership probabilities generated by the RS based predictive model for the SZ group using clinical and demographic measures ($r = 0.5$, $P = 3.297e\text{-}5$, $df = 61$, Coefficient of Determination = 25.1, $df = 61$). The usage of a wrapper approach with an early stopping enabled us to obtain a feature selection probability profile for our clinical and demographic sample. Current age, age of onset of psychotic symptoms, conceptual disorganization, emotional withdrawal, uncooperativeness and motor retardation yielded the highest values for selection probability, above 0.75. The analysis of the weights estimated by the SVR indicate that higher PANSS positive symptoms scores such as conceptual

disorganization as well as higher scores on the PANSS general symptoms scale such as motor retardation are predictive of high SZ group membership probabilities.
Discussion: We were able to predict the class membership probabilities derived from a multivariate predictive model based on clinical and demographical data. Our study suggests that two of the most important features are age of unset of psychotic symptoms and current age. This is in line with recent studies that point out that SZ patients may experience accelerated brain ageing and that the pathological process which causes an early age of onset could also be responsible for more pronounced abnormal connectivity patterns. The high predictive weight of the PANSS scores, current age and age of onset strongly suggests that our RS predictive model reflects the disease severity and chronicity.

S26. A comparison of B cell repertoire in cerebrospinal fluid of healthy individuals and patients with schizophrenia

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Background: B and T cells are key players of the adaptive immune system. B cells express immunoglobulin receptors that can bind and effectively react to a multitude of antigens. However, very little is known of the B cell repertoire in the cerebrospinal fluid (CSF) of healthy individuals and patients with schizophrenia. The primary objective of this project was to sequence immunoglobulin produced by B cells in the CSF of both schizophrenia patients and healthy individuals in order to test the hypothesis that the CSF B cell repertoire in patients affected by schizophrenia is different from that of healthy individuals. We also compared immunoglobulin produced by CSF B cells and peripheral blood (PB) B cells to determine whether these populations differ.
Methods: Paired samples of CSF and PB from healthy volunteers and patients were obtained and single B cells were isolated via FACS. The immunoglobulin repertoire encoded by these B cells was determined using high-throughput deep sequencing technology. The data was analyzed to determine: VH, DH, and JH family and subfamily usage, N region addition, CDR3 length, and somatic mutation.
Results: After analyzing sequences from 3 schizophrenia patients and 3 healthy controls, our results suggest that,
– In both patients and controls, B cells in the CSF do not recapitulate PB B cells but represent a select subpopulation
– VH family usage is different in CSF B cells of patients with schizophrenia compared to CSF B cells of healthy controls
– Increased mutations are seen in CSF B cells from patients compared to controls
– Average complementarity determining region 3 (CDR3) length of CSF B cells in patients is longer than in controls
– Average N region length is similar in CSF B cells from patients and controls
Discussion: Our results suggest a difference in the immunoglobulin repertoire of B cells in the CSF of schizophrenia patients compared to healthy individuals. Although the B cell repertoire in PB of healthy individuals is comparable to that of patients, the difference in CSF B cells suggests selection of a particular subset in CSF of patients that could be responsible or contributory to disease pathology. This novel finding also opens new questions regarding antibodies targeting brain-specific tissue in individuals affected by schizophrenia. The knowledge gained from this study may ultimately aid in evaluating the relationship between clinical symptoms and immune dysfunction through study of B cell antibodies in patients with schizophrenia.

S27. Improving treatment of patients with schizophrenia – glutamate as a marker for choice of treatment

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Background: Insufficient treatment response to dopaminergic antipsychotics constitutes a major challenge in the treatment of patients with schizophrenia. A treatment-resistant subgroup of patients might be characterized by primarily glutamatergic disturbances since cross-sectional studies have found elevated levels of glutamate (glu) in the brain area termed anterior cingulate cortex (ACC) of non-responder patients early in the disease but no dopaminergic dysfunction (Egerton 2012, Demjaha 2014). Elevated levels of the glu metabolite glutamine (gln) have also been found in both the ACC and the thalamus in antipsychotic-naïve first-episode schizophrenia (FES) patients (Théberge 2002, Théberge 2007) suggesting that glutamatergic disturbances are part of the pathophysiology although the relationship to symptoms is unclear at present (Meritt 2013). Glu regulates regional cerebral blood flow (rCBF) (Attwell 2010) that might also be disturbed in cortical and subcortical areas.
Here, we wish to test the hypothesis that increased glutamate levels in the ACC and left thalamus in initially antipsychotic-naïve patients with FES can predict poor treatment response to antipsychotic compounds that inhibit dopaminergic activity. In secondary analyses we will explore the association between levels of glutamate and treatment outcome after 6 weeks, changes in rCBF, and symptom severity.
Methods: Longitudinal study of 30 initially antipsychotic-naïve FES patients and matched healthy controls. Levels of glutamate are measured with proton magnetic resonance imaging (1H-MRS) in ACC and left thalamus and estimated with LC-Model. rCBF is measured with 30 pairs of perfusion weighted and control scans of cerebrum before and after 6 weeks of treatment with aripiprazole.
Clinical outcome is measured with positive and negative symptom scale (PANSS).
Results: To date 17 patients have been recruited and 9 completed follow-up. Preliminary analyses reveal no baseline differences between patients and healthy controls. A significant reduction was found in left thalamic Glu/Cr levels of patients from baseline to 6 weeks follow-up from 1.35 ± 0.18 to 1.21 ± 0.17 ($t(8) = 2.49$, $P = 0.016$, two-tailed) as well as a decrease of blood flow in Anterior Cingulum from 1.18 ± 0.14 to 1.07 ± 0.10 ($t(7) = 3{,}62$, $P = 0.008$, two-tailed). A non-significant reduction in ACC Glu/Cr levels from 1.52 ± 0.30 at baseline to 1.39 ± 0.27 at follow-up was also found. The analysis of blood flow in subcortical regions is ongoing.
Discussion: The data represent work in progress and the results should therefore be interpreted with caution. Future analyses after inclusion of the entire sample are expected to reveal if levels of glutamate in ACC and left thalamus prior to treatment can predict treatment outcome. Furthermore, secondary analyses can evaluate if patients not responding to antipsychotic treatment have persistently high levels of glu after 6 weeks.

S28. Quantification of the serum levels of NR1 and NR2 NMDA receptor in patients in the first episode psychosis

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Background: Ionotropic glutamate receptors, such as N-Methyl-D-Aspartate (NMDA), are involved in physiopathology of several psychiatric disorders.[1] NMDARs are described as heteromeric complexes incorporating different subunits within a repertoire of three types: NR1, NR2 and NR3. The expression of functional NMDAR requires the coexpression of at least one NR1 and one NR2. Recent

findings suggest that plasma glutamatergic amino acid levels may be a significant biological marker that reflects the condition, especially in severely affected patients.[2]. A meta-analysis showed that peripheral glutamate levels in schizophrenics were significantly higher than in controls, but more comprehensive research is needed to understand the relationship between glutamate levels in the blood and in the brain.[3] The aim of this study was to quantify the serum levels of the NR1 and NR2 NMDAR subunits in patients with first episode psychosis (FEP), compared with siblings, as a high-risk group for greater likelihood of exposure to the same genetic and environmental risk factors, and healthy controls.
Methods: This is a case-control study of FEP in the region of Ribeirão Preto, Brazil. The control group was composed of healthy individuals who had not psychosis lifelong, matched with patients by age and sex. We collected 5 to 10 ml of peripheral blood sample in an EDTA tube when the diagnosis was established. Serum quantification of NR1 and NR2 NMDAR subunits was performed by ELISA. Data were analyzed by ANOVA, using the log-transformed values of NR1 and NR2 concentration.
Results: We included 166 FEP (mean age = 30.34, SD = 12.2; 64% males), of these 84 with the diagnosis of psychotic disorders, mainly schizophrenia, 51 with bipolar disorder and 31 with depressive disorder. In addition to patients, we included 77 siblings and 166 controls. The serum levels of NR1 [F(4) = 11.492, $P < 0.001$] and NR2 subunits [F(4) = 63,513, $P < 0.001$] were significantly lower in patients (psychotic disorders - mean NR1 = 1.34 pg/ml, SD = 0.83; mean NR2 = 0.47 pg/ml; SD = 0.26; bipolar disorder - mean NR1 = 1.41 pg/ml, SD = 1.10; mean NR2 = 0.40 pg/ml; SD = 0.26; depressive disorder - mean NR1 = 1.15 pg/ml, SD = 0.92; mean NR2 = 0.41 pg/ml; SD = 0.26) compared to both siblings (mean NR1 = 1.92 pg/ml, SD = 0.46; mean NR2 = 0.85 pg/ml; SD = 0.95) and healthy volunteers (mean NR1 = 1.75 pg/ml, SD = 0.62; mean NR2 = 0.72 pg/ml, SD = 0.20).
Discussion: Until now, there are no reports about the peripheral quantification of the NR1 and NR2 NMDAR subunits in severe psychiatric disorders. However, it has been shown that elevated serum levels of NR2 subunit could be associated as a candidate biomarker for ischemic stroke.[4] Because some studies indicate that psychiatric disorders are due to the abnormalities of one or more of the NMDAR subunits, it is demanding a better understanding of the functioning of this receptor for both normal human development and in pathological conditions.

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S29. Human protein atlas enabled neuroproteomic profiling of body fluids

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Background: The Human Protein Atlas (www.proteinatlas.org) currently contains more than 25.000 validated antibodies targeting 17.000 proteins corresponding to approximately 86% of the encoded human proteins. The publicly available portal contains several millions of high-resolution images generated by immunohistochemistry on tissue microarrays and confocal microscopy for subcellular localization. The antibodies are antigen-purified and the long-term objective is to generate paired antibodies towards all human protein targets. A systematic biomarker discovery approach has been implemented, utilizing various array-based platforms in combination with the massive antigen and antibody resource.
Methods: Proteomic profiling of serum, plasma and CSF in multi-disease cohorts are performed with large number of peptides and antigens on planar microarrays for the analysis of autoimmunity repertoires with subsequent verifications with suspension bead arrays. Large set of samples are also profiled with massive numbers of antibodies on highly multi-parallel suspension bead arrays which utilizes magnetic color-coded beads functionalized with antibodies to generate protein profiles from labeled samples for biomarker discovery.
Furthermore, the initial protein profiling and exploration of a large serum RPPA will also be described. We have generated what is according to our current knowledge the largest serum microarray ever produced. It contains more than 12 000 serum samples collected within the TwinGene cohort (2004-2008, Sweden) and it comprises both monozygotic and dizygotic twin pairs.
Results: The results from broad scaled autoimmunity and antibody-based neuroproteomic profiling of body fluids with analysis both within and between several psychiatric disorders with a focus on schizophrenia utilizing the different platforms will be presented.
Discussion: The emerging possibilities of global affinity proteomic-based protein profiling of csf, plasma and serum will hopefully be able to provide the scientific community with a set of proteins that potentially can dramatically change the molecular understanding within psychiatric diseases.

S30. Effects of OMEGA-3 PUFA on the vitamin E and glutathione antioxidant defense system in individuals at ultra-high risk of psychosis

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Background: Oxidative stress and impaired antioxidant defenses are reported in schizophrenia and are associated with disturbed neurodevelopment, brain structural alterations, glutamatergic imbalance, increased negative symptoms, and cognitive impairment. There is evidence that oxidative stress predates the onset of acute psychotic illness. Here, we investigate the effects of omega-3 PUFA on the vitamin E and glutathione antioxidant defense system (AODS).
Methods: In 64 help-seeking UHR-individuals (13–25 years of age), vitamin E levels and glutathione were investigated before and after 12 weeks of treatment with either 1.2 g/d omega-3 (PUFA-E) or saturated fatty acids (SFA-E), with each condition also containing 30.4 mg/d alpha-tocopherol to ensure absorption without additional oxidative risk.
Results: In multivariate tests, the effects on the AODS (alpha-tocopherol, total glutathione) were not significantly different ($P = 0.13$, $P = 0.11$, respectively) between treatment conditions. According to univariate findings, only PUFA-E caused a significant alpha-tocopherol increase, while PUFA-E and SFA-E caused a significant gamma- and delta-tocopherol decrease. Total glutathione (GSHt) was decreased by PUFA-E supplementation.
Discussion: Effects of the PUFA-E condition on the vitamin E and glutathione AODS could be mechanisms underlying its clinical effectiveness. In terms of the vitamin E protection system, PUFA-E seems to directly support the antioxidative defense at membrane level. The effect of PUFA-E on GSHt is not yet fully understood, but could reflect antioxidative effects, resulting in decreased demand for glutathione. It is still necessary to further clarify which type of PUFA/antioxidant combination, and in which dose, is effective at each stage of psychotic illness.

S31. Low levels of vitamin D poorly responsive to daylight exposure in patients with therapy-resistant schizophrenia

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Background: Low vitamin D levels are associated with schizophrenia, but the possible association between vitamin D levels and illness severity or duration of exposure to daylight has hardly been investigated. Aims of this research project were to compare vitamin D levels in therapy-refractory severely ill schizophrenia patients and

members of staff. Additionally, to investigate the influence of daylight exposure on vitamin D levels in patients.
Methods: Vitamin D was measured in patients with therapy-resistant schizophrenia in April, after the winter, and in patients and staff members in June, after an exceptionally sunny spring. Vitamin D levels in April and June were compared in patients, and levels in June were compared in patients and staff. The influence of daylight was taken into account by comparing the time patients spent outdoors during the day with the recommended minimum time for adequate vitamin D synthesis, and by comparing time spent outdoors in patients and staff.
Results: Patients had high rates of vitamin D deficiency (79-90%) and lower levels of vitamin D than staff members ($P < 0.001$), independent of skin pigmentation. In patients, vitamin D levels did not normalize, despite the considerably longer than recommended exposure of the skin to daylight ($P < 0.001$) and the longer exposure in patients than in staff members ($P = 0.003$).
Discussion: The vitamin D deficiency of therapy-resistant schizophrenia patients is pronounced and cannot be explained by differences in skin pigmentation or by an inactive, indoor lifestyle on the ward. Even theoretically sufficient exposure of the patients to daylight did not ameliorate the low vitamin D levels.
While vitamin D deficiency probably plays a role in somatic health problems, it may also play a role in schizophrenia. Interestingly, exposure to daylight during an unusually sunny spring was not sufficient to correct the vitamin D deficiency seen in the patients. This emphasizes the need to measure and correct vitamin D levels in these patients.

S32. EEG coherence as a trait marker of schizophrenia

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Background: The disconnectivity of brain circuit is considered as a core feature of schizophrenia. EEG coherence is known to reflect the connectivity in brain circuit. To investigate EEG coherence as a potential trait marker for schizophrenia, we examined the differences of EEG coherence among patients with schizophrenia, siblings and controls.
Methods: Eighteen patients with schizophrenia were recruited from one psychiatric hospital in Korea. Sixteen individuals of patient's healthy siblings and 15 healthy controls were recruited. Resting-state eyes-closed electroencephalography (EEG) was recorded in 19 channels. EEG coherence was calculated. The statistical differences of EEG coherence among patients with schizophrenia, healthy siblings and healthy controls were examined using ANOVA.
Results: EEG coherence was increased in patients with schizophrenia compared with healthy controls in beta frequency bands of F8O2, F3T5 and F4T6. EEG coherence of sibling group was not statistically different from healthy control group in beta frequency bands but was shown in the middle range between patients with schizophrenia and normal controls. In delta frequency bands of C3C4 and T5T6, EEG coherence of sibling group was significantly increased compared with that of healthy controls.
Discussion: These findings suggest that the increases of EEG coherence in schizophrenia and healthy siblings compared with healthy controls imply the possibility of EEG coherence as a trait marker for schizophrenia.

S33. Cognitive and psychosocial correlates of suspicious young minds: a UK-Hong Kong follow-up study of 9- to 16-year-olds

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Background: Paranoia, or excessive suspiciousness of others, is a disabling condition affecting patients with psychosis and more commonly than previously thought, the general population (Freeman, 2006). In the first large-scale study of 8- to 14-year-olds from the UK and Hong Kong ($N = 2498$), Wong, Freeman, & Hughes (2014) documented the prevalence, structure, and correlates of childhood suspiciousness using a new dimensional measure of mistrust (Social Mistrust Scale). One limitation of this study however was the sole reliance on child-reported questionnaires. To further extend this literature, the current multi-informant (child-, peer-, parent-reports) follow-up study of trusting and persistently mistrustful children aimed to reassess the relative contributions of cognitive and psychosocial risk factors in explaining childhood mistrust.
Methods: This cross-sectional study involved 118 9- to 16-year olds ($M = 11.96$, $SD = 1.95$ years, female = 52.5%) reassessed at 6- 12-months ($M = 8.9$ months, $SD = 1.6$) as part of a UK-Hong Kong study of social mistrust. During a 1- hour interview session, trusting (scoring < 3) and persistently mistrustful children (scoring > 3 at both time-points) defined by the social mistrust scale were matched (country, age, gender, school) and completed a battery of tasks assessing theory of mind, executive function, cognitive reasoning bias (cognitive), loneliness, depression, bullying experiences, and hostile attributional bias (psychosocial risk factors) hypothesized to predict levels of mistrust. Further details about participant demographics are published elsewhere (see. Wong, Freeman, & Hughes, 2014).
Results: Mistrustful and trusting children did not differ in age, gender, country, socioeconomic status, and verbal ability ($p > .05$ for all). Performance on theory of mind, executive function, and reasoning bias also did not predict levels of mistrust (ps $> .05$). Parent-reports of mistrust were unrelated to child-reported mistrust ($rs = .16$), but were correlated with the child's self-reported depression ($rs = .30$, $p < .001$) and isolation rated by peers ($rs = .21$, $p < .001$) to the same magnitude. Peers perceived mistrustful children as being less popular ($B = 2.50$, $SE = .88$, $p < .001$) than trusting children, controlling for peer-rated trustworthiness and sociability. Mistrustful children were more likely to self-report frequent victimisation ($B = 3.28$, $SE = .92$, $p < .001$) and elevated levels of hostile attributional bias toward others ($B = .09$, $SE = .03$, $p < .01$) compared to trusting children. These effects held up after controlling for depression ($p = .15$), likelihood of being a bully ($p = .37$) and feelings of loneliness ($p = .61$). No interactions were found ($p = .92$). The final model explained 50% of the variance in mistrust ($\chi 2(7, N = 104) = 47.45$, $p < .001$).
Discussion: Child-reported mistrust corroborated with peer-reports of trustworthiness and social problems more than parent-reports, which supports the convergent validity of the social mistrust scale. Child reported peer victimization and hostile attribution toward others may be potential correlates for childhood suspiciousness cross-sectionally. These findings tentatively support a psychosocial explanation of mistrust (rather than cognitive dysfunction); however, replication, and multi-informant longitudinal studies are needed to determine the causal directions of these relationships.

S34. Twelve-month psychosis-predictive value of the ultra-high risk criteria in children and adolescents

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Background: The validity of current ultra-high risk (UHR) criteria is under-examined in help-seeking minors, particularly, in children below the age of 12 years. Thus, the present study investigated predictors of one-year outcome in children and adolescents (CAD) with UHR status.
Methods: Thirty-five children and adolescents (age 9–17 years) meeting UHR criteria according to the Structured Interview for Psychosis-Risk Syndromes were followed-up for 12 months. Regression analyses were employed to detect baseline predictors of conversion to psychosis and of outcome of non-converters (remission and persistence of UHR versus conversion).
Results: At one-year follow-up, 20% of patients had developed schizophrenia, 25.7% had remitted from their UHR status that, consequently, had persisted in 54.3%. No patient had fully remitted from mental disorders, even if UHR status was not maintained. Conversion was best predicted by any transient psychotic symptom and a disorganized communication score. No prediction model for outcome beyond conversion was identified.

Discussion: Our findings provide the first evidence for the predictive utility of UHR criteria in CAD in terms of brief intermittent psychotic symptoms (BIPS) when accompanied by signs of cognitive impairment, i.e. disorganized communication. However, because attenuated psychotic symptoms (APS) related to thought content and perception were indicative of non-conversion at 1-year follow-up, their use in early detection of psychosis in CAD needs further study. Overall, the need for more in-depth studies into developmental peculiarities in the early detection and treatment of psychoses with an onset of illness in childhood and early adolescence was further highlighted.

S35. High-risk symptoms for psychosis through adolescence: are there age-related peculiarities in the profile of negative symptoms?

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Background: High-risk symptoms for psychosis (HRS) are common among adolescents and can be predictive of later psychosis especially when positive symptoms persists (Dominguez *et al.*, 2011) or when linked to negative symptoms (NS) and poor global functioning (Addingtonn and Heinssen, 2012). However, it is still unknown whether there are developmental peculiarities in the presentation of HR-NS in young age groups. OBJECTIVE: To study the profile of NS and functional scores of a sample of young adolescents who meet criteria for HRS by comparing their clinical and functional profile with a group of old adolescents with HRS.
Methods: Sample included 89 PRS subjects from a prospective longitudinal study including help-seeking subjects who met HRS criteria (Child and Adolescent Psychiatry and Psychology departments of Hospital Clínic and San Joan de Déu, Barcelona). 42 subjects were 14 years old or younger (Young adolescents group, Y-Ad, mean age = 13.6, SD = 1.1). 47 subjects were 15 years old or older (Old adolescents group, O-Ad, mean age = 16.4, SD = 0.9). Inclusion criteria: age 10-17 years, meeting criteria for 1) attenuated positive or negative symptoms in the previous 12 months, 2) brief intermittent psychotic symptoms, 3) first or second degree relative with schizophrenia or schizotypical disorder plus impairment of functioning. Exclusion criteria: IQ < 70 and a diagnosis of neurodevelopmental disorder (ND). Instruments: The Semistructured Interview for Prodromal Syndromes and Scale of Prodromal Symptoms (SIPS/SOPS) were administered by expert child and adolescent psychiatrists and psychologists. The Hamilton Depression Rating Scale (HDRS, Hamilton, 1960) to assess depressive symptoms and the Young Mania Rating Scale (Young *et al.*, 1978) for manic symptoms. The Social Communication Questionnaire (Rutter *et al.*, 2003) to assess autism spectrum features in the sample. The social and Role functioning Scales (GF:S and GF:R, Cornblatt *et al.*, 2007) to rate functioning. An estimation of the IQ was derived from the Wechsler Scales of Intelligence for children or adults.
Results: Young and old adolescent groups were similar in gender ($P = 0.055$), SES ($P = 0.104$) and IQ (Y-Ad = 95.2 ± 14.2; O-Ad = 100.1 ± 12.8, $P = 0.128$). Regarding functioning, both groups had mean scores around 5 in role functioning (Y-Ad = 5.6 ± 1.3; O-Ad = 5.6 ± 1.2) and around 6 in social functioning (Y-Ad = 6.4 ± 1.1; O-Ad = 6.4 ± 1.5) ($P > 0.940$). There were no significant differences among groups in the SOPS total NS scores (Y-Ad = 11.4 ± 5, O-Ad = 12.1 ± 5.6, $P = 0.550$). However, ANOVAs for individual NS showed that older adolescents had higher mean scores in the N3-Expression of emotion ($P = 0.026$) and N4-Experience of emotions and self ($P = 0.015$) while younger adolescents had higher mean scores in the N5-Ideational Richness ($P = 0.008$). Old adolescents had also more depressive symptoms accordantly to the HDRS ($P = 0.033$). No differences were found in manic symptoms or autistic features ($P > 0.113$). When depressive symptoms were controlled for, differences between groups in N3 and N4 were no longer significant but remained statistically significant for N5.

Discussion: Both young and old adolescents with HRS were moderately impaired in their social and role functioning, which is consistent with previous literature (Cornblatt *et al.*, 2012). Old adolescents had higher difficulties with expression and experience of emotions but these differences were mainly account by depressive symptoms. Poorer ideational richness appeared as a specific symptom for young adolescents. The results showed age-related peculiarities in the presentation of HR negative symptoms throughout development.

S36. Relationship between emotional and reasoning schemata about self and others and type of delusional symptoms in a sample of child and adolescents at clinical risk for psychosis

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Background: Cognitive models of psychosis have postulated that the two different types of delusions (Persecutory delusions - Paranoia and Grandiose delusions) might be related differently to distinct psychological processes. Persecutory delusions (paranoia) has been associated to low self-esteem, self-critical thinking, and extreme negative beliefs about self (Garety 2013) and grandiose delusions have been related to mood-congruent disorder, specifically mania (Lake 2008), or to high self-esteem, low levels of depression, or less negative self-schemas (Moritz 2010). So, although there is evidence from psychotic subjects, there is sparse literature on at risk samples, and this data might have a crucial interest to know whether these schemes are trait versus status markers for psychosis. In this poster we present preliminary data about schemata in a sample of patients at risk of psychosis and the relationship between the emotional and cognitive processes and the attenuated delusional symptoms.
Methods: Participants were recruited at a prospective, naturalistic, multi-site and longitudinal study conducted in help-seeking child and adolescents at risk for psychosis. The sample consists of $N = 89$ patients at risk and $N = 39$ healthy controls, but only 25 subjects (14 psychosis risk and 11 controls) were assessed in their emotional and cognitive schemata. All psychosis risk subjects met Criteria of Prodromal Syndromes (COPS) using the Structured Interview for Prodromal Syndromes (SIPS) (McGlashan, 2010). Psychological processes were assessed using The Brief Core Schema Scales (BCSS, Fowler *et al*, 2006), that provides a self-report of schemata concerning self and others (Negative-self, N-S; Positive-self, P-S; Negative-other, N-O; Positive-other, P-O). The attenuated psychotic symptoms were assessed using the SIPS. Data analysis was ruled using the SPSS 20.0 statistical package.
Results: There were no significant differences between groups on gender ($P = 0{,}897$) but were differences on age ($P = 0{,}024$). We found differences between clinical and controls, based on scores in the 4 BCSS subscales. Healthy subjects scored higher on the 2 scales of Positive schemata (both positive Self and Other) and subjects at risk had higher intensity of Negative schemata (Self and Others). Group differences were significant for the P-S ($P = 0{,}004$) and there was a tendency to the significance for the N-O schemata ($P = 0{,}057$).
Also, we found statistically significant associations between cognitive schemata and some attenuated psychotic symptoms. Specifically, we found that the Unusual thought content / Delusional ideas (P1) severity was positively associated with negative schemes, both N-S ($r = 0{,}544$; $P = 0{,}044$) and N-O ($r = 0{,}551$; $P = 0{,}051$), and was negatively associated with P-O ($r = -0{,}594$; $P = 0{,}032$) (more severity of delusional ideas correlated to less positive beliefs about others).
In addition we observed a significant and negative association between the intensity of P-O and the severity of Persecutory ideas (paranoia) (P2) ($r = -0{,}575$; $P = 0{,}040$). Paranoia was also positively associated to the N-O scale ($r = 0{,}622$; $P = 0{,}023$). Grandiosity (P3) was significant and negatively correlated with the intensity of the P-O schemata ($r = -0{,}789$; $P = 0{,}01$). Finally, it is noteworthy that the P-S schema was not associated with any of the attenuated psychotic symptoms.

Discussion: Data from at risk patients is consistent with literature in patients with psychosis. Although the small sample size, if we can confirm these results in a larger sample, findings could indicate the likely presence of cognitive and emotional schemata related with the risk for developing different types of delusional attenuated symptoms.

S37. Abnormal involuntary movements are linked to psychosis-risk in children and adolescents: results of a population-based study

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Background: Altered motor behavior has consistently been reported in medication-naïve adult patients with schizophrenia and first episode psychosis and adults at clinical high risk for psychosis (CHR). This study is the first to evaluate the prevalence of abnormal involuntary movements in a community sample of children and adolescents with and without CHR.
Methods: We examined CHR in 102 children and adolescents aged 8–17 years from the general population of the Canton Bern. Attenuated and brief intermittent psychotic symptoms, as well as basic symptoms, were assessed using the Structured Interview for Psychosis Risk Syndromes and the Schizophrenia Proneness Instrument, Child & Youth Version. Motor symptoms were assessed using the Abnormal Involuntary Movement Scale (AIMS). Additionally, psychosocial functioning, a neurocognitive test battery, and DSM-IV Axis I disorders were examined.
Results: Eleven (10.8%) participants met CHR criteria, 13 (12.7%, 5 with and 8 without CHR) met criteria for increased abnormal involuntary movements (AIMS ≥ 2). Both AIMS total scores and the percentage of children with AIMS ≥ 2 were significantly higher in the CHR group. Psychosocial functioning was reduced in subjects with abnormal involuntary movements, and movement abnormalities were linked to deficits in attention and perception but not to the presence of non-psychotic mental disorders.
Discussion: Our findings suggest that abnormal involuntary movements are linked to psychosis risk in children and adolescents from the general population. Thus, abnormal involuntary movements might represent an additional useful and easily accessible predictor of psychosis.

S38. Interaction between DISC1 mutation and cannabis exposure in adolescence results in aberrant behavioral and neurobiological phenotypes in a translational mouse model of schizophrenia

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Background: Cannabis abuse in adolescence is associated with increased risk of psychosis and conversion to schizophrenia. Δ-9-tetrahydrocannabinol (THC) is the primary psychoactive component of cannabis. DISC1 is a driver for major mental illness by influencing neurodevelopmental processes biologically. The aim of the present study is to establish a clinically relevant mouse model of severe mental illness such as schizophrenia based on host (DISC1) X environment (THC administration) interaction.
Methods: Wild-Type (WT) and DN-DISC1 mice were injected with THC (10 mg/kg) or vehicle for 10 days during mid-adolescence-equivalent period. Behavioral tests assessed exploratory activity (open field, light-dark box test) and working memory (novel object recognition test). Electrophysiological effect of THC was evaluated using hippocampal slices. Hippocampal cannabinoid receptor type 1 and Brain-derived neurotrophic factor (BDNF) protein levels were measured. Over expression of BDNF was conducted using stereotactic delivery of a lentiviral vector to the hippocampus.
Results: THC significantly interacted with host perturbance in DISC1 by eliciting behavioral deficits in DN-DISC, but not in WT mice, in terms of exploratory activity and working memory. Deficits in working memory in THC-treated DN-DISC1 mice were associated with reduced short-term synaptic facilitation. THC-treated WT mice responded with elevated hippocampal BDNF, which was not observed in the THC-treated DN-DISC1 mice. Over-expression of BDNF in the hippocampus of THC-treated DN-DISC1 mice prevented the impairment in working memory.
Discussion: DN-DISC1 mice display increased susceptibility to develop aberrant neuropsychiatric behavioral and biochemical phenotypes following adolescent sub-chronic THC administration, in a BDNF dependent manner. We hereby suggest a DN-DISC1 X THC interaction as a gene X environment mouse model for schizophrenia.

S39. The danish high risk and resilience study – via 7 -a cohort study of 520 7 year old children born of parents diagnosed with either schizophrenia, bipolar disorder or neither of these two mental disorders

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Background: Severe mental illnesses like schizophrenia and bipolar disorder are known to be diseases that to some extent, but not entirely can be understood genetically. For schizophrenia the dominating hypothesis is that it is a neurodevelopmental disorder, and that genes, environment as well as gene-environment-interactions contribute to the risk of developing the disease.
Aim: We aim to analyse the influences of genetic risk and environmental factors in a population of 7-year-old children with either 0, 1 or 2 parents diagnosed with schizophrenia spectrum psychosis or bipolar disorder, on psychopathology, and neurocognitive, neuromotor, and psychosocial development. We hypothesize that a larger proportion of children growing up with an ill parent will display abnormal or delayed development, behavioural problems or psychiatric symptoms compared to the healthy controls.
Methods: We are establishing a cohort of 520 7 year old children and both their parents for a comprehensive investigation with main outcome measures being neuro cognition, behaviour, psychopathology and neuro motor development of the child. Parents and children will be examined with a battery of instruments. The participants are recruited via Danish registers to ensure representativity. Data from registers concerning social status, birth complications, somatic illnesses and hospitalization are included in the database.
Psychological and relational factors like emotional climate around the child, degree of stimulation and support in the home and attachment style are also investigated.
Results: Recruitment was successful since only about 20% of the invited families declined to participate, equal for all groups. Results expected in autumn 2016.
Discussion: Results are not available yet, but in this large, clinical study many aspects already call for attention, e.g. that some of these families may need specialized early intervention to prevent deterioration of the child's daily function and maybe also prevent development of later mental illness

S40. Aberrant linguistic salience attribution as a risk factor for psychosis-proneness: insights from the TWINSSCANCHINA study

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Background: Mis-assignment of linguistic salience to objectively meaningless auditory information could result in extraction of spurious speech in unintelligible noise (i.e., "speech illusion"). Experimentally, speech illusion could be tested by asking participants to report any speech heard in multispeaker babble in which phonetic density is so high that word detection is virtually impossible. Previous studies suggest speech illusion predicts transition to schizophrenia spectrum disorder in individuals displaying prodromal signs of psychosis (Hoffman *et al.*, 2007), and correlates with scores on the Schizotypal Personality Questionnaire in the general population (Morton, Nicolson & Linscott, 2013). This study seeks to clarify the relationship between speech illusion and psychosis proneness in a Chinese subclinical population using a psychobabble task. It is hypothesized that the length of speech illusion predicts higher psychosis proneness.
Methods: Data were collected from 198 Chinese twin-sibling participants aged between 15-22 (mean = 16.45; SD = 1.16) with no known familial or personal history of mental disorder. Speech illusion was measured by the psychobabble task (Hoffman, 1999). Participants listened to multispeaker babble derived from 6 overlapping recordings of neutral texts in Chinese, and were instructed to repeat out loud any words or phrases they believed they had heard. Participants' reported words were then compared against the original texts so as to identify spurious words (speech illusion). The outcome measure of interest was the longest speech illusion (LSI) score (i.e., number of characters in the longest phase generated). Psychosis proneness was measured using the validated Chinese version of Community Assessment for Psychic Experiences (CAPE-C15): a self-report 15-item questionnaire designed to measure psychosis proneness through tapping the frequency and level of distress of psychotic-like experiences (PLE) in the general population. CAPE-C15 includes dimensions of positive symptom (e.g., hallucinations and delusions), negative symptom (e.g., poverty of speech and affective flattening) and depressive experiences (e.g., crying about nothing and feeling like a failure). Multilevel linear modeling was employed to account for increased covariance between subject pairs.
Results: 20% of participants reported one or more spurious word, with LSI range being 0-4 (mean = 1.07; SD = .741). Multilevel linear modelling revealed that LSI significantly predicted CAPE-C15 positive dimension "frequency and distress" scores (b = 0.59, 95%CI = 0.036, 1.138, $P = 0.037$).
Discussion: Our results suggest that non-clinical individuals who heard longer spurious speech reported more frequent and distressing positive PLE. Based on this, it is possible to speculate that the tendency to extract coherent speech (a phrase), which is difficult to dismiss as misperception, could lead to distressing hallucinations later on. We suggest that the spurious, perceived-coherent speech commands attention and further top-down processing of "meaning". Since spurious speech are typically context-free, idiosyncratic explanations might have to be used to explain their existence and meaning, leading to delusion-like experiences. Taken together with evidence that LSI predicted clinical transition to schizophrenia spectrum disorders (Hoffman *et al.*, 2007), it is possible to further speculate that this mechanism could underlie clinical hallucinations. Through the use of a subclinical population, our findings suggest that speech illusion was not due to the downstream consequences of medication or illness experience in psychotic patients, supporting it as a potential risk mechanism.

S41. The role of autoimmunity on neurodevelopment: study on offspring of systemic lupus erytematosus patients

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Background: The idea of an association between psychopathology, autoimmunity and inflammation is receiving growing interest. A pro-inflammatory condition has been associated to development of psychiatric symptoms from early lifetime. In an autoimmune condition as Systemic Lupus Erythematosus (SLE), maternal antibodies (Ab) have been posited to affect in-uterus neurodevelopment of fetus, possibly contributing to increased risk for learning disabilities, anxiety and depression symptoms. In adult SLE, a subset of the anti-dsDNA Ab – the anti-DWEYS Ab - have been suspected to cause psychiatric symptoms, by cross-reacting against the NR2 subunit of the NMDA receptor, and causing neuronal damage and apoptosis.
Purpose: To compare immunological, neuropsychological and psychopathological profiles of offspring of women with SLE during pregnancy (SLE-O), with healthy controls without history of maternal SLE (HC).
Methods: Sample: SLE-O ($n = 21$, mean age 14,9, %female 40%), HC ($n = 34$, m.a. 15,1, %female 48%). No difference was found between the two groups.
Data were collected on:
- pregnancy and delivery, immunity and Ab condition, serum levels of 12 cytokines;
- cognitive function - Wechsler Intelligence Scale for Children and Adults (WISC-IV and WAIS-R) and other batteries;
- *psychopathology*: K-SADS-PL, and screening scales for anxiety, depression and recent stress.
Blood samples were collected in fasting status and frozen at -80º. Statistical analysis performed with SPSS.20.
Results: SLE-O show:
- Differences in delivery conditions, immunity profile (lower leukocytes, higher cytokines and anti-DWEYS Ab) and some neuropsychological tests.
- A tendency for higher scores in screening scales for anxiety and depression. No significant difference in recent stress level.
- A high prevalence of clinical or subclinical psychiatric diagnosis (described prevalence of axis I diagnose in young population is 10-22%).

Table 1. Relevant comparisons

	HC	*SLE-O*	*P-value*
	median (IQ range)	*median (IQ range)*	
Obstetrical Complication Scale (range 0-30)	1,5(1-3)	4(2-7)	0,006**
Gestation_week	40(39-40)	38(34-40)	0,004**
Birth weight (kg.)	3,2(3-3,4)	3,03(2,48-3,45)	0,294
Leukocyte count (10E9/L)	7,25(6,45-8,74)	5,64(4,84-6,51)	0,001**
Neutrophile count	3,75(3-5)	2,9(2,4-3,5)	0,004**
Lymphocyte count	2,4(1,9-2,9)	1,9(1,6-2,5)	0,049*
DWEYS Ab	0,07(0,05-0,10)	0,15(0,12-0,20)	< ,001**
IFN-g (pg/mL)	0(0-0)	0,2(0-1,07)	0,026*
IL1b	0(0-0)	0,71(0,39-0,94)	< ,001**
IL2	0(0-0)	0,39(0,13-3,24)	< ,001**
IL10	0(0-0)	0,56(0,12-1,02)	< ,001**
IL5	0(0-0)	0(0-0,31)	0,001**
IL4	0(0-0)	2,52(1,51-6,65)	< ,001**
IL6	0(0-0,38)	0,82(0,46-1,81)	< ,001**
SCARED^ total score (cutpoint = 15)	13(9-19)	16,5(12,5-24)	0,085
Beck Depression Inventary (cutpoint = 13)	2(0-5)	5(1-8)	0,061
Stressful Life Events Scale	14(6-27)	20(10-42)	0,258
Time of Copy (typical score = T.S.)	59(51-61)	45(36-58)	0,001**
London Tower- Transgression of rules (T.S.)	52(35-52)	52(52-53,5)	0,002**
Learning abilities - text redaction (T.S.)	55(45-65)	47(43-55)	0,039*

significantly different at *: $P < 0,05$, **: $P < 0,01$.
^SCARED = Screen for Child Anxiety Related Disorders.

Table 2. KSADS-PL results in SLE-O. n (%)

DSM-IV clinical diagnosis: YES	5 (24%)
ADHD	2 (10%)
TOURETTE/TIC DIS	1 (5%)
OCD	1 (5%)
ANXIETY	1 (5%)
DSM-IV subclinical diagnosis	
SUBCL. ANXIETY	9 (43%)
SUBCL. ADHD	4 (19%)
SUBCL. OCD	1 (5%)
NO DIAGNOSIS	7(33%)
TOTAL	21

Discussion: Results suggest differences between SLE-O and HC in immunological profile, cognitive performance and psychopathology. If confirmed, it should be determined whether they depend on prenatal autoimmune insult, altered autoimmune condition, or environmental stressors, like maternal health.

S42. Is it still correct to differentiate between early and very early onset psychosis?

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Background: It remains unclear whether very early onset psychosis (VEOP; ≤ 12 years of age) and early onset psychosis (EOP; onset 13-17 years of age) are homogeneous in their clinical presentation. We investigated the predictive value of age of psychosis onset for severity, functioning and demographic variation by: 1) comparing groups based on traditional cut-offs for age of psychosis onset, and 2) using receiver operating characteristic (ROC)-curve calculations, without a priori age of onset cut-offs.
Methods: Participants in this study were 88 (45 female, 43 male) children and adolescents consecutively admitted to the Child and Adolescent Neuropsychiatry Unit of the Clinical and Research Hospital Bambino Gesù of Rome with a recent onset of psychosis. Patients had psychosis onset between ages 6.7 and 17.5 years (M = 13.74, SD = 2.37, median = 14.1) and had no previous drug treatment for psychosis (typical/atypical antipsychotics).
Results: There were no significant group differences between VEOP and EOP in terms of gender, urban environment, diagnosis of schizophrenia or a family history of psychotic illness. The VEOP group showed a significantly shorter duration of untreated illness (DUI) and duration of untreated psychosis (DUP) than the EOP group and lower functioning scores. Groups did not differ significantly on psychotic, depressive and anxiety symptoms, or IQ.
When applying ROC-curves to the lowest three quartiles of positive psychotic symptoms scores, the optimal age-cut-off was 14.0 years (sensitivity = 0.62; specificity = 0.75). For the highest quartile of functioning scores, the optimal differentiating cut-off for age of psychosis onset was 14.7 years (sensitivity = 0.71; specificity = 0.70). To investigate the validity this newly identified age cut-off, univariate analyses were rerun dividing groups based on age of psychosis onset < 15 or ≥ 15 years of age. The younger group had significantly higher positive symptoms and lower functioning. They also had higher total psychotic symptoms and DUI. There were no significant group differences on negative or general symptoms, depressive and anxiety symptoms, IQ, DUP, or demographic and diagnostic variables.
Discussion: Larger samples of patients, assessed at presentation and followed-up, are necessary to clearly examine clinical presentation and outcome as a function of social and neural development to better understand if the differentiation between VEOP and EOP is justified. This will aid the development of predictive diagnostic tools, more accurate prognosis prediction, and age-tailored therapeutic interventions.

S43. Clinical profile and predictors of outcomes in outpatients with prodromal psychosis in Shanghai, China

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Background: In a previous epidemiological study, we reported on the ascertainment of "clinical high risk" (CHR) individuals at the Shanghai Mental Health Center (SMHC), and the outcomes of a subsample of individuals. This current study aimed to replicate these earlier findings with a new sample of CHR individuals to confirm the clinical factors associated with transition to psychosis and to improve the accuracy of prediction weights.
Methods: A sample of 100 CHR participants visiting the SMHC for the first time and psychotropic medication naive (at baseline) were selected based on screening and face-to-face interviews. The Structured Interview for Prodromal Syndromes (SIPS) was used for CHR ascertainment. A naturalistic 10-month follow-up was conducted, and the conversion determination was made according to clinical information received from clinician reports, telephone interviews of CHR individuals or their caregivers, or face-to-face interviews using the SIPS. A forward stepwise logistic regression was used to assess predictors of psychosis, with transition as the dependent variable and the demographic and clinical factors (e.g., age, positive symptoms) as the independent variables. These results were tested for replication of previous findings that had suggested that poorer functioning, symptoms and clinicians' judgment would help to predict the conversion of psychosis.
Results: A total of 91 (of 100) CHR participants completed the clinical 10-month follow-up (91.0%), 22 (29.1%) of the 91 completers transitioned to a psychotic disorder over the course of follow-up. When converter and non-converter baseline characteristics were compared, the most significant differences were found in GAF (Global Assessment of Functioning) score drop ($P = 0.02$) and the disorganized symptom score ($P = 0.011$). A logistic regression model was used to evaluate the effect of demographic and clinical variables on conversion risk, including age, gender (40 factors in total). Results indicated that the P1 symptom (Unusual thought content) (OR = 6.728, $P = 0.016$), functional impairments (OR = 1.112, $P = 0.023$), and severity of overall disorganized symptoms (OR = 1.420, $P = 0.006$) were found to predict which CHR participants were more likely to develop full psychosis within a 10 month follow-up period of time.
Discussion: Chinese CHR participants from this study had a similar transition rate as those in our previous epidemiological investigation, and comparable with those of specialized help-seeking samples world-wide. Functionally deteriorating clinical participants who are suffering from attenuated psychotic symptoms warrant attention and effort of early intervention in China.

S44. Mechanisms of transmission of health and risk in parents with schizophrenia or bipolar disorder and their offspring (the WARM study)

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Background: Approximately half of infants of parents with complex mental health problems such as psychosis and mood disorder develop mental disorders themselves and thus have a severely increased risk compared to the normal population. The purpose of this study is to establish the feasibility of developing a cohort of pregnant women with severe mental disorder and to identify biological and psychosocial transmission mechanisms involved in the development of 'risk' and 'resilience' in the offspring. A High-Risk developmental trajectory in infants is likely to be caused by a complex interaction between multiple biological, psychological and social factors. The WARM study focuses specifically on examining the impact of physiological stress-

sensitivity (cortisol), attachment, care-giving and the familial and social context for care-giving.
Methods: The project is a longitudinal cohort study, identifying and recruiting women during pregnancy presenting in four groups: 1) lifetime DSM-V diagnosis of schizophrenia ($n = 50$); 2) lifetime diagnosis bipolar disorder ($n = 50$); lifetime diagnosis of moderate/severe depression ($n = 50$); non-clinical control ($n = 50$). The cohort will be recruited in Denmark and Scotland. After baseline assessment antenatally, mothers and their infant's will be followed up at 1-7 days, 4, 16-weeks and 12-months postnatal. We are measuring symptoms (PANSS, Bech, MADRS), stress-sensitivity (maternal and infant salivary cortisol), maternal intelligence (Reynolds Intellectual Screening Test), maternal attachment (Self-report and interview, Adult Attachment Interview, Adult Attachment Projective, Psychosis Attachment Measure), neonatal behaviour (NNNS), mother-infant interaction (Caregiving Inventory, Still Face procedure) and social factors (significant others, childhood trauma, demographics).
Results: After 8 months of recruitment we have identified 182 potential participants and have recruited $n = 50$ participants. Our recruitment data indicates that identification of mothers with a diagnosis of Schizophrenia is consistent with a population birth rate of 0.02% of total births, which is similar to estimates from national registries. Our rate of consent for non-affective psychosis is 27% of those eligible and the rate for bipolar disorder is 43% of those eligible. We present preliminary data on baseline symptoms and birth data on the initial sample.
Discussion: The WARM study is in the process of establishing a cohort of pregnant women with severe mental disorder. Our data highlight the challenges of recruiting and retaining this clinical group into a research study and also yield valuable information on the baseline symptomatology of high-risk mothers.

S45. Genome-wide methylation changes following early and late prenatal immune activation: focus on the prefrontal cortex

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Background: Epidemiological and experimental evidences demonstrate that maternal exposure to infection during gestation is an environmental risk factor for a variety neurodevelopmental disorders, such as schizophrenia and autism. Moreover, the precise timing of the prenatal infection seems to be critical, as it can determine specific clusters of behavioral and morphological phenotypes in the offspring. Thus, we used a specific animal model of prenatal immune challenge to investigate the possible molecular mechanisms underlying differences and similarities in specific clusters of behavioral abnormalities brought on by infection at two different time points in pregnancy. First of all, we compared adult behavioral features in offspring born to mothers subjected to infection early or late during gestation. Secondly, we investigated the possible molecular mechanisms underlying such abnormalities, focusing our attention on how prenatal infection could affect DNA methylation patterns in the prefrontal cortex.
Methods: C57BL/6 mice were treated with the synthetic viral mimetic poly(I:C) (5 mg/kg, i.v.) or control (saline, i.v.) solution on gestation day 9 or on gestation day 17. Offspring were subjected to cognitive and behavioral testing in adulthood, and then whole genome capture-sequencing DNA methylation analysis and subsequent q-PCR validation were performed on the prefrontal cortex.
Results: Prenatal exposure to Poly(I:C) led to a variety of behavioral abnormalities, some of which were common to both time points, while others, as for example prepulse inhibition, were specific to one time point. Specific and overlapping changes were also observed when considering the DNA methylation analysis in the prefrontal cortex. In particular, both early and late exposure to prenatal infection led to extensive changes in DNA methylation, and a significant portion of these differentially methylated regions is common to both time points of infection. Different genes, such as Mid1, Ntm and Nrxn2, stood out as top candidates for deeper investigation based on their involvement in neurodevelopment and psychiatric disorders.
Discussion: Our results provide new insight into the molecular mechanisms mediating the association between prenatal infection and adult vulnerability to psychiatric disorders, and, more specifically, provide further knowledge regarding the impact of the precise timing of the infection. Moreover, our results uncover possible targets of future studies and point to a possible role of DNA methylation in mediating the detrimental effects of prenatal immune challenge, consistent with similar reports in human studies.

S46. Neurochemical changes underlying antipsychotic phenotype in mGlu4 knockout mice

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Background: In variety of our previous studies we showed that mGlu4 receptor is a promising target in the antipsychotic drug discovery. Its activation, with both mGlu4 agonists and positive modulators induced clear antipsychotic-like effect in animal models, that was 5-HT1A, and, to some extent, GABAB-dependent. Moreover we showed that the lack of mGlu4 receptor in knockout mice results in antipsychotic-like phenotype that was observed as the decreased sensitivity of these mice to the psychostimulant effect of DOI, manifested as the decreased number of episodes in DOI-induced head twitches test when compared to wild type mice. In the present studies we tried to established, which neurochemical changes may develop in these mice that could be responsible for observed effect. We focused on serotonergic and GABAergic signaling.
Methods: We used DOI-induced head twitches test, in which we compared wild type and mGlu4 KO animals response to DOI. We also investigated, if that effect was reversed with the administration of GABAB or 5-HT1A antagonists (CGP55845 and WAY100635, respectively). After behavioral experiments, prefrontal cortices, hippocampi and striata were dissected and the level of factors important in schizophrenia were measured, e.g GAD65 and GAD67, enzymes responsible for GABA synthesis, and 5-HT1A receptors. Both mRNA and protein level were measured, with the use of RT-PCR and Western blotting techniques, respectively.
Results: mGlu4 KO animals showed the decreased number of head twitches after administration of DOI. Both GABAB and 5-HT1A antagonists reversed this effect in KO animals, having no activity in their wild type counterparts. mRNA analysis revealed decreases in the 5-HT1A production in the prefrontal cortex and increases in GAD65 and GAD67 production in prefrontal cortex and hippocampus of mGlu4 animals, and those changes were accompanied with the changes in protein level.
Discussion: mGlu4 receptor is strongly involved both in the pathophysiology and pharmacotherapy of schizophrenia, however, the exact mechanisms that underlie its functioning are poorly investigated. However our results indicate that GABAergic and serotonergic systems play a crucial role in the mGlu4-mediated actions.

S47. Differential regulation of ventral tegmental area dopamine neurons by infralimbic prefrontal cortex and lateral habenula: implications for schizophrenia

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Background: Dopamine system abnormalities have long been recognized for their contributions to the pathophysiology of schizophrenia. Recently, interest has focused on how specific subsets of DA neurons within the ventral tegmental area (VTA) may contribute to unique psychological processes. For example, neurons that are more involved in the processing of reward-related information and vulnerable to acute and chronic stress have been localized preferentially to more medial portions of the VTA. Conversely, more laterally located VTA DA neurons project to the associative striatum and thus have more involvement in salience and cognition. Heightened activity in these associative-related lateral DA neurons is

particularly pronounced in animal models of the hyperdopaminergic state observed in schizophrenia. In the present study, we sought to identify the circuitry regulating the activity of medially vs. laterally located DA neurons in order to identify potential involvement of these regions in the hyperdopaminergic state present in schizophrenia. We chose to focus on two regions that have well-established abilities to modulate the DA system: infralimbic prefrontal cortex (ILPFC) and lateral habenula (LHb).
Methods: We performed single-unit extracellular recordings of identified VTA DA neurons from anesthetized rats following LHb or ILPFC pharmacological activation or inhibition using localized micro-infusion of N-methyl-D-aspartate (NMDA) or tetrodotoxin (TTX), respectively. Specifically, we made 9 electrode passes in a preset pattern spanning the medial-lateral extent of the VTA in order to determine the number of DA neurons firing (population activity), their firing rate and pattern.
Results: Activation of either ILPFC or LHb in normal rats potently suppressed VTA DA neuron population activity ($P < 0.05$), albeit in different patterns. ILPFC activation primarily affected medial VTA DA neurons, whereas LHb activation inhibited more central and lateral VTA DA neurons. However, neither manipulation induced either global or location-specific effects on firing rate or bursting of VTA DA neurons. Inhibition of the ILPFC or LHb with TTX each resulted in increased number of spontaneously active DA neurons, however no clear differences in laterality were observed. Neither inhibition of ILPFC nor LHb with TTX induced a change in average firing rate or bursting.
Discussion: In the present study we show that both ILPFC and LHb have bidirectional control over the firing of VTA DA neurons. Furthermore, ILPFC appears to have greater influence over motivationally-relevant medial DA neurons, while LHb appears to have greater influence over more lateral cognitive DA neurons. Finally, while both regions possess the ability to alter the number of spontaneously active DA neurons, neither appear to exert potent effects on group-averaged firing rate or burst firing of these neurons. Collectively, these data suggest that the ILPFC and LHb may exert differential modulatory roles over distinct subsets of DA neurons within the VTA Such differences could account for the presence of comorbidity of affective disorders and schizophrenia that are believed to result from modulation of the DA system in opposite directions.

S48. A randomised controlled trial of cognitive behavioural therapy versus non-directive reflective listening for young people at risk of developing psychosis: the detection and evaluation of psychological therapy (DEPTH) trial

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Background: Intervention trials for young people clinically at risk (AR) for psychosis have shown cognitive behavioural therapy (CBT) to have promising effects on treating psychotic symptoms. However many of these trials have compared CBT to supportive counselling and have not focused on functional outcomes. Our trial compared CBT to an active control condition in the treatment of young people AR for psychosis.
Methods: This study was a single-blind randomised controlled trial for young people AR for psychosis (aged 14-35 years) comparing CBT to Non Directive Reflective Listening (NDRL) in addition to standard care, with a six month treatment phase and 12 months of follow up.
Results: There were 57 young people with a mean age of 16.5 years randomised for treatment. The rate of transition to psychosis was 5%, with all three transitions occurring in the CBT condition, at baseline, two months and five months respectively. The active control condition, NDRL, resulted in a significantly greater reduction in distress associated with psychotic symptoms compared to CBT. Both CBT and NDRL showed reductions in the frequency and intensity of psychotic symptoms over time. There were no significant treatment effects on global, social or role functioning.
Discussion: Compared to other trials, our participants were higher functioning, younger and experiencing lower levels of psychotic like experiences. The significant treatment effect for our active control condition, NDRL, supports the recommendations for a stepped care approach in the treatment of young people AR for psychosis.

S49. Selective estrogen receptor modulation increases dorsolateral prefrontal cortex activity during emotional inhibition in schizophrenia

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Background: People with schizophrenia show impaired response inhibition in conjunction with decreased neural activity in the dorsolateral prefrontal cortex (DLPFC). DLPFC activity during emotional response inhibition correlates positively with circulating estrogen levels in healthy females and with circulating testosterone in men with schizophrenia. Here, we tested the extent to which the selective estrogen receptor modulator (SERM) raloxifene could modify neural activity during a language-based emotional go/no-go task in men and women with schizophrenia. We also predicted that the neural response to raloxifene will vary depending on estrogen receptor alpha (ESR1) genotype in people with schizophrenia.
Methods: Twenty-one men and women with schizophrenia participated in a 13-week, randomized, double-blind, placebo-controlled, crossover adjunctive treatment trial of the SERM raloxifene administered orally at 120 mg daily. Effects of raloxifene versus placebo on brain activity were assessed using functional magnetic resonance imaging (fMRI) during an emotional inhibition test. Functional ESR1 genotype changes within intron 1 were determined by TaqMan allelic discrimination assay.
Results: Relative to placebo, treatment with raloxifene increased neuronal activity in the DPLFC during inhibition of negative words in men and women with schizophrenia. The increased BOLD signal in the DLPFC was more pronounced in ESR1 genotype that predicted higher ESR1 levels in the DLPFC. A separate confirmatory Region Of Interest analysis comparing 21 people with schizophrenia to 23 healthy controls demonstrated that raloxifene restores DLPFC activity to normal levels in people with schizophrenia.
Discussion: Selective estrogen receptor modulation by raloxifene facilitates activation of the DLPFC during inhibition of negative emotions in men and women with schizophrenia. People with schizophrenia having a specific ESR1 genotype displayed increased DLPFC activity during inhibition of emotional words with raloxifene administration relative to those carrying the ESR1 risk genotype. These results support a role for estrogen receptor modulation of prefrontal neural activity in both men and women with schizophrenia and suggest that ESR1 genotype may be informative of treatment response to raloxifene.

S50. Aggresivity management in schizophrenia diagnosed patients using calcium channel alpha-2-delta ligands

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Background: Hostility, aggresivity and excitement are important dimensions of schizophrenia, with significant impact on the patients' clinical status. Pharmacological interventions designed to control such symptoms are not so varied, consisting mainly of antipsychotics and benzodiazepines. Mood-stabilizers are associated with mixed results, so their use in clinical practice is not so wide. We tested the hypothesis of alpha2delta calcium channels ligands are eficacious agents in schizophrenia diagnosed patients with aggresivity and related symptoms.
Methods: A group of 12 patients, 8 male and 4 female, diagnosed with schizophrenia (both according to DSM 5 criteria), admitted in our department for acute psychotic episodes, received atypical

antipsychotics (olanzapine $n=4$, risperidone $n=3$, amisulpride $n=3$, aripiprazol $n=1$, quetiapine $n=1$). All these patients had a Positive and Negative Syndrome Scale (PANSS) excited component score (excitement, hostility, tension, uncooperativeness, poor impulse control) - PANSS-EC over 20 at the admission. Patients received also pregabalin ($n=6$) 300-600 mg, flexible dose, or gabapentin ($n=6$) 900-1200 mg, flexible dose, and were monitored every other day for 10 days, and every week for a month after that, using PANSS, PANSS-EC, Clinical Global Impression –Severity (CGI-S), and Global Assessment of Functioning (GAF). Inclusion criteria: age 18-65, using of two contraception methods during treatment, ability to sign informed consent, PANSS over 70. Exclusion criteria: other psychiatric comorbidities, unstable organic conditions, suicidal ideation or/and behavior, treatment rezistent schizophrenia. Last observation carried forward and intent-to-treat analyses were used for statistic interpretation of data.
Results: After 6 days patients improved significantly compared to baseline on PANSS-EC ($P<0.01$) on either pregabalin or gabapentin group, with no statistical significant differences between the two groups (-6.8, and -7.2, respectively). The improvement remained significantly to baseline throughout the 4 weeks of the study on PANSS-EC. The overall PANSS score decreased also gradually, with no significant differences between the 5 antipsychotics used. CGI-S evolution reflected the PANSS-EC score improvement, while GAF correlated more closely to the PANSS global score.
Discussion: Alpha-2 delta calcium channels ligands are efficient in controlling aggresivity and related symptoms, and their onset of action could be detected early (day 6) and the positive effect maintained during the 4 weeks of the study.

S51. Weight reduction with reboxetine treatment: a double-blind, placebo-controlled study of reboxetine and citalopram as adjuncts to atypical antipsychotics

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Background: Patients with schizophrenia exhibit a reduced life expectancy mainly due to metabolic-related pathologies, such as cardiovascular disease or type 2 diabetes mellitus. Although diverse factors have been associated with this increased risk of morbidity and mortality, excess body weight, extremely prevalent, has been considered as one the most responsible features. Among patients with severe mental illness, excess body weight can be attributed to unhealthy lifestyles, personal genetic profile, as well as the metabolic effects of psychotropic medications, above all antipsychotic drugs. Prior reports have suggested diverse adjunctive treatments, with dissimilar levels of efficacy, for weight reduction in patients with schizophrenia. In view of the extent of the problem, we aim to estimate the rate of weight change over 6 months in patients treated with reboxetine in comparison with citalopram and placebo as adjuncts to second generation antipsychotics (olanzapine and risperidone).
Methods: Double-blind, randomized, placebo-controlled clinical trial: 90 patients treated with a stable dose of either olanzapine or risperidone were randomly assigned to complete a 6-month period of adjunctive treatment with reboxetine 8 mg/d (34 patients), citalopram 30 mg/d (23 patients) or placebo (33 patients).
Results: In a mixed model regression analysis, weight variations over time were significantly associated with baseline body mass index, age and gender (male) while reboxetine was also associated with weight reduction compared with citalopram and placebo. No significant association was found for tobacco use, medical or familial history.
Discussion: Our results do support weight reduction when combining reboxetine with atypical antipsychotics in patients with schizophrenia over a 6-month period.

S52. Effects of community mental health service in subjects with early psychosis

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Background: The use of a multidisciplinary team approach aimed at improving clinical symptoms and socio–occupational functioning is essential for increasing the likelihood of recovery among individuals with early psychosis. Thus, the aim of the present study was to investigate the effects of community-based mental health services on the symptoms and socio–occupational functioning of subjects with early psychosis.
Methods: The present study included participants who were self- or hospital-referred to our Mental Health Promotion Center and who agreed to participate in diverse individual and group programs. The participants were prospectively followed for 1 year.
Results: During the follow-up period, the medication adherence rate remained high, the recovery rate substantially increased, and the scores on the Positive and Negative Syndrome Scale (PANSS), Psychotic Symptom Rating Scale-Delusion and Auditory Hallucinations subscales (PSYRATS-D/AH), Global Assessment of Functioning (GAF), Interpersonal Sensitivity Measure (IPSM), and Social Functioning Questionnaire (SFQ) significantly improved over time. The present findings suggest that the 1-year outcome of subjects with early psychosis can be improved by diverse community-based psychosocial interventions.
Discussion: The present findings suggest that the Mind Flower service effectively reduced the clinical symptoms and improved the socio–occupational functioning of clients with early psychosis. The implications of the present study are that traditional hospital-centered treatment regimens should be expanded to incorporate community-based psychosocial interventions to maximize the likelihood of achieving recovery in subjects with early psychosis.

S53. Results of an exploratory phase II study with MIN-101, a 5-HT2a/sigma2 antagonist, for the treatment of schizophrenia

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Background: Current treatments for schizophrenia are effective in some but not all patients and do not benefit negative symptoms or cognitive deficits which are prevalent in this disease. MIN-101 has a novel mechanism of action combining 5-HT2a and sigma2 antagonism. Preclinical work suggests that this combination might affect negative symptoms and cognition.
Methods: This was an exploratory multi-center, double-blind, parallel-arm, placebo-controlled study of MIN-101 32 mg BID (64 mg daily) in patients with schizophrenia. Patients were randomized 1:1 to placebo or MIN-101. Patients had PANSS total score >60, and were not selected for specific positive, negative, or cognitive symptoms. The study consisted of 3 phases: an inpatient washout period of 3-9 days, an inpatient 3- day single blind placebo lead-in, and a 12 week double-blind treatment phase. Patients could transition to ambulatory care after 2 weeks of treatment. Assessments included PANSS and Brief Assessment of Cognition in Schizophrenia (BACS). Treatments were compared using Mixed Model Repeated Measures analysis after 28 and 84 days of the double blind phase. The primary efficacy endpoint was the change from baseline in the PANSS total score after 28 days of treatment. Safety was monitored at each visit.
Results: Of the 84 patients in the ITT population, 48 (57.1%) remained in the study at D28, when the primary efficacy measurement occurred. The PANSS total score mean changes at D28 were -6.2, ($P=0.017$), and

-3.2, ($P = 0.210$), respectively for placebo and MIN-101. There was no statistically significant difference on PANSS total score observed between treatments. On the PANSS 5-factor Negative Subscale at D84 the mean changes were +0.3 ($P = 0.7924$) and -3.1 ($P = 0.0177$) for placebo and MIN-101, respectively, and the 2 treatments were statistically significantly different ($P = 0.045$). No other comparisons between treatments were statistically significantly different. On the BACS the MIN-101 arm was numerically better than placebo at all post-baseline visits on the Total Score, Token motor, and List Learning and Verbal Fluency tasks. MIN-101 was well tolerated and induced no significant changes in vital signs or physical examination. Weight and waist circumference showed little change over the 3-month study. MIN-101 induced no increase in prolactin levels and no significant change in safety lab parameters. The mean change from baseline in QTcF was higher at all visits in MIN-101 group compared to placebo, with the mean change from baseline < 10 ms at all time-points but three (D6, D14 and D28), and a maximum of +11.7 ms (and -0.4 ms for placebo) on D14. There was no clinically significant cardiac related AE.
Discussion: This was an exploratory study of an antipsychotic with a novel mechanism of action. The purpose of this study was to assess signals among multiple efficacy measures to optimize design of future studies. It was powered based on published change in PANSS total score in patients treated with known antipsychotics, but the dropout rate was higher than anticipated. There was a strong placebo effect in this trial, which has been shown to correlate with negative study outcome. Nevertheless the changes seen on the negative subscale of the PANSS are promising, and are explored in a current study. The effects on cognition are also be important, if replicated. The overall safety & tolerability profile was very encouraging with the possible exception of QTc effects; a new formulation of MIN-101 which reduces Cmax is being tested, which should reduce these effects.

S54. Sex and gender differences in emerging psychosis – results from the Basel FePsy project

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Background: Sex and gender differences in schizophrenic psychoses have often been described, especially regarding age of onset and course of the disorder. Little is known, however, regarding sex or gender differences in emerging psychosis, i.e. the prodromal phase of psychosis and its first episode.
Methods: Within the Basel FePsy (Früherkennung von Psychosen) study, we examined consecutively all patients referred to the specialized Early Detection Clinic of the University Psychiatric Hospital Basel, covering the catchment area of the county of Basel and followed them up over at least 5 years regarding the question of later transition to psychosis. All patients were assessed regarding different domains, amongst others symptomatology, neuropsychology, MRI and different endocrinological blood tests.
Results: Based on 126 at-risk mental state (ARMS) and 97 first episode psychosis (FEP) patients we found no significant gender differences regarding psychopathology. Regarding neurocognition, women performed better in verbal learning and memory independent of the diagnostic group. By contrast, men showed a shorter reaction during the working memory task. In a subgroup we found hyperprolactinemia in 27% of antipsychotic-naïve patients, mainly in women. Pituitary volumes were considerably larger in women than in men and increased in emerging psychosis (FEP and ARMS patients with later transition to psychosis $>$ ARMS patients without later transition to psychosis and healthy controls).
Discussion: With this multidomain project we could show that during emerging psychosis there are probably no significant gender differences in symptomatology. Gender differences in neurocognition seemed to be similar in patients with emerging psychosis to those in the healthy general population. The most striking gender differences we found were regarding psychoendocrinology and neuroimaging. Both hyperprolactinemia and pituitary volume were much more increased in women than in men with emerging psychosis. As prolactin is a well-known stress hormone and is produced in the pituitary, these latter findings might indicate that emerging psychosis is associated with more stress for women than for men.

S55. Increasing signal detection in clinical trials: improving fidelity of instruments

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Background: Treatment effects in schizophrenia can be subtle. Even small imprecision in measurement can lead to false negative results. In the current pharmacoeconomic climate such failures can lead to the permanent abandonment of potentially beneficial treatments. One strategy to improve measurement is to conduct consistency checks in the use of measures.
Methods: ISCTM (International Society for CNS Clinical Trials and Methodology) convened a working group of Positive and Negative Syndrome Scale (PANSS) experts who met over the last 2 years. The goal was to develop consistency flags for the PANSS. These flags were applied to the NEWMEDS data and also to CATIE. In addition strategies to cross-check Clinical Global Impressions (CGI) and Calgary Depression Scale for Schizophrenia (CDSS) and the PANSS were developed.
Results: Twenty-three flags were identified and divided based on extent to which they represent error (Possibly, Probably, Very probably (or definitely)). The seven most common inconsistencies in order of extent to which the workgroup determined that they represent error were as follows: 1. Same response on ALL items from previous visit; 2. if Depression (G5) is moderately severe or greater then Motor retardation (G7) should be at least mild; 3. Lack of spontaneity (N6) should be at least 2 pts $>$ than N3 Poor rapport; 4. If either Hostility (P7) or Poor impulse control (G14) is $>$ mild then the others should not differ by more than 2 points; 5. Tension (G4) should not be greater than Anxiety (G2); 6. If Hallucinatory behavior (P3) is moderately severe or greater then Preoccupation (G15) should be at least moderately severe; 7. If Conceptual disorganization (P2)is moderately severe or greater then Difficulty in abstract thinking (N5) should be at least moderately severe. Almost 40% of NEWMEDS and CATIE ratings had at least one flag raised, and approximately 10% had two flags raised. Based on the literature establishing cutting points for clinical depression on the CDSS the following concordance of PANSS depression item and CDSS is suggested: PANSS depression item 1-Absent = CDSS 0 to 2, 2-Minimal = 3, 3-Mild = 4-5, 4-Moderate = 5-6, 5-Moderately Severe = 7-9, 6-Severe = 9 or greater. Based on the literature the following PANSS ranges for CGI scores were derived CGI-S of 3 Mildly ill, PANSS range of 55 to 80; CGI-S of 4 Moderately ill PANSS in range of 71 to 92 and CGI-S of 5 Markedly ill with a PANSS in the 88 to 100 range.
Discussion: Analyzing items within the PANSS, as well as comparing the PANSS items to ratings on other scales, can help to identify potentially incorrect ratings which may be remediated with rater training and could also be used to develop a metric for rater selection.

S56. Combining aerobic exercise and cognitive training decreases negative symptoms and improves social functioning in first episode schizophrenia: a UCLA pilot RCT

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Background: Meta-analyses have indicated that the beneficial effects of cognitive training (CT) for schizophrenia patients extends to psychiatric symptoms and functioning, but the effect sizes for symptoms are smaller than for cognitive deficits. Meta-analyses have also shown that various forms of exercise (E) in schizophrenia patients are associated with symptom reduction, improved quality of life, and increased social functioning. We examined whether combining cognitive training and aerobic exercise could improve symptoms and social functioning compared to cognitive training alone. First episode schizophrenia patients were selected to maximize treatment effects before patterns of chronic disability develop. The goal of this RCT is to estimate the effect sizes of this novel intervention.
Methods: In this pilot RCT, 21 patients with a recent first episode of schizophrenia were assigned to Cognitive Training plus Exercise (CT&E: $n = 11$) or Cognitive Training alone (CT; $n = 10$) for 6 months. The CT&E intervention involves 24 weeks of cognitive training, 4 hours

per week, plus aerobic exercise, four 30- minute sessions per week. The first 12 weeks involved neurocognitive training (BrainHQ), using auditory training exercises. The second 12 weeks involved social cognitive training (SocialVille). The exercise intervention consisted of aerobic conditioning exercises for 150 minutes per week, including 45 minutes at UCLA two days a week and 30 minutes at home two days a week. Intensity of aerobic exercise was tailored to maintain an individualized target heart rate zone. A weekly one-hour Bridging Skills Group was designed to aid generalization of training. Symptoms were assessed every two weeks with the BPRS and SANS, and social functioning was assessed every 3 months with the Global Functioning Scale: Social (GFS).
Results: A Generalized Linear Mixed Model (GLMM) was used to compare the trajectories of changes in symptom severity and level of social functioning. Analysis of the BPRS negative symptom factor indicated that CT&E patients showed a significantly larger decrease in expressive negative symptoms vs CT alone ($F(1,235) = 8.4$, $P < .01$, Cohen's $f = .19$) with a decrease of 0.7 ($d = .47$) for the CT&E group vs decrease of.1 ($d = .07$) for the CT group. Analysis of trajectories for SANS Expressive symptoms also showed a significant difference over time for the two treatment conditions ($F(1,235) = 5.9$, $P = 0.02$, Cohen's $f = .16$), with a decrease for the CT&E group of.7 ($d = .44$) vs a decrease in the CT alone group of.2 ($d = .12$). However, the SANS Experiential subscale showed no differential effect of treatment ($F(1,236) = 0.6$, $P = .44$). For BPRS depression there was a nonsignificant tendency toward greater reduction for the CT&E group ($F(1,211) = 3.04$, $P = .08$, Cohen's $f = .12$). Analysis of GFS Social Functioning trajectories showed a tendency that neared statistical significance, indicating greater improvement for the CT&E group from 0 to 6 months ($F(1,19) = 4.2$, $P = .054$, Cohen's $f = .47$, equivalent to Cohen's $d = 94$).
Discussion: Our preliminary findings support the use of exercise to boost the effects of cognitive training on expressive negative symptoms. We found significant reductions in BPRS negative symptoms and on the SANS expressive factor which includes Blunted Affect and Alogia. Adding exercise to cognitive training also might aid improvement in depression. The addition of exercise tended to improve social functioning more than cognitive training alone, with measurable effects that are not yet statistically significant. Our ongoing study supports previous work, extends prior studies to first episode schizophrenia patients, and suggests that exercise may enhance the impact of cognitive training beyond cognition to both symptoms and community functioning.

S57. Why do clinical trials fail so often in schizophrenia? A quantitative systems pharmacology approach to account for the effect of comedications and genotypes

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Background: The development of new therapeutic interventions in schizophrenia poses substantial challenges resulting in a low success rate and prompting many companies to exit the field. Possible reasons include the variability of patient populations, the translational disconnect between animal models and the clinical situation and the lack of understanding of the biological pathways involved in the disease. Here we address the impact of comedications and genotypes on the clinical phenotype and propose to use the concept of virtual human patients as a novel modeling technology to optimize the clinical trial design.
Methods: Quantitative Systems Pharmacology (QSP) is a mechanism-based computer simulation of biophysically realistic cortico-striatal-thalamo-cortical neuronal circuits for pharmacological research questions spanning the spectrum from discovery to clinical development. The model is an accurate representation of the associative and meso-limbic circuit between dorso-lateral and ventromedial cortex and their respective basal ganglia regions that drives symptoms of schizophrenia and incorporates the direct, hyperdirect and indirect pathway in addition to a number of dopaminergic, serotonergic, adrenergic and cholinergic GPCR that modulate the firing dynamics in different parts of the circuit. Schizophrenia pathology is introduced quantitatively using human imaging data on the degree of hyperstriatal activity and cortical dysfunction. The model is calibrated using historical clinical trials
Results: Using this model of 'virtual patients', we show how different combinations of drugs and smoking affect different clinical outcomes such as PANSS Total, EPS liability and cognitive performance. Combining antipsychotics usually does not result in improved PANSS Total outcome, except for quetiapine while in many cases clinical performance is reduced and side effects such as EPS and prolactin levels are increases. When considering augmentation therapy with acetylcholinesterase inhibitors and memantine in addition to smoking, most of the combinations show a negative pharmacodynamic interaction on cognitive readouts, with the exception of olanzapine.
Discussion: This study suggests that virtual patient simulation can identify the combinations that show a positive pharmacodynamic interaction and optimize clinical trial design or rationalize polypharmacy in real-life settings.

S58. Scoring discrepancies and site performance in the administration of the PANSS

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Background: Numerous clinical trials of schizophrenia have recently failed, some in costly late stages of clinical development (Goff, 2014), increasing the challenge of developing new treatments. The high failure rate in psychosis trials has, in part, been due to imprecision in endpoint measurement that introduces noise. The Positive and Negative Syndrome Scale (PANSS) is a complex scale that is prone to administration and scoring errors that can contribute to poor interrater reliability. Central Review methodology utilizes recordings of assessments and source documents to help ensure quality of interviews and consistency of ratings across study sites. Subsequent feedback to site raters is designed to improve their assessments and standardize the cohort of site raters. The goal of the present study was to examine error rates in the administration and scoring of the PANSS across raters and sites.
Methods: 288 assessments of the PANSS in two multisite, randomized, double-blind, placebo-controlled clinical trials of schizophrenia were evaluated. The PANSS is a 30-item scale with three major subscales: Positive, Negative, and General Psychopathology. After conducting the subject interview, raters completed scoring based on unique scoring anchors and conventions for each item. The 288 assessments were completed by a total of 79 raters at 58 investigative sites. Score discrepancies in the PANSS were identified via review of video recordings and source documents by a cohort of expert calibrated reviewers. Site performances in scoring discrepancies were also examined.
Results: Central review of assessments identified very high percentages of reviews with two or more discrepancies between the expert raters and the site raters. 92% of the reviews contained at least two errors in the total score. On the subscale level, two or more discrepancies were observed in 58% of reviews for Positive Symptoms, 71% for Negative Symptoms, and 83% for General Psychopathology. Analysis of performance by site indicated that a majority of the sites had very high percentages of reviews with two or more errors ($>90\%$).
Discussion: The PANSS is a complex scale that is challenging to score, resulting in poor rater reliability. Central Review methodology can help improve interrater reliability through detection and remediation of scoring errors. A platform for electronic clinical outcome assessments (eCOA) with real-time clinical guidance, auto-calculation of scores and prompts for missing data and out-of-range errors can standardize PANSS administration and scoring, thereby improving signal detection. Such eCOA platforms would have alerted 73% of site raters in the present study to at least one potential error (Williams, *et al.*, 2015).

S59. Initial development of a patient reported outcome measure of experiences with cognitive impairment associated with schizophrenia

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Background: Cognitive impairment is a pervasive feature of schizophrenia and a major contributing factor to functional impairment and disease burden. There are many existing instruments for the measurement of cognitive impairment based on clinicians' assessment or performance on a variety of cognitive tests. However, there is currently no reliable, validated patient-reported outcome measure of the everyday experience of cognitive impairment from the patient's point of view. Such a measure would provide a complimentary outcome to other existing instruments and fill an important gap in current assessments. This report describes the initial development and content validity of a novel patient-reported outcome measure, the Patient Reported Experience of Cognitive Impairment in Schizophrenia (PRECIS).
Methods: An initial conceptual model was constructed based on existing literature and expert input. A first round of patient interviews was conducted for concept elicitation and item generation. A second set of interviews and cognitive debriefing with patients was conducted to evaluate the draft item pool. Revisions to the conceptual model and draft items were made at each stage.
Results: Eighty patients were interviewed for concept elicitation and item generation. A further twenty-two patients participated in interviews and cognitive debriefing on the initial item pool. The initial conceptual model included seven domains: memory, attention, executive functioning, communication/social cognition, impaired perception, flat cognition, and metacognitive abilities. Within domains, some concepts were modified, removed, or added after the interviews. The name of the domain "flat cognition" was revised to "sharpness of thought;" and the domain impaired perception was removed due to infrequent endorsement by patients and potential overlap with positive symptoms.
The initial item pool consisted of 53 items covering 26 concepts in the six domains. The initial draft instrument used a 1 week recall period and a 5-category response scale from 'not at all hard' to 'very hard'. At debriefing, most participants reported that the questionnaire was 'very' or 'quite' complete in covering their experiences of cognitive impairment (16 of 19 responding, 84%) and of an acceptable length (19 of 22, 86%). Fifteen items were removed due to insufficient ease of comprehension, and 3 items were removed due to redundancy. Minor revisions were made to most of the remaining 35 items and to the instructions based on specific participant feedback.
Discussion: This qualitative study initiated development of a valid and reliable patient-reported outcome measure of the subjective experience of cognitive impairment in schizophrenia. There may be important differences between how patients perform on standardized tasks (i.e. their objective level of impairment) and how burdened they feel as a result of their cognitive problems (i.e. their subjective level of disability). The PRECIS instrument has been developed in accordance with industry best practices and to be consistent with guidance from regulatory authorities. The patient-centric development and iterative revision process has led to a measure with a high degree of content validity for a well-defined concept of interest. Qualitative data show a high degree of comprehension and comprehensiveness, and the instrument is now undergoing quantitative psychometric evaluation in the context of a clinical trial. The PRECIS will be further revised based upon the results of this psychometric evaluation, and may eventually provide an invaluable tool for the direct assessment of patients' experiences with cognitive impairment.

S60. Efficacy and safety of paliperidone palmitate 3-month versus 1-month formulation in schizophrenia: global and Asian subgroup analysis of a randomized, double-blind, non-inferiority study

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Background: Paliperidone palmitate (PP) 3-month formulation (PP3M), a long-acting injectable antipsychotic, has recently been approved in the US for the treatment of schizophrenia. This sustained release formulation of PP provides an extended dosing interval of once every 3 months, i.e., 4 doses per year. This study aimed to demonstrate noninferiority of PP3M to PP1M in patients with schizophrenia previously stabilized on PP1M, and to compare efficacy and safety outcomes in the Asian subgroup with the total patient population.
Methods: This was a randomized, double-blind (DB), parallel-group, multicentre, non-inferiority, phase 3 study (NCT01515423). After screening, patients (18 to 70 years) diagnosed with schizophrenia DSM-IV-TR and a total Positive and Negative Syndrome Scale (PANSS) score between 70 and 120 entered a 17-week, flexible-dose, open-label (OL) phase to receive PP1M. Patients meeting predefined stability criteria entered a 48-week, DB phase and were randomized (1:1) to receive either the stabilized fixed dose of PP1M (50, 75, 100, or 150 mg eq.) or PP3M (175, 263, 350, or 525 mg eq. [3.5 multiple of PP1M]) in the deltoid or gluteal muscle. Primary efficacy endpoint was the percentage of patients who remained relapse-free at the end of the DB phase. Secondary efficacy endpoints included the changes from baseline to end of DB phase in PANSS total and subscale scores, Clinical Global Impression-Severity (CGI-S) score and Personal and Social Performance (PSP) score. Safety parameters including treatment-emergent adverse events (TEAEs) were also assessed.
Results: Of 1429 patients enrolled during OL, 1016 (Asians: $n = 344$) entered DB phase. Asian subgroup was 52% female and total population was 47% female. Mean (SD) age (years) was younger in Asians (36.0 [12.05]) vs total population (38.7 [12.08]). Mean OL baseline (SD) BMI (kg/m2) was normal in Asians (24.4 [4.13]) and lower than the total population (26.5 [5.05]). Kaplan-Meier estimate of difference (95% confidence interval [CI]) between PP3M and PP1M groups who remained relapse-free at end of DB was similar between Asian subgroup (1.7% [-5.5%; 8.9%]) and total population (1.5% [-2.3%; 5.3%]); the lower bound of CI of the difference was larger than prespecified noninferiority margin of -15%. LS mean differences (95% CI) between PP3M and PP1M in change from baseline to end of DB phase: PANSS total score – Asians: 0.3 (-2.26; 2.80) vs total: 0.9 (-0.61; 2.34); CGI-S score – Asians: -0.1 (-0.24; 0.10) vs total: 0.0 (-0.05; 0.13); PSP score – Asians: -0.3 (-2.48; 1.80) vs total: -0.5 (-1.73; 0.64). Incidence of TEAEs in DB was higher in Asian patients (PP3M: 81.2%, PP1M: 75.9%) vs total population (PP3M: 67.9%, PP1M: 66.4%); TEAE of weight increased was higher in Asian subgroup (PP3M: 31.2%, PP1M: 31.0%) vs total (PP3M: 20.8%, PP1M: 21.3%).
Discussion: PP3M was noninferior to PP1M and was similarly tolerable in Asian subgroup and in total population, for patients with schizophrenia, previously stabilized on PP1M.

S61. Toward a negative symptom system of schizophrenia: a network approach

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Background: Recent research on the measurement and treatment of negative symptoms has attained mixed success. An approach to illuminate reasons for that may be to conceptualize negative symptoms as a system using network analysis. Using network analysis we aim to examine negative symptoms to: (I) identify negative symptom severity networks; (I) identify the most central negative symptoms; (III) contrast negative symptom networks.
Methods: Item level Scale for the Assessment of Negative Symptoms (SANS) data were re-analyzed from three clinical trials that compared placebo and amisulpride to 60 days. Participants had chronic

schizophrenia and predominantly negative symptoms ($n = 487$). Symptom networks were tested at baseline for severity and on change with mixed models for the total sample, as well as in amisulpride and control samples.
Results: Within baseline and endpoint networks: symptoms grouped into Affect, Poor responsiveness, Lack of interest, and Apathy-inattentiveness; the most central symptom was Decreased Spontaneous Movements and least on Grooming and Hygiene. These networks did not statistically significantly differ. For the adjusted change score networks Affect, Poor responsiveness and Lack of interest remained, but Apathy-inattentative symptoms split. In the total group, amisulpride and placebo on Poverty of Speech was the most central item. In the total and amisulpride groups the least central item was Grooming and Hygiene, whereas in the placebo group it was inappropriate affect. The placebo and amisulpride networks did not significantly differ.
Discussion: This is first study to consider negative symptoms as a network. Results demonstrated: (I) a replicable negative symptom system; (II) symptoms with high centrality (e.g., poverty of speech) that may be future treatment targets.

S62. Outcomes of maintenance antipsychotic treatment versus discontinuation strategies following remission from first episode psychosis: a systematic review and meta-analysis

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Background: Although remission of symptoms is common in patients with first episode psychosis, evidence to guide prophylactic treatment with antipsychotics post remission has been limited to placebo controlled trials with relatively short follow-up until recent trials investigating discontinuation strategies.
Methods: We performed a systematic review of the literature using the Cochrane guidelines as a framework. We included prospective, parallel control group or experimental studies that specifically compared maintenance antipsychotic treatment in first episode psychosis samples to those in which a discontinuation strategy or intermittent treatment strategy was employed. Studies were included if patients were defined as in remission of psychotic symptoms prior to the commencement of the comparison and relapse rates were reported for at least 6 months. MEDLINE, Embase, PsycINFO, and all Cochrane library bibliographic databases were searched from their date of inception to February 2015. Primary outcome was relapse rate; secondary outcomes included hospitalization rate, symptoms, functioning and side-effects. We performed a meta-analyses, and meta-regression where possible in order to test potential explanations of our findings.
Results: 9 studies were included in the review, which in total included 751 participants; average length of follow-up was up was 2.06 years. There was a greater risk of relapse in the discontinuation groups compared to the maintenance treatment groups (overall risk difference (RD) of 0.25). The pooled risk difference was lower when hospitalisation was considered as the outcome (RD 0.12). There was heterogeneity in study results. Subgroup analysis suggested that the pooled RD of relapse was lower in studies with a longer follow-up period, a targeted discontinuation strategy as opposed to placebo, studies with a higher relapse threshold and studies with a larger sample size. Meta-regression demonstrated that the results were only significantly different for targeted discontinuation versus placebo trials, and smaller versus larger trials. A narrative review only, was possible for other outcomes, which highlighted differences in quality of life and functional outcomes between maintenance and discontinuation groups.
Discussion: There is a higher risk of relapse and hospitalisation in those who undergo a graded or intermittent discontinuation strategy compared to a maintenance antipsychotic therapy. However the effect size is relatively small in first episode psychosis patients. These differences are lower than previous studies and might be explained by smaller differences between more real world strategies that include graded discontinuation as opposed to placebo. Few studies include functioning as an outcome but there appears to be no functional benefit reported for maintenance therapy in these trials.

S63. Prediction of transition to psychosis in patients with a clinical high risk for psychosis: a systematic review of methodology and reporting

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Background: Meta-analyses suggest that among help seeking patients with a clinical high risk (CHR) for psychosis only about one third develop psychosis within 5 years and about one third is having a clinical remission within 2 years. Hence, in order to improve clinical decision making in these patients, recent research efforts have been increasingly directed towards estimating the probability of developing frank psychosis on an individual level using multivariable clinical prediction models. However, despite considerable research efforts in this area, no psychosis risk prediction model has yet been adopted in clinical practice. One possible reason for the lack of progress in this area could be the widespread use of poor methods. Thus, the aim of this study was to systematically review the methodology and reporting of studies developing or validating models predicting psychosis in CHR patients using rigorous quality criteria.
Methods: A systematic literature search was carried out (up to September 18, 2015) in order to find all studies that developed or validated a multivariable clinical prediction model predicting the transition to psychosis in CHR patients. Data were extracted using a comprehensive item list which was based on the recently published Checklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS) and current methodological recommendations of text books and articles on clinical prediction modelling.
Results: Eighty-six studies met the inclusion criteria. Although all included studies had applied a multivariable prediction model, most of them did not directly aim at developing a model for clinical practice. Instead, they made use of these models for hypothesis testing or aimed at evaluating the predictive potential of certain predictors or assessment domains. Consequently, only 7 studies (8%) were classified as model development studies and 79 (92%) as predictor finding studies. None of the retrieved studies performed a true external validation of an existing model. The average number of events per considered predictor variable (EPV) was 1.8 and 3.1 in model development and predictor finding studies, respectively. Only 2 studies (2.5%) had an EPV of at least 10, which is the recommended minimum for sufficient power. Internal validation was carried out in only 13 studies (15%) and six of these used inefficient or severely biased methods, such as split-sampling or cross-validating only the final model and thereby not taking into account the uncertainty introduced by variable selection. Other frequently observed modelling approaches not recommended by methodologists included univariate screening of candidate predictors, stepwise variable selection with low significance threshold, categorization of continuous predictor variables, and poor handling and reporting of missing data.
Discussion: Our systematic review revealed that poor methods and reporting are widespread in prediction of psychosis research. Since most studies relied on relatively small sample sizes, did not perform internal or external cross-validation, and applied modelling strategies that are prone to overfitting and overoptimistic predictive performance estimation, the results of these studies must be interpreted with great caution. To enhance progress, future studies should develop prediction models in accordance with current methodological recommendations and guidelines, such as the recently published Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement.

S64. The practical implications of metacognitive psychotherapy in psychosis: findings from a pilot study

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Background: In preparation for a multicenter randomized controlled trial a pilot study was conducted investigating the feasibility and acceptance of a shortened version (12 vs. 40 sessions) of an individual metacognitive psychotherapy.
Methods: Twelve participants with a diagnosis of schizophrenia were offered twelve sessions of Metacognitive Psychotherapy (MERIT). Effect sizes were calculated for metacognitive capacity as measured by the Metacognition Assessment Scale – A.
Results: Nine out of twelve patients finished treatment. Non-significant moderate to large effect sizes were obtained on the primary outcome measure. Results are discussed in the context of informing the randomized controlled trial currently in progress.
Discussion: This study suffers from limitations typical to a pilot study; notably a small sample size and lack of a control group. Sufficient evidence of efficacy was obtained to warrant further investigation into the method. Effect sizes and drop-out suggest an estimated required sample size of 120.

S65. Long-term effectiveness of aripiprazole once-monthly is maintained in the qualify extension study

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Background: The QUALIFY (QUAlity of LIfe with AbiliFY Maintena®) study is the first to directly compare two pharmacologically different atypical long-acting injectable antipsychotics on a measure of health-related quality of life and functioning as the primary outcome. The primary analysis showed superior improvements with the dopamine D2 partial agonist aripiprazole once-monthly 400 mg (AOM 400) vs the dopamine D2 antagonist paliperidone palmitate once-monthly (PP) on the Heinrichs-Carpenter Quality-of-Life scale (QLS) total score (Naber *et al.* 2015, NCT01795547). This extension study evaluated the long-term safety, tolerability, and effectiveness, of continued AOM 400 treatment in patients with schizophrenia who completed the QUALIFY study.
Methods: This was an open-label, flexible-dose, 28-week extension study (NCT01959035) in patients who received AOM 400 treatment and completed the lead-in QUALIFY study ($n = 100$). At entry into the lead-in study, the patients were out-patients, ages 18 to 60 years, with schizophrenia according to DSM-IV-TR. In the extension study, patients received 6 monthly injections of AOM 400, with safety and effectiveness data collected at each visit. The 24-week treatment extension period allows, when aggregated to the data from the lead-in study, for nearly one year of data on the safety and effectiveness of AOM 400 in the maintenance treatment of schizophrenia. Effectiveness data comprised health-related qualify of life and functioning assessed with the QLS total and Clinical Global Impression – Severity of Illness (CGI-S) scores, and changes from baseline were assessed with a mixed model for repeated measures in the extension study alone and in the lead-in and extension study combined.
Results: Of the 88 patients enrolled and treated in the extension phase, 77 (88%) completed the study. The reasons for withdrawal were adverse events ($n = 5$), withdrawal of consent ($n = 4$), lost to follow-up ($n = 1$) and other reasons ($n = 1$). The treatment-emergent adverse events (TEAEs) with highest incidence during the extension study were weight increased (6/88, 7%), toothache (3/88, 3%) and headache (3/88, 3%). Three patients (3%) had serious adverse events of alcoholism, dysphoria, and gastrooesophageal reflux disease (1 patient each). Effectiveness assessed during the extension study was maintained with AOM 400 treatment, with continued minor improvements from baseline: the least squares mean (LSM) change [95% confidence interval] from baseline of the extension to week 24 was 2.32 [-1.21; 5.85] in QLS total score and -0.10 [-0.26; 0.06] in CGI-S score. In these patients, the aggregated LSM changes from baseline of the lead-in study to week 24 of the extension were 11.54 [7.45; 15.64] for QLS total score and -0.98 [-1.18; -0.79] for CGI-S score.
Discussion: Continued long-term treatment with AOM 400 was safe and well tolerated in patients rolling over from the lead-in QUALIFY study. In terms of effectiveness, the completion rate in the extension was close to 90% with robust and clinically meaningful improvements on health related quality of life and functioning being maintained, as measured with QLS and CGI-S. These results further support the clinical benefits of AOM 400 for long-term treatment in patients with schizophrenia.

S66. ITI-007 exhibits unique pharmacology: combined results from positron emission tomography (PET) studies in healthy volunteers and patients with schizophrenia

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Background: ITI-007 is a first-in-class investigational new drug in clinical development for the treatment of schizophrenia. Through synergistic actions via serotonergic, dopaminergic and glutamatergic systems, ITI-007 represents a novel approach to the treatment of schizophrenia and other neuropsychiatric disorders. ITI-007 is a potent antagonist at 5-HT2A receptors, a mesolimbic/mesocortical dopamine phosphoprotein modulator (DPPM) with activity as a pre-synaptic partial agonist and post-synaptic antagonist at dopamine D2 receptors, a mesolimbic glutamate GluN2B receptor phosphoprotein modulator and a serotonin reuptake inhibitor. Phase 2 clinical trial (ITI-007-005) data indicated that 60 mg ITI-007 was effective in reducing symptoms of schizophrenia with a safety and side effect profile similar to placebo (Lieberman *et al.*, Biological Psychiatry, 2015 online ahead of print). The purpose of the present studies was to determine brain occupancy of ITI-007 at key pharmacological targets thought to mediate its efficacy, including dopamine D2 receptor occupancy (D2RO).
Methods: Healthy volunteers (Clinical Study ITI-007-003) or patients with stable schizophrenia who were washed off their antipsychotic medications at least two weeks inpatient (ITI-007-008) received a baseline scan and up to 3 post-treatment scan(s). Healthy volunteers were evaluated after a single dose of ITI-007 (10, 20, 30, or 40 mg) and patients with schizophrenia received ITI-007 (60 mg) once daily for approximately two weeks, to plasma steady state. Carbon-11-Raclopride, carbon-11-M100907, and carbon-11-DASB were used as the radiopharmaceuticals for imaging striatal D2 receptors, cortical 5-HT2A receptors, and striatal serotonin transporters, respectively. Brain regions of interest were outlined using magnetic resonance tomography (MRT) with cerebellum as the reference region. Binding potentials were estimated using a simplified reference tissue model. D2RO was expressed as percent change in the binding potentials before and after ITI-007 administration.
Results: In healthy volunteers, ITI-007 (10 mg) demonstrated high occupancy (>80%) of cortical 5-HT2A receptors and low occupancy of striatal D2 receptors (~12%). D2RO increased with dose. ITI-007 (40 mg) resulted in peak occupancy up to 39% of striatal D2 receptors and 33% of striatal serotonin transporters. In patients with schizophrenia, 60 mg ITI-007 demonstrated ~40% D2RO.
Discussion: Taken into context with data from other clinical trials (ITI-007-005 and ITI-007-301) in which ITI-007 60 mg was effective in reducing psychosis in patients with schizophrenia, ITI-007 was effective at relatively low striatal D2 receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D2 receptors. This mechanism

along with potent interactions at 5-HT2A receptors, serotonin reuptake inhibition and indirect glutamatergic modulation likely contributes to the efficacy with improved psychosocial function. As such, ITI-007 represents a novel approach to the treatment of schizophrenia.

S67. Psychiatric stability maintained in tardive dyskinesia subjects treated with valbenazine

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Background: Tardive dyskinesia (TD) is a persistent movement disorder induced by chronic neuroleptic exposure, for which there are currently no FDA-approved treatments. Valbenazine (VBZ; NBI-98854) is a novel, highly selective vesicular monoamine transporter 2 inhibitor under investigation for use in TD that exhibited favorable safety in earlier studies. KINECT 2 (NCT01733121) was a dose-escalating trial evaluating safety and efficacy of VBZ for TD, demonstrating significant and clinically meaningful improvement vs placebo. The present analysis evaluated the psychiatric status of subjects across the trial.
Methods: KINECT 2 was a prospective, randomized, double-blind, 6-week, placebo-controlled trial in subjects with schizophrenia, mood disorder or gastrointestinal disorder with moderate or severe TD. VBZ or placebo (1:1) were administered once daily. All subjects randomized to VBZ received 25 mg through Week 2, then the dose was titrated to 50 mg or maintained at 25 mg; at Week 4 the dose was titrated to 75 mg, maintained or reduced to the previous dose. After Week 6, subjects completed a 2-week follow-up. The primary endpoint (previously reported) was Week 6 change from baseline (CFB) in Abnormal Involuntary Movement Scale (AIMS) score vs placebo. AIMS videos were scored by two blinded central raters. Safety assessments were analyzed descriptively and included the following psychiatric scales: the Positive and Negative Syndrome Scale (PANSS), Young Mania Rating Scale (YMRS), Montgomery-Asberg Depression Rating Scale (MADRS), Calgary Depression Scale for Schizophrenia (CDSS), and the Columbia Suicide Severity Rating Scale (C-SSRS).
Results: A total of 102 subjects were randomized; 76% of VBZ subjects reached the maximum dose of 75 mg. The Safety population was 51 (VBZ) and 49 (placebo) subjects. Antipsychotics, antidepressants, and anxiolytics were the most common concomitant medications, taken by $\geq$40% of subjects in each group. Week 6 CFB in AIMS score (primary endpoint) was significantly greater for VBZ vs placebo ($P = 0.0005$). Psychiatric status measured by psychiatric rating scales remained stable or improved from baseline to Week 6 for both groups, as shown by CFB in: PANSS scores for positive symptoms VBZ -0.6 vs placebo -1.0, negative symptoms VBZ 0.5 vs placebo -0.9, and general psychopathology VBZ -0.5 vs placebo -0.7, MADRS VBZ -1.5 vs placebo -0.2, CDSS VBZ -0.9 vs placebo -0.7, and YMRS VBZ -1.1 vs placebo -0.3. The percentage of subjects with suicidal ideation/behavior as measured by the C-SSRS for VBZ vs placebo was 5.9% vs 2.0% (screening) and 5.9% vs 0% (Weeks 2-8).
Discussion: Across psychiatric scales, there was no apparent increase in psychopathology, depression or suicidality with VBZ, and psychiatric status remained stable or improved in subjects with underlying schizophrenia, schizoaffective disorder, depression or bipolar disorder. Together with favorable efficacy findings, these results indicate that VBZ may be a promising therapy for TD.

S68. Safety, tolerability, and pharmacokinetics of TAK-063, a PDE10A inhibitor, after a single dose in healthy Japanese and non-Japanese subjects

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Background: TAK-063 is in clinical development for the treatment of schizophrenia. TAK-063 selectively inhibits phosphodiesterase 10A (PDE10A), which hydrolyzes both cyclic adenosine monophosphate and cyclic guanosine monophosphate. Current evidence suggests that inhibition of PDE10A may be beneficial in the treatment of schizophrenia by modulating, indirectly or directly, the effects of glutamatergic and dopaminergic systems. The objective was to characterize the safety, tolerability, and pharmacokinetics (PK) of TAK-063 following single oral dosing in healthy subjects.
Methods: This was a randomized, double-blind, placebo-controlled, single-dose study in healthy Japanese and non-Japanese subjects. Upon completion of inclusion and exclusion criteria, 84 subjects were enrolled in 6 cohorts ($n = 14$ per cohort) and randomized to TAK-063 or placebo with 11 subjects (i.e., 5 Japanese, 6 non-Japanese) in each cohort receiving a single dose of TAK-063 (3, 10, 30, 100, 300, or 1000 mg) and 3 subjects (i.e., 1 Japanese, 2 non-Japanese) receiving a matching placebo under fasted conditions. Subjects receiving 100 mg TAK-063 also received 100 mg TAK-063 under fed conditions after a washout period. Safety assessments included adverse event (AE) reporting, clinical laboratory tests, physical examination, electrocardiogram (ECG), vital signs, and suicidal assessments. Serial plasma and urine samples were collected for determination of TAK-063 and M-I metabolite concentrations. PK parameters were derived using noncompartmental methods.
Results: Administration of TAK-063 was generally safe and well tolerated with no serious AEs. The most common treatment-related AEs (TEAEs) under fasted conditions for all TAK-063 doses combined were somnolence, postural orthostatic tachycardia, orthostatic hypotension, nausea, vomiting, dizziness, and headache. Under fasted conditions, plasma concentrations of TAK-063 and M-I peaked approximately 3 to 4 hours postdose and subsequently declined ($T½ = 15$-25 hours), with renal elimination playing a minor role. Increases in exposure to TAK-063 and TAK-063 M-I were less than dose proportional. Under fed conditions, TAK-063 was more slowly absorbed and resulted in greater oral bioavailability of TAK-063 (up to 2-fold in Cmax and AUC values), relative to fasted conditions. No substantial differences were noted between Japanese and non-Japanese subjects in TEAE incidence or PK of TAK-063 and M-I.
Discussion: A single dose of TAK-063 (range 3-1000 mg) was well tolerated in Japanese and non-Japanese subjects. Somnolence was the most common AE and increased in frequency and intensity with increasing dose. Nonlinear PK was observed across the evaluated dose range for TAK-063; this is likely due to solubility-limited oral bioavailability, which was enhanced with the co-administration of food.

S69. Five-year follow-up of a randomized-controlled trial on 2-year vs. 3-year specialized early intervention for young patients presenting with first-episode psychosis

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Background: Literature has indicated superior efficacy of early intervention (EI) over standard care (SC) on illness outcome of first-episode psychosis (FEP). Our previous randomized-controlled trial (RCT) further demonstrated that FEP patients receiving an extended 1-year EI (i.e. 3 years) had better functional outcome than those with 2-year EI (Chang *et al*., 2015). Yet, whether beneficial effects of 3-year (vs. 2-year) EI could be sustained after service termination remains unknown.
Methods: This is a follow-up study of our previous RCT cohort aiming to compare clinical and functional outcomes between EI and SC groups 5 years after initial presentation for their FEP. Of the 160 patients from the initial cohort, 143 completed 5-year symptom and functional assessments, 7 refused evaluation, 4 died and 6 defaulted follow-up.
Results: No significant between-group (EI: $n = 76$; SC: $n = 67$) differences were observed in socio-demographics, premorbid adjustment, duration of untreated psychosis, and baseline symptom and functional levels. At 5-year follow-up, EI patients did not differ from SC counterparts in PANSS positive ($P = 0.58$) and negative symptom scores ($P = 0.94$), and CDSS total score ($P = 0.27$) for depression. There were no between-group differences in functional levels as measured

by SOFAS ($P = 0.19$) and RFS ($P = 0.30$). The two groups did not differ in relapse and admission rates. Nonetheless, EI group had significantly better subjective quality of life in mental health domain (by SF36; $P = 0.028$) than SC group.
Discussion: Our findings indicated that, although an extended 1-year (3-year) EI significantly improved clinical and functional outcomes in FEP patients at 3-year follow-up when compared to 2-year EI, these therapeutic gains could not be sustained at 5 years when the specialized service was terminated. Further research is warranted to determine an optimal duration of EI for psychosis.
References: Chang WC, Chan GHK, Jim OTT, Lau ESK, Hui CLM, Chan SKW, Lee EHM, Chen EYH. Optimal duration of an early intervention programme for first-episode psychosis: randomised controlled trial. British Journal of Psychiatry 2015; 206:492-500.

S70. Probabilistic reinforcement learning in patients with first-episode schizophrenia-spectrum disorder: preliminary results of a 1-year follow-up study

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Background: Substantial evidence indicates reinforcement learning (RL) deficits in schizophrenia patients. Most research has focused on patients with chronic illness. Relatively few studies have been conducted to examine RL in first-episode samples. There is a paucity of longitudinal data in the early course of illness. Our previous analysis on RL performance at baseline, using Go/NoGo paradigm (Waltz *et al.*, 2011), suggested impaired reward-driven learning in the presence of relatively intact punishment-driven learning in patients with first-episode schizophrenia-spectrum disorder. We aimed to investigate RL in this first-episode cohort 1 year after study intake.
Methods: This report is based on an ongoing prospective 1-year follow-up study examining probabilistic RL performance in patients with first-episode DSM-IV schizophrenia, schizoaffective disorder or schizophreniform disorder. The current analysis focused on cross-sectional comparison of RL performance on a computerized Go/NoGo task at 1-year follow-up between 26 patients and 28 matched healthy controls. A brief battery of cognitive assessments was re-administered to patients and controls at follow-up.
Results: There was no significant between-group difference in age, sex and educational level. Patients had lower overall cognitive function than controls. Repeated-measures analysis of variance (ANOVA) revealed main effects of group on accuracy rate ($F1,52 = 5.1$, $P = 0.03$; controls performing better than patients), block ($F2,104 = 87.8$, $P < 0.001$; performance improving over time), and valence ($F1,52 = 54.1$, $P < 0.001$; performance better with positive than negative stimuli) across training phase. No significant valence x block or group x valence interaction was observed. Concerning Go-response rates to stimuli in test/transfer phase, a two-way ANOVA showed no significant main effect of trial-type or group x trial-type interaction. We found no significant differences between patients and controls in rapid RL measures (win-stay and lose-shift scores at block 1 and across training phase) and overall Go-response rate (or Go-response bias).
Discussion: Contrary to our previous findings at baseline, we failed to observe any differential impairment between positive and negative RL. The current analysis also showed lack of Go-response bias and rapid learning deficits in patients, which, nonetheless, is consistent with data of our baseline investigation. Completion of 1-year follow-up assessment with a larger sample size will help provide a more definitive conclusion on the trajectory of RL in first-episode schizophrenia-spectrum disorder.
References: Waltz JA, Frank MJ, Wiecki TV, Gold JM. Altered probabilistic reinforcement learning and response biases in schizophrenia: behavioral evidence and neurocomputational modeling. Neuropsychology 2011;25:86-97.

S71. Testing differents domains of social cognition in the prediction of social functioning in patients with schizophrenia

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Background: Interest in social cognition is growing because it appears to be a key determinant of daily functioning in patients with schizophrenia. However, both social cognition and functional outcome are broad constructs covering multiple abilities. As no unifying model of social cognition has been described yet, there is no agreement on which domains or measures of social cognition may be the more relevant in order to be considered as putative predictors of functioning. This study aims to compare two specific domains of social cognition (Theory of Mind and affect processing) as possible predictors of social functioning in persons with schizophrenia.
Methods: 35 individuals diagnosed with schizophrenia and 29 controls completed the assessment of symptom severity (PANSS), neuropsychological status (MATRICS domains), social cognition (Penn Emotion Recognition Task ER-40, Reading the Mind in the Eyes Test, and The Hinting Task HT) and other functional measures (Social Scale Functioning, SFS). Data were analysed following a Hierarchical Regression analyses in a cross-sectional study.
Results: The regression model based on higher social cognition measures like Hinting Task and ER-40 is able to explain the larger part of the variance of social functioning (47%, R2 = 0. 47). Different model of prediction combining basic cognition and the domains appeared to be statistically significant but always being able to explain less variance than the combination of HT and ER-40). Eyes Reading test was not included in any valid model (t = -0.706; p 0.373).
Discussion: Scores on social cognitive tests like the Hinting task (HT) and Penn Emotion Recognition Test (ER-40) seem to be more related to social functioning than others, like the Reading the Mind in the Eyes Reading Test or basic neurocognition. Combination of measures of different levels of social cognition (Emotion Processing and Theory of Mind) may be the best approach in order to predict social functioning from social cognitive variables in patients with schizophrenia.

S72. Validation of the tablet-based brief assessment of cognition (BAC App) for assessment of cognition in schizophrenia

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Background: The Brief Assessment of Cognition in Schizophrenia (BACS) is a pen-and-paper cognitive assessment tool that has been used in hundreds of research studies and clinical trials, and has normative data available for generating age- and gender-corrected standardized scores. A tablet-based version of the BACS called the BAC App has been developed. This study compared performance on the BACS and the BAC App in patients with schizophrenia and healthy controls.
Methods: 48 patients with schizophrenia and 50 demographically matched healthy controls from three academic research centers were assessed with the BACS and the BAC App.
Results: In both groups, the distributions of standardized composite scores for the tablet-based BAC App and the pen-and-paper BACS were indistinguishable, and the between-methods mean differences were not statistically significant. The discrimination between patients and controls was similarly robust with the BAC App ($d = 1.34$) and the BACS ($d = 1.24$). The between-methods correlations for individual measures in patients were $r > 0.70$ except Token Motor ($r = 0.43$) and Tower of London ($r = 0.61$). In patients, performance between the test methods was not significantly different on any test except the Token Motor Test. When data from the Token Motor Test were removed, the between-methods correlation of composite scores improved to r = .88

(df = 48; $P < .001$) in healthy controls and r = .89 (df = 46; $P < .001$) in patients, consistent with the test-retest reliability of each measure.
Discussion: The tablet-based BAC App generates results consistent with the traditional pen-and-paper BACS. These data support the notion that the BAC App can now be used in clinical trials and clinical practice.

S73. To act as one while remaining two -- self-other distinction in children at risk for psychosis

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Background: In daily life people rarely act in social isolation. To ensure fluent and efficient social interaction people have to take into account the actions of others (i.e., self-other integration). At the same time people have to distinguish their own actions from those of others (i.e., self-other distinction). This is essential for regulating one's own behavior, develop a personal identity, or feel responsible for one's own behavior. Normally, the integration and distinction of self and other is a well-balanced process, occurring without much effort or conscious attention. However, not everyone is blessed with the ability to balance self-other distinction and integration. That is, people suffering from psychosis typically struggle to distinguish self and other. For example, some psychotic patients may feel that they are being controlled by others (e.g., delusions of control), while other patients may feel control over other people (e.g., delusions of grandiosity). Recent research suggests that such abnormalities in self-other processing are already present in early stages of psychosis and might even be predictive of psychosis onset in symptomatic and high risk individuals. This raises the question whether children at risk for developing psychosis also show difficulties in distinguishing self and other during social action coordination.
Methods: The extent to which people distinguish own and others' actions has been extensively examined by using the social Simon task. In this task, participants respond with right key presses to one of two stimuli (e.g., red or green dots) that appear at the left, middle, or right side of the computer screen. A hand on the left side of the screen responds to the other stimuli. This task requires people to distinguish own (right) and other's (left) actions in terms of action planning and execution. To the extent that participants distinguish their own 'right' actions from the other's 'left' actions, participants respond slower to stimuli that are spatially incongruent (e.g., presented to the left). This is also known as the social Simon effect. Fifty-four children (Mage = 16.09, SD = 2.29) of schizophrenia patients (SZ; $N = 17$), children of patients with bipolar depression (BD; $N = 20$), and children of healthy controls (HC; $N = 17$), performed this social Simon task.
Results: A repeated measures ANOVA with spatial congruency (incongruent, neutral, congruent) as within subjects variable and offspring group (SZ, BD, HC) as between subjects variable revealed a main effect of spatial congruency, $F(2,50) = 7.96$, $p = .001$, $\eta p2 = .24$, with faster reaction times for spatially congruent (M = 353.02, SD = 50.40) compared with spatially incongruent (M = 363.98, SD = 55.63) stimuli. This indicates that the children were capable of distinguishing own and others' actions. There were no main ($F(2,51) = 1.86$, $p = .17$, $\eta p2 = .07$) or interaction ($F(2,51) = .63$, $p = .54$, $\eta p2 = .02$) effects of the risk for psychosis.
Discussion: In line with previous research, we replicated the social Simon effect in children. In contrast to our expectations, this social Simon effect did not differ between children of healthy controls and children at high familial risk for developing psychosis. This suggests that children with a familial risk of developing psychosis risk are equally capable of using spatial information to distinguish own and others' actions. Future research would have to reveal whether children at high risk are also capable of using social information (e.g., identity, skin color) to distinguish own and others actions and how this affects their social relationships.

S74. Analysis of AKT1 and cannabis moderation effects on psychotic experiences and cognitive performance in healthy subjects

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Background: Genes such as AKT1 and environmental factors such as cannabis use have been associated with both an altered cognitive performance and the risk for developing psychotic experiences (PE). It has been suggested that deterioration of cognition may precede the first episode of psychosis (Cannon *et al*, 2000). Moreover, psychotic experiences (PE) have been described as relatively frequent in subjects from the general population assuming the existence of a continuum of risk between healthy subjects and psychotic patients (Verdoux *et al*, 2002).
Our aim was to analyse the effect of life time cannabis use, AKT1 variability and their interaction on the development of PEs and also on cognitive performance.
Methods: Psychotic experiences (CAPE), neurocognitive performance (CPT-IP, WMS-R, WCST), cannabis use and SNPs at the AKT1 gene (rs2494732 and rs1130233) were examined in a sample of 445 Caucasian subjects from the general population.
Results: A significant relationship between cannabis use and higher CAPE negative scores was observed ($P = 0.007$). No main effect of AKT1 SNPs or AKT1-cannabis interaction was found on any of the two CAPE dimensions. Cannabis use was not associated with any neurocognitive measure. A main effect of AKT1 was found on CPT d' shapes (rs1130233: $P = 0.001$, rs2494732 $P = 0.005$). Individuals with the genotype AA-rs1130233 and CC- rs2494732 presented better scores on this task.
Discussion: The results for cannabis consume effect on psychosis liability are consistent with those found in other studies, which have shown an association between the exposure to this environmental risk factor and both psychotic disorders and PEs (Henquet *et al*, 2005; Moore *et al*, 2007; Hides *et al*, 2009). In reference to cognitive performance, the AKT1 moderation of cannabis-induced cognitive alterations has been previously reported in psychotic disorders (van Winkel *et al*, 2011). Our results add to this evidence by showing the AKT1 effects on measures of sustained attention independently of cannabis use in healthy subjects.
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S75. Are cognitive functions deteriorating during the first 5 years after an early-onset psychosis?

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Background: Early onset types of schizophrenia and bipolar disorder have a low prevalence ranged between 0.1 and 3%. Studies have shown that child and adolescent forms of these disorders are more severe and are related with neurodevelopmental abnormalities.
Regarding cognitive deficits, neuropsychological impairments have been considered as core traits of both diseases and are present from the early stages of the disease to the more chronic states. Follow-up studies in early onset schizophrenia (EOS) have shown that in children and adolescent who develop schizophrenia, cognitive deficits are

stable and there are some areas such as verbal memory or attention were a decrease in performance can be observed (Frangou *et al* 2013). Follow-up studies including cognition in pediatric bipolar disorder are very scarce (PBD). Their results showed that children and adolescent improved in some cognitive areas such as attention, working memory, visual memory and visuospatial perception. There is conflicting evidence between these studies in terms of executive functions and verbal memory where one study found an important improvement (Lera-Miguel *et al* 2015) and other didn't (Pavuluri *et al* 2009). To our knowledge there are no longitudinal studies where early onset schizophrenia and pediatric bipolar samples were compared. The objectives of this study were: to study cognitive performance at five-year follow-up in a sample of first episode psychosis (FEP) and to analyze different patterns of evolution depending on the diagnoses.
Methods: This is part of the child and adolescent first episode psychosis study, CAFEPS. At baseline, the sample included 107 patients with a first episode psychosis and 98 healthy controls matched by age, gender and socio-economic status. At two year follow-up 75 FEP patients and 79 HC were evaluated. Finally at five years follow-up a total of 73 FEP and 63 HC were assessed. The cognitive assessment included the following cognitive areas: global attention, working memory, learning and memory and executive functions.
To perform the statistical analyses all direct scores were converted to z scores (which have a mean of 0 and a standard deviation of 1) based on the healthy control group performance at baseline. Z scores were calculated in such a way that higher scores always reflect better performance. To test if there were significant differences at longitudinal level a mixed model analysis was conducted. In the first step, Total PANSS score, age, gender, antipsychotic medication, the duration of untreated psychosis, and the diagnoses were included in the model. In the second step, those variables that were not significant in the model were excluded and the mixed model was repeated.
Results: All groups improved over time in attention ($Z = 4.636$; $P < 0.001$) and executive function ($Z = 5.575$; $P < 0.001$). Working memory performance remained stable over time. Regarding significant differences between groups, both FEP groups (schizophrenia and bipolar disorder) performed worse than the HC group in all cognitive domains: attention (EOS: $Z = -4.289$; $P < 0.001$; PBD: $Z = -2.814$; $P = 0.004$), working memory (EOS: $Z = -2.68$; $P = 0.007$; PBD: $Z = -2.173$; $P = 0.024$), verbal memory (EOS: $Z = -5.606$; $P < 0.001$; PBD: $Z = -4.97$; $P < 0.001$), and executive functions (EOS: $Z = -7.951$; $P < 0.001$; PBD: $Z = -5.993$; $P < 0.001$),. No significant differences were found between the first episode schizophrenia and the bipolar disorder group in any cognitive domain.
Discussion: EOS and PBD improved over time in attention and executive functions. EOS and PBD showed lower scores than HC in all cognitive domains. Moreover, both groups shared cognitive difficulties.

S76. A comparison of neurocognitive batteries after single dose modafinil in early schizophrenia and health

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Background: Modafinil induces moderately consistent neurocognitive improvements in healthy volunteers, sometimes slowing performance while improving it. Early schizophrenia patients show some similar effects, making it a potential cognitive enhancer. Benefits are less clear in chronic schizophrenia. Drug effects have not been compared directly in health and illness, and studies used the CANTAB battery not the FDA-accepted MATRICS Consensus Cognitive Battery (MCCB). We compared modafinil's effect on performance on the CANTAB and MCCB in early schizophrenia sufferers and healthy volunteers, hypothesizing that modafinil would enhance strategy, working memory, set shifting and social cognition in both groups.
Methods: 46 patients from Manchester Mental Health & Social Care NHS Trust and South London & Maudsley NHS Foundation Trust, with DSM-5 schizophrenia, schizophreniform or schizo-affective disorder, took 200 mg modafinil or placebo in a double-blind cross-over design with order allocated by minimisation, stratified by smoking habit and site. 2 hours post dose they started the CANTAB and MCCB neurocognitive batteries. 26 age-matched Healthy Volunteers (HVs) from Manchester followed the same protocol. Uncorrected *P* values were derived using pkcross in STATA 12.0 to test modafinil's specific effect in each group and mixed effects models to test differences between groups in modafinil's effects. Effect sizes (Glass' delta) were calculated with placebo SD.
Results: In HVs modafinil improved MCCB social cognition (d0.16, p0.003) while MCCB composite score changed non-significantly (d0.15, p0.074). No MCCB domain significantly improved in schizophrenia but there was a difference from HVs in visual learning (p0.033): HVs improved (d0.35, p0.087) while patients worsened (d-0.21, p0.108).
HVs improved on some CANTAB measures of rapid visual processing (RVP_A d0.4, p0.035 & probability of a hit d0.41, p0.029) and immediate verbal recall (d0.40, p0.045) after modafinil. Modafinil slowed patients' completion of a strategy task (Stockings of Cambridge median latency d0.50, p0.038) but improved a measure of Paired Associate Learning (6 shapes: d0.19, p0.023). CANTAB yielded no significant differences between HVs and patients.
Discussion: Like other studies in the field sample size and uncorrected *P* values provide limitations but these results were still comparable to some past data, despite modafinil's effects differing from most of our specific predictions. Some CANTAB tasks appeared more sensitive to modafinil's effects but did not reveal significant differences between groups. The only significant differences between HVs and patients was in MCCB visual learning, with patients performing worse than HVs after treatment. This is difficult to evaluate in the absence of such differences on the CANTAB. MCCB identified significant improvements in HVs' rather than patients' social cognition (though the difference was not significant) but CANTAB contains no such task. Modafinil enhanced specific aspects of cognition in both health and early schizophrenia but each battery performed differently.

S77. Theory of mind functioning is no longer a natural process in prodromal psychosis: a model of social cognition compensated by neurocognition

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Background: Neurocognitive and social cognitive deficits have been observed in patients with psychosis and in those with attenuated psychosis syndrome (APS). However, it is unclear how this decline contributes to the progression of psychosis. We hypothesized that the model of cognitive interaction is altered in individuals with APS compared to healthy controls. Specifically, we hypothesized that Theory of Mind (ToM) deficits among APS subjects would increase their dependence on neurocognition when interpreting others' mental states. Moreover, we predicted that the combination index of ToM and neurocognition would improve the prediction of conversion to psychosis in those at-risk.
Methods: A sample of 83 APS individuals, identified through the Structured Interview for Prodromal Syndromes [SIPS], and 90 healthy controls (HC; matched on age, gender, and education) were assessed by comprehensive cognitive tests (MATRICS Consensus Cognitive Battery; Faux-Pas Task, FP; Reading-Mind-in-Eyes Tasks, RMET).The cohort also completed a one-year follow-up. The relationship between ToM performance and each domain of MCCB scores were characterized using linear trend lines. A set of regression lines were drawn to highlight the trend of APS subjects compared to HC subjects. A Structural Equation Modeling (SEM) analysis was conducted to estimate the effects of neurocognition on ToM functioning in 2 datasets (the APS and HC groups).
Results: A comparison of cognitive performance revealed significantly higher scores in the HC group compared to the APS group in all domains. In the APS group, ToM was associated with an apparent increase in neurocognition, but this trend was not evident in the HC group. In the APS cohort, 78 subjects (94.0%) completed the follow-up

at 1 year. Of these individuals, 20 subjects (25.6%) transitioned to a psychotic disorder over the course of follow-up. Exploratory binary logistic regression analysis identified the interaction effects in neurocognition and ToM sub-domains (Faux Pas-No Faux Pas Story test × MCCB-visual learning [the Revised Brief Visuospatial Memory Test]) and total scores (FP × MCCB) as significant predictors of conversion. Using the new index of combined neurocognition and ToM scores, the sensitivity for predicting psychosis-proneness was 75% and the specificity was 72%. A structural equation modeling analysis demonstrated that the paths from neurocognition to ToM were all statistically significant in the APS dataset. However, in the HC dataset, the paths from neurocognition to RMET were not significant. *Discussion*: Our data suggest that APS subjects likely infer others' intentions using compensation by neurocognition. A composite index of neurocognition and ToM could improve the validity of predictive models of future conversion to psychosis, which may have clinical implications for early identification of those at-risk. Additionally, these results are also very important for combined ToM and neurocognitive rehabilitation strategies, which could be a more effective intervention for subjects in the attenuated and pre-onset stages of psychosis.

S78. Improvement in depressive symptoms and functioning in schizophrenia: a treatment study

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Background: Depressive symptoms are common in schizophrenia, and have been linked to impairment in functioning. However, cross-sectional studies have found quite small relationships between depression and functioning. Longitudinal and treatment studies such as the present one are required to clarify this issue. The objective of this post-hoc analysis was to investigate the effects of improvement in depressive symptoms on cognitive performance and functional capacity in patients followed for up to 6 months after acute phase treatment.
Methods: A 6-week randomized, placebo- and active-controlled trial of lurasidone in patients with an acute exacerbation of schizophrenia, followed by a 6-month, double-blind, continuation study was conducted. Depressive symptoms, cognitive performance, and functional capacity were assessed with the Montgomery-Asberg Depression Rating Scale (MADRS), CogState computerized cognitive battery, and the UPSA-B, respectively.
Results: Depressive symptoms improved in the lurasidone 80 mg/d and 160 mg/d groups compared to the placebo group at week-6 (LOCF) (both $P < 0.001$). Similar results were observed in the quetiapine XR 600 mg/d group ($P < 0.001$). Reduction in depressive symptoms mediated an improvement in functional capacity during the initial, 6-week, randomized, trial for both lurasidone and quetiapine XR-treated patients ($P < 0.001$). At month-6 of the double-blind, continuation study, reduced depressive symptom severity was significantly associated with improved neurocognitive performance and increased functional capacity (all $P < 0.05$) across the treatment groups. Lurasidone demonstrated significant improvement in neurocognitive performance (vs. quetiapine XR), both before (Cohen's $d = 0.49$, $P < 0.05$) and after adjustment for reduction in depressive symptoms (Cohen's $d = 0.45$, $P < 0.05$).
Discussion: These findings suggest that there are significant mediating relationships between reduction in depressive symptoms and improvement in both cognitive performance and functional capacity in patients with schizophrenia. These relationships were found across both acute and continuation study phases.

S79. Social cognition over time in individuals at clinical high risk for psychosis: findings from the NAPLS-2 cohort

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Background: The NIMH Workshop of Social Cognition in Schizophrenia defines social cognition as a function that involves the perception, interpretation and processing of information that underlies social interactions. Deficits in social cognition are well evidenced in schizophrenia, both in the established illness and prior to the illness onset. Compared to healthy controls (HC), individuals at clinical risk of psychosis (CHR) are said to show deficits in social cognition similar to those observed in patients experiencing the first episode of psychosis (FEP). These deficits have been observed in several domains of social cognition, such as theory of mind (ToM), emotion recognition and social perception. In the current study, the aim was to examine: firstly, the stability of three domains of social cognition (ToM, social perception and facial emotion recognition) over time; secondly, the longitudinal association between social cognition and clinical symptoms; and thirdly, the role of social cognition in the development of psychosis in the CHR sample.
Methods: Participants were recruited as part of the multi-site NIMH funded North American Prodrome Longitudinal Study (NAPLS 2) that consisted of 764 CHR individuals and 280 HC recruited across the eight NAPLS 2 sites. All CHR participants were required to meet the Criteria of Prodromal Syndromes (COPS) using the Structured Interview for Psychosis-risk Syndrome (SIPS).
Results: All analyses were performed using IBM SPSS version 23 and SAS version 9.2. Six hundred and seventy-five CHR participants (389 males and 286 females) with a mean age $M = 18.5$, $SD = 4.25$ years and 280 HC (136 males and 128 females) with a mean age of $M = 19.7$, $SD = 4.72$ years completed four tests of social cognition at three different time points (baseline, 1 year and 2 years) as part of their participation in the NAPLS 2 study. Participants in the HC group were significantly older than those in the CHR group (19.7 vs. 18.5 years respectively), and had significantly more years of education (12.7 vs. 11.3 respectively). The majority of all study participants were Caucasian (62.6% CHR and 59.6% HCs), born in USA or Canada (92.0% CHR and 90.4% HC), single (95.0% CHR and 95.0% HCs), students (82.5% CHR and 81.1% HCs) and currently not employed (75.0% CHR and 54.0% HCs). Of those 675 CHR participants, 86 had transitioned to psychosis during the two year study period. Social cognition was not associated with attenuated positive symptoms at any time point in the study. Similarly, those CHR individuals who developed a psychotic disorder during the course of the study did not differ on any of the measures of social cognition at baseline from those who did not develop psychosis. However, the CHR group performed poorer on all tests of social cognition across all time points compared to HC. Furthermore, performance on all but one social cognitive test improved over time in both groups.
Discussion: The current longitudinal study demonstrated mild to moderate, but persistent ToM and social perception impairments in those at CHR for psychosis compared to age and gender matched healthy individuals. Future research would benefit from exploring social cognitive heterogeneity and a possible associations between distinct social cognitive profiles and functional and cognitive outcomes in CHR.

S80. Dysexecutive impairment in first-episode of schizophrenia

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Background: Deficit in executive functions may be central to schizophrenia and it is present in adolescents at risk of developing

the disease [ultra-high risk], in patients with a first outbreak of schizophrenia, and apparently in their first-degree relatives. Mild to moderate impairments on executive functions tests have particularly been described in patients with a first-episode of schizophrenia. In aged schizophrenic patients, a more severe cognitive impairment has been described that mainly involves executive functions. Executive dysfunction has been significantly associated with psychosocial impairment in this disease. Despite its importance, there are still few studies that analyze the disexecutive behaviors' in FES.
We compared executive functions and disexecutive behaviors' of a group of first-episode schizophrenia [FES] patients and a group of healthy participants using the Modified Six Elements Test [MSET], the Modified Wisconsin Card Sorting Test [MWCST], the Frontal Assessment Battery [FAB], the Questionnaire which probes symptoms of Dysexecutive syndrome [DEX] and the Behavioral Dysexecutive Syndrome Inventory [BDSI].
Methods: We evaluated 22 stable FES from 17 to 29 years of age. They met the clinical and DSM-IV-TR criteria for schizophrenia [SCID-I]. FES patients were rated on the Positive and Negative Syndrome Scales [PANSS]. Their scores on the Positive Syndrome Scale ranged from 7 to 13 [mean = 8.5 ± 2.0] and on the Negative Syndrome Scale ranged from 7 to 28 [mean = 16.8 ± 6.2], corresponding to mild schizophrenia. During the evaluations of our study, FES took a single atypical antipsychotic medication. Computed cerebral tomography of 20 patients showed no brain abnormalities. Every participant verbally confirmed that they correctly understood the procedure and the tasks. 20 healthy controls, matched with FES by age, gender, and years of education, were also included in the study. For both FES and control, exclusion criteria were: [a] brain disease other than schizophrenia, [b] mental retardation, [c] substance abuse, or [d] electroconvulsive therapy. The study was approved by the regional ethics committee for biomedical research of the University of Chile, Faculty of Medicine. Executive functions were estimated using MSET, MWCST, and FAB. Dysexecutive behaviors' were estimated using DEX and BDSI.
Results: We found that the control group demonstrated significantly greater Executive functions efficiency than FES patients in the MSET, MWCST, and FAB tests. Patient group demonstrated significantly greater disexecutive behaviours than FES patients in the DEX and BDSI questionnaires.
Discussion: Schizophrenics patients may demonstrate the most significant alterations in executive functions, a first-order cognitive process. This may consequently lead to cognitive disorders in second-order functions, memory, or social language. Executive dysfunction is manifested in dysexecutive behaviors, which may account for most problems patients face in their daily lives. In our research, FES patients are impaired in disexecutive behaviors' suggesting that executive deficit may be a primary impairment during the progression of the disease. Better comprehension of dysexecutive behaviors can help us understand the social adjustment disorders of schizophrenia. Further studies are needed to explore the evolution of dysexecutive disorders over the course of the disease, and its response to pharmacological and non-pharmacological treatments. It is also important to investigate the longitudinal course of executive dysfunction in schizophrenia because this dysfunction is already present in children who later develop schizophrenia, and maturation of executive functions extends into young adulthood.

S81. Meta-analysis of cognitive performance in drug-naïve patients with schizophrenia

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Background: Cognitive deficits represent a significant characteristic of schizophrenia. However, a majority of the clinical studies have been conducted in antipsychotic drug treated patients. Thus, it remains unclear if significant cognitive impairments exist in the absence of medication. This is the first meta-analysis of cognitive findings in drug-naïve patients with schizophrenia.
Methods: Cognitive data from 23 studies encompassing 1106 patients and 1385 controls published from 1992 to 2013 were included. Tests were to a large extent ordered in cognitive domains according to the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) battery. Analysis was performed with STATA using the random-effects model and heterogeneity as well as Egger's publication bias was assessed.
Results: Overall the results show that patients performed worse than healthy controls in all cognitive domains with medium to large effect sizes. Verbal memory, speed of processing and working memory were three of the domains with the greatest impairments. The pattern of results is in line with previous meta-analytic findings in antipsychotic treated patients.
Discussion: The present meta-analysis confirms the existence of significant cognitive impairments at the early stage of the illness in the absence of antipsychotic medication.

S82. Comprehensive assessment of auditory perception and its relation to impaired emotion recognition in schizophrenia

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Background: Basic perceptual processes, such as auditory pitch processing, are impaired in schizophrenia and may explain key social deficits such as the ability to identify emotions in other people. These auditory deficits may be closely linked to the neural circuits relevant for the development of psychotic symptoms and thus may be useful predictors of psychosis onset and promising therapeutic targets. However, previous work in this area has focused on a relatively narrow assessment of auditory deficits and a lack of information regarding the relationship between basic auditory processing deficits and impairments in emotional processing and cognition.
Methods: We have assessed 83 patients with schizophrenia and 73 healthy controls between the ages of 18 and 60 on a comprehensive battery of tasks spanning the four empirically derived domains of auditory function. We explored group differences across the battery of basic auditory tasks using between-groups t-tests. We also explored the relationship between basic auditory processing and auditory emotion recognition within the patient group using correlational analysis.
Results: We observed significant group differences in the ability to identify emotion in vocal samples and in several basic auditory skills, including 3 of the 4 domains of auditory function. Performance on all of the basic auditory tests correlated with auditory emotion recognition at the $P < .01$ level in the patient group, with 9 out of 13 tests correlating with emotion recognition at $r = .40$ or greater. Partial correlational analysis suggested that after controlling for cognition, the basic auditory skills that were most robustly correlated with emotion recognition were sinusoidal amplitude modulation detection at 60 Hz. ($pr = -.36$, $P < .001$), formant discrimination ($pr = .27$, $P < .05$) and embedded tone detection ($pr = .27$, $P < .05$).
Discussion: Previous research has indicated a correlation between basic pitch processing deficits and impairments in auditory emotion recognition in individuals with schizophrenia. Our results build upon this finding and suggest that patients exhibit broad deficits in basic auditory processing that are correlated with impaired recognition of emotion in voice. Of particular note, tests that require frequency processing in the range at which the auditory system is able to phase lock to the stimulus waveform or envelope periodicity were amongst the most impaired auditory skills in the patients and the most highly correlated with emotion recognition. These results suggest that impaired phase-locking in auditory brain structures in individuals with schizophrenia may be associated with difficulty identifying emotion from the vocal properties of speech.

S83. Cognitive remediation and occupational outcome in schizophrenia spectrum disorders: a 2 year follow-up study

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Background: Neurocognitive impairment is prominent in schizophrenia, significantly related to poor occupational outcomes and a

predictor of poor engagement in vocational rehabilitation programs. Supported employment (SE) and Individual Placement and Support (IPS) are the principle evidence-based approaches in vocational rehabilitation for people with severe mental disorders with beneficial short- and long-term effects. However, despite superior outcomes regarding competitive employment rates, people with schizophrenia still face numerous occupational challenges and as many experience unwanted job discontinuations. Hence, augmenting SE/IPS programs in order to optimize occupational outcomes may be advantageous. The strong relationship between neurocognition and functional outcome underlines the importance of targeting neurocognitive impairments through interventions such as cognitive remediation (CR) as a means to improve occupational functioning. In the present study, we aimed to explore the long-term effects of CR combined with vocational rehabilitation on neurocognition and occupational functioning in participants with broad schizophrenia spectrum disorders using cognitive behavioral therapy (CBT) focused vocational rehabilitation as a comparison.
Methods: The current study is part of the Job management program study (JUMP), a multisite vocational rehabilitation program for adults with psychotic disorders. JUMP is a collaborative effort between health and welfare services. Participants were offered a 10 month extensive vocational rehabilitation program consisting of competitive or sheltered work, close collaboration between health and vocational services, employers and employment specialists in addition to either CR or CBT. One hundred and thirty one persons with schizophrenia spectrum disorders were assigned to receive either CR or CBT combined with vocational rehabilitation. Neurocognition (measured with the MATRICS Consensus Cognitive Battery (MCCB)), occupational status and number of hours worked were assessed at baseline, end of treatment and after 2 years (follow-up). Linear mixed models were conducted for the MCCB domains to estimate change over time. Logistic and hierarchical multiple regression analyses were employed to examine predictors of occupational status and number of hours worked.
Results: Neurocognition improved significantly from baseline to follow up in the CR group on verbal learning ($F = 4.9$, $p = .03$). There was also a trend for problem solving ($F = 2.89$, $p = .08$). There were no significant improvements in the CBT group.
None of the baseline or posttreatment neurocognitive domains predicted occupational status at follow up in either of the two groups. However, the change in the neurocognitive composite score between baseline and posttreatment was a significant predictor of hours worked at follow up in the CR-group ($t = 3.18$, $p = .005$). In the CBT group, education was the only significant predictor ($t = 3.99$, $p = .001$).
Discussion: Participants improved on several neurocognitive domains in the CR group, however only significantly on verbal learning. There were also some improvements in the CBT group, none however significant. Cognitive remediation seems to generalize to occupational outcome, not with regard to occupational status but to number of hours worked. Additional analyses of subgroups will help further elaborate these findings in order to identify characteristics, such as level of neurocognitive impairment, learning potential etc., of those who might benefit more from either CR or CBT in this vocational rehabilitation program.

S84. Improvement of executive functions using the occupational goal intervention method in patients with treatment -resistant schizophrenia: results of the follow-up phase

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Background: Executive Functions (EF) are complex cognitive processes comprising various dimensions such as initiative, planning, cognitive flexibility and decision-making. EF are highly compromised in patients with schizophrenia. The Occupational Goal Intervention is a method designed to improve EF and was proven to be effective in patients less severe cases of schizophrenia. However OGI was never tested in patients with Treatment Resistance Schizophrenia (TRS). The aim this study was to test the efficacy of EF in patients with TRS in comparison with neutral handicraft activities by a randomized controlled trial in three phases: baseline, endpoint and follow-up.
Methods: A randomized controlled trial, single blinded 54 participants initially, ages 18-55, were randomized to EG or CG. The patients were evaluated before (T0) and after treatment (T1) and after 6 month follow-up without intervention (T2). Thirty- nine patients completed the study until the moment. To measure EF we used the Behavioral Assessment of Dysexecutive Syndrome (BADS) as primary outcome variable. As secondary outcome we used the Direct Assessment of Functional Status (DAFS-BR), which measures functional aspects and the Independent Living Skills Survey (ILSS-BR) which measures the occupational performance of patients in basic and instrumental activities of daily living. Other cognitive functions were measured by a standard neuropsychological battery. Both groups realized 30 sessions over a period 14-15 weeks and follow-up. Mixed Model Analysis and Effect Sizes (Cohen's d) were used to evaluate efficacy.
Results: Groups showed no differences at baseline in terms of demographic variables and degree of severity. At T1 the OGI showed to be more effective improving EF as measured by the BADS Total $d = 0.73$, DAFS Total $d = 0.58$ and ILSS- BR $d = 1.12$. At T2 we obtained the following results: BADS total $d = 0.69$; DAFS Total $d = 0.40$ and ILSS–BR $d = 1.19$. Mixed Model Analysis showed improvement (time x group interaction) only with the ILSS-BR Inventory. We found no improvement in terms of neuropsychological variables in both analyses.
Discussion: During the intervention the OGI method showed to be effective improving EF in patients with TRS, with medium to high effect sizes as measured by the BADS, DAFS scales. Families' perception of the improvement was also an important aspect, as observed by the high effect sizes of the ILSS-BR Inventory. However, after the 6 months follow-up period without treatment, such improvement was lost, despite the fact that families continue to observe an improvement. The OGI method showed no impact over neuropsychological functions as measured by standard neuropsychological tests.

S85. Cognitive impairment as a vulnerability marker for psychosis: the role of childhood trauma

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Background: Cognitive impairment is increasingly recognized as a prominent vulnerability factor for psychosis. Childhood trauma deserves attention in this context, as it is highly prevalent in patients and is associated with cognitive dysfunctioning. We investigated whether increased exposure to early traumas can explain the reduced cognitive performance associated with a vulnerability to experience psychotic symptoms, in non-clinical adults with and without psychotic experiences ($N = 202$), to prevent disease-related bias.
Methods: We included 101 non-clinical individuals with psychotic experiences (auditory verbal hallucinations) and 101 controls. Participants did not meet criteria for DSM-IV diagnosis. Neuropsychological assessment included several cognitive domains, childhood trauma was rated using the Childhood Trauma Questionnaire Short Form (CTQ-SF).
Correlations between CTQ-SF score and cognitive test scores were calculated using non-parametric Spearman's rho. To address the effect of childhood trauma, we conducted step-wise regression analyses for those cognitive measures that were significantly lowered in individuals with psychotic experiences in our previous study. Group was included as a predictor in the first step, CTQ-SF score was added in the second step for the following outcome measures: verbal inhibition, working memory, verbal abilities, and verbal intelligence.
Results: Individuals with non-clinical psychotic symptoms reported more childhood trauma as indicated by the CTQ-SF ($M = 45.1$, $SD = 15.7$), compared to controls ($M = 36.4$, $SD = 8.6$), $t = 23.7$, $P < .001$. Associations between cognitive performance and CTQ-SF score were corrected for multiple analyses, using Bonferroni correction ($p < .0036$). Childhood trauma was related to reduced verbal inhibition (Stroop interference: $\rho = .210$, $P = .003$). Childhood trauma

was unrelated to other cognitive measures (ρ -.167 to.110, all $P > .0036$).
Childhood trauma fully explained the previously found association between reduced verbal inhibition and non-clinical psychotic features, as group was no longer a significant predictor for Stroop interference when adding CTQ-SF score. Childhood trauma also accounted for the association between non-clinical psychotic symptoms and reduced working memory. Childhood trauma was of no explanatory value with regard to the association between psychotic features and reduced verbal abilities, nor intelligence.
Discussion: Our results indicate that a history of childhood trauma is an underlying factor for the association between cognitive impairment and psychotic experiences, especially executive functioning and working memory. These cognitive domains are largely supported by the prefrontal cortex, which are especially vulnerable to stress. Our results are not only relevant for the field of schizophrenia and related psychotic disorders, as multiple psychiatric disorders are characterized by impairments in executive functioning and working memory as well as increased exposure to trauma, including depression, post-traumatic stress disorder, and bipolar disorder. In these conditions, the mechanisms may be similar, which implies that prevention of childhood trauma could be a mean to forestall severe dysfunction from cognitive impairments in psychiatric disorders.
Our results imply that childhood trauma increases the vulnerability for psychotic symptoms later in life, by showing its potential impact on executive functioning and working memory performance. We emphasize the need for future studies to establish whether early cognitive dysfunction constitutes an independent general vulnerability marker for psychosis, or if it (partly) results from the neurobiological consequences of trauma early in life.

S86. Emotional intelligence and non-social cognition in schizophrenia and bipolar-I-disorder

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Background: The different patterns of Emotional Intelligence (EI) deficits in schizophrenia and bipolar disorder are not yet well understood. This study compares EI levels among these groups and highlights the potential impact of non-social cognition on EI.
Methods: 58 schizophrenia and 60 bipolar outpatients were investigated using the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) and the Brief Assessment of Cognition in Schizophrenia (BACS). Analyses of covariance were performed with adjustment for the BACS composite score.
Results: Compared to bipolar subjects, schizophrenia patients showed significantly lower levels in both EI and non-social cognition. After adjustment for the BACS composite score, the difference in EI was lost. The mediation analysis revealed that differences between schizophrenia and bipolar patients in strategic EI are almost fully attributable to the mediating effect of non-social cognition.
Discussion: Our findings suggest that in both schizophrenia and bipolar patients EI is strongly influenced by non-social cognitive functioning. This has to be taken into account when interpreting MSCEIT data in comparative studies in serious mental illness and emphasizes the importance of cognitive remediation.

S87. The cognitive underpinnings of multitasking of daily life activities in persons diagnosed with schizophrenia: validation of a new model

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Background: Difficulties in everyday life activities are core characteristics of persons diagnosed with schizophrenia and in particular for complex activities and those involving multitasking abilities (Semkovska *et al.*, 2004; Laloyaux *et al.*, 2014), such as preparing a meal, doing the shopping or maintaining a professional activity. These multitasking activities share certain characteristics: the person has to (1) carry out and alternate between different tasks that vary in terms of priority, difficulty and duration; (2) define the tasks' targets; and (3) deal with unexpected problems during the realization of these tasks (Burgess, 2000). However, typical cognitive tests are not suitable to assess multitasking abilities as it is a separate cognitive function (Burgess *et al.*, 2009). Moreover, at present, patients' multitasking abilities and the cognitive underpinnings of multitasking have not been adequately examined in the literature. In order to do so, we recently developed a computerized real-life activity task designed to take into account the complex multitasking nature of certain everyday life activities in which participants are required to prepare a room for a meeting – the Computerized Meeting Preparation Task (CMPT). Using this task, the aim of the present study was to evaluate multitasking abilities in schizophrenia and to create and validate a new cognitive model.
Methods: Fifty-seven individuals diagnosed with schizophrenia and 39 matched healthy controls completed the CMPT. During the CMPT, participants find themselves in a virtual room that they have to prepare for a meeting while also respecting a list of instructions (e.g. the correct placement of the guests and required objects), dealing with interruptions (e.g. a phone call), solving problems (e.g. required objects that are missing) and remembering prospective memory instructions (e.g. give an object to an avatar). Patients were also evaluated with an extensive battery of standard cognitive tests.
Results: Results demonstrated that performance on the CMPT significantly differentiated patients and healthy controls in the total time to complete the task, the initiation measure, following the instructions, number of forgotten objects, planning efficiency, control of actions, and ability to deal with distractors. Based on these results, a cognitive model of multitasking abilities was also created (Structural Equation Modeling), indicating that multitasking abilities rely on the coordination of five different cognitive domains: retrospective memory, energization (i.e. process related to initiation and sustaining a response), planning, flexibility and prospective memory. Finally, a double dissociation was observed in which some patients were found to present impaired performances on the CMPT but preserved performance on standard cognitive measures, whilst others showed the opposite profile.
Discussion: In this study, we evaluated the performance of schizophrenia patients on a novel computerized task involving the multitasking nature of real world activities. The results suggest that the CMPT possesses good sensitivity. Moreover, a new cognitive model of multitasking abilities was created and validated that may stimulate both research and clinical practice. Finally, we found evidence of a double dissociation between multitasking abilities and typical cognitive performance measures, suggesting that multitasking abilities rely on cognitive functions that are not assessed with standard cognitive tests. Because multitasking is a key characteristic of many everyday life activities, these results suggest that adding measures of multitasking abilities should aid prediction of everyday functioning.

S88. Cognitive architecture of individuals at risk to psychosis: findings from lyriks

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Background: Cognitive deficits are a key feature of schizophrenia and multiple reviews have confirmed the role of cognition as a risk factor for schizophrenia and psychotic illnesses. However, little is known about the psychometric architecture and longitudinal trajectory of cognition in individuals at risk for psychosis. Elucidating the longitudinal cognitive architecture of individuals at risk will facilitate research on early clinical identification and intervention.
Methods: 557 participants were included in the current study. All participants were assessed clinically with the CAARMS structured interview, and participants were assigned to either the healthy control or UHR groups. There were 384 healthy controls, 154 UHR subjects

and 17 UHR converters to psychosis. Analysis was also conducted using the UHR Remitter ($N = 84$) and UHR Non-Remitter ($N = 89$) categorization. Participants with neurological disorders or injuries, colour blindness, or current substance abuse were excluded. A cognitive battery that included the Brief Assessment of Cognition in Schizophrenia (BACS), CPT-IP, WMS-III Spatial Span, WASI Vocabulary, High-Risk Social Challenge (HiSoC) task, Snakes in the Grass, Perceptual Closure, and Babble Task were administered to all participants over 24 months with 6 monthly follow ups. Cognitive trajectories, baseline prediction of group membership and cognitive architecture were examined. Cognitive trajectory differences across groups (linear mixed modelling), prediction of group membership with baseline cognition (ordinal logistic regression) and the covariance structure for candidate tasks (factor analysis) were investigated in the current sample.
Results: I) Cognitive tests that showed significant longitudinal group x time interaction were further examined. Fluency, BACS Symbol Coding, Snakes in the Grass, and CPT-IP showed significant longitudinal improvements over time for the HC vs UHR vs UHR-Psychosis model while Verbal Memory, Snakes in the Grass and Fluency improved for the HC vs Remitter vs Non Remitter model. Group interaction effects appeared to be driven by baseline differences. II) Ordinal logistic regression revealed that the BACS symbol coding was most discriminatory across groups, followed by HISOC, CPT-IP and Snakes in the Grass. This was true using either the HC vs UHR vs UHR-Psychosis or HC vs Remitter vs Non-Remitter model. Effect sizes were similar. III) Exploratory Factor Analysis (EFA) revealed that there were at least 5 domains subserving the covariance structure of candidate tests from earlier analyses. Factor 1 = HISOC; Factor 2 = CPT-IP; Factor 3 = Fluency; Factor 4 = g; Factor 5 = Snakes in the grass. The factor structure between Healthy Controls and Remitters were broadly similar, whereas stronger covariances were observed across tests in the Non-Remitters resulting in several cross loadings of tests across domains.
Discussion: Group membership differentiation appeared to be driven by differences in the covariance structure between groups – particularly in UHR individuals who do not remit over time. Results indicate that not only was test performance poorer in individuals who did not remit and and/or convert, but that the factor structure underlying cognitive performance appeared to differ between the remitters and non-remitters. The psychometric structure of non-remitters is consistent with cognitive deficits observed in dementia and schizophrenia. Underlying biological substrates, associated with risk to psychosis could manifest in cognitive performance long before first episode psychosis or schizophrenia onset.

S89. Familiality of cognitive performance and its relationship with the neurocognitive evolution profile in psychotic patients

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Background: Cognitive deficits are considered core features of psychotic disorders (Green, 2004) and they are an important determinant of quality of life and everyday functioning in people with these disorders (Tolman & Kurtz, 2012). Moreover, cognitive impairment can also be observed in nonpsychotic family members of psychotic patients (Cella, Hamid, Butt, & Wykes, 2015) which highlight a familial component for the relationship between cognitive impairments and psychotic disorders. Our goal was to evaluate: i) which neurocognitive traits were familial among families with one psychotic patient affected and ii) to explore the relationship between familiality of cognition and the patients' course/evolution of cognitive performance.
Methods: Familiality was explored in 71 psychotic patients and 153 healthy first degree relatives (60 mothers, 48 fathers and 45 siblings), which underwent clinical assessments and neurocognitive battery tests (IQ: WAIS; Working memory: phonemic and semantic fluency, Wisconsin Card Sorting Test; Attention (CPT)). For a subsample of 30 patients, cognitive profile was re-evaluated after 4 years from inclusion. The strength of the familial effect in the complete sample was measured by calculating the family-level residual intraclass correlation coefficient (ICC) and its confidence interval (CI). A three-level linear mixed model (LMM) with the cognitive as the dependent variable, sex, center, age, education years and mean phenotype as fixed effect covariate and family as random effects (subjects nested within families) was used in order to obtain the Intrafamilial resemblance score (IRS). Then, for those variables that were familial (ICC with a P value < 0.05) each family was classified according to the level of familiality (IRS) obtaining a continuous parameter score from the family-pairs differences. All analyses were implemented with the Stata v. 13 (StataCorp, 2013) mixed command.
Results: We found statistical differences between patients and first-degree relatives for: gender, age, education years and IQ ($P < 0.001$). Significant familial aggregation was found for Intelligence quotient (IQ) (ICC (95%CI) = 0.197 (0.034 to 0.359), $P < 0.001$), phonemic fluency (ICC (95%CI) = 0.286 (0.126 to 0.446), $P < 0.001$) and semantic fluency (ICC (95%CI) = 0.212 (0.058 to 0.366), $P < 0.001$), reflecting that the strength of the familial effect for this variables was moderate. Significant IRS was obtained for IQ and phonemic fluency ($P < 0.001$), classifying these families according to their level of familiality. No correlation was found between IRS IQ and IRS phonemic fluency (r2 = 0.02, $P = 0.75$). The level of familiality (IRS) of IQ and Phonemic fluency was not significantly related with the cognitive performance evolution of the patient.
Discussion: In conclusion, these results suggest that intelligence quotient, phonemic and semantic fluency are familial in a family sample of psychotic patients. Despite that different studies have found that patients and relatives display deficits on a variety of neuropsychological tasks (Reichenberg, 2005), we have detected that only IQ, phonemic and semanticfluency were familial. Moreover, although we would have expected that the cognitive course evolution of patients was different according IQ or phonemic fluency familiality levels, we could not detect any difference. In this sense, more studies are required to further explore the role of familiality in the evolution over the course of the illness.
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S90. EEG mu-rhythm suppression in patients with schizophrenia and schizoaffective disorder and its relation to psychopathology

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Background: The current research suggests that abnormal mirror neuron activity, as indicated by altered EEG mu rhythm suppression, exists among patients with schizophrenia. However, it is not known whether these alterations are also common in schizophrenia spectrum disorders. The aim of the present study was to elicit the properties of the mu rhythm using motion imagery task in patients with first episode of schizophrenia and schizoaffective disorder and to investigate its relation to psychopathology in both groups of patients.
Methods: We measured EEG spectral power (SP) of mu-rhythm (in right-handed 157 subjects (schizophrenia patients (SCH) $N = 50$, patients with schizoaffective disorder (SAD) $N = 30$, and healthy subjects (HC) $N = 77$) matched by age, gender and years of education, at rest and while performing a motion imagery task (with eyes closed). Mean mu-rhythm spectral power (SP) in the 8-13 Hz range for the F3, F4, C3, Cz and C4 electrodes was calculated in rest and in task conditions. The association of mu-rhythm SP and psychopathological scores as measured by PANSS, were subsequently approached with the correlative analysis using Pearson correlation coefficient.

Results: In the resting state, the group effect was found in group x electrode interaction (F (2,127) = 3.67; $P = 0.029$). Post-hoc test using Fisher LCD revealed the elevated SP in C4 ($p \leq 0.01$) in SCH and SAD as compared to controls. In task condition we observed less suppression of mu rhythm in SCH in contrast to HC ($F(2,127) = 3.27$, $P = 0.04$), post-hoc test showed a significant difference in C3 ($p \leq 0.01$) and Cz ($p \leq 0.01$). There was no difference between HC and SAD except for the decreased suppression of mu rhythm in right frontal area (for F4, $P < 0.05$). In schizophrenia, mu rhythm suppression in F3 positively correlated with the severity of negative symptoms ($r = .36$, $P < .05$), whereas in schizoaffective disorder patients, the mu rhythm reactivity was associated with the severity of positive symptoms in F4 ($r = .39$, $P < .05$) and in C4 ($r = .39$, $P < .05$)
Discussion: The results are consistent with the previous reports demonstrating a substantial lack of mu-rhythm suppression in schizophrenia patients. The mu rhythm characteristics in patients with schizoaffective disorder were closer to schizophrenia in the resting state and resembled those in controls while performing the task. As we show, the mu rhythm reactivity in schizophrenia and schizoaffective disorder is associated with the symptoms severity. However, this association is diverse that might indicate the distinct disruptions of the mechanisms involved into the cognitive processing in schizophrenia and in schizoaffective disorder. The project was supported by MH CZ - DRO (NIMH- CZ, 00023752) and by the grant of Russian Foundation for Humanities No. 14-06-00304a.

S91. The relationship between cortisol and cognitive functions in the psychosis prodrome and those at clinical high-risk in NAPLS2

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Background: Both increased hypothalamic pituitary adrenal (HPA) axis activity, indexed by elevated cortisol, and impaired cognitive functioning have been observed in those at risk for psychosis. In both healthy subjects and individuals with established psychosis, elevated cortisol is associated with neurocognitive impairment in declarative memory and executive functions. This suggests the HPA axis plays a role in specific cognitive impairments and may be associated with chronic deficits in those with psychosis. No published study has investigated the possible link between basal cortisol measures and cognitive deficits in those at clinical high risk (CHR) for developing psychosis.
Methods: The current study examines the relationship between cortisol and cognitive functions in 748 CHR adolescents, as well as 217 healthy controls in the second phase of the North America Prodrome Longitudinal Study (NAPLS2). Up to three salivary cortisol samples were collected 30 minutes apart and aggregated using the mean of all available measurements. Cognitive functions were assessed using the MATRICS battery and five other tasks tapping functions shown to be affected in psychosis. Cognitive performance was aggregated using exploratory factor analysis. Both linear and quadratic associations between basal cortisol and cognitive functions were tested after controlling for significant covariates. This is based on previous studies showing associations between cognitive impairment and both elevated and reduced cortisol, suggestive of an "inverted U" shaped relationship.
Results: Maximum likelihood factor analysis of the cognitive data yielded executive function/visual, verbal, attention and working memory, and declarative memory abilities factors, accounting for 59% of the variance in cognitive performance. After controlling for age and time of cortisol sampling, the CHR group performed more poorly on all cognitive factors ($F(1,745) = 14.23$, 7.44, 52.42, 26.56, respectively; all $P < .01$) and demonstrated higher cortisol values ($F(1,745) = 5.50$, $P = .019$). No relationships between cortisol and cognition were significant in the overall sample. However, in those with low cortisol (1st quartile, $n = 191$) a negative quadratic relationship between cortisol and attention/working memory abilities ($R2 = .43$, $\beta = -1.72$, $t(13) = -2.17$, $P = .05$) and declarative memory abilities ($R2 = .06$, $\beta = -.63$, $t(126) = -.63$, $P = .05$) was evident only in those who later transitioned to psychosis and the overall CHR group, respectively. These associations were also significant when collapsed across all diagnostic groups. In those with high cortisol (4th quartile, $n = 187$), those who later developed psychosis demonstrated a negative quadratic relationship between cortisol and executive function/visual abilities ($R2 = .29$, $\beta = -1.82$, $t = -2.43$, $P = .03$). No linear relationships were significant.
Discussion: Results provide evidence for a curvilinear relationship between cortisol and executive functioning and declarative memory abilities that is moderated by psychosis risk status. Visual inspection supports an "inverted U" shaped pattern. Cortisol accounted for more variance in executive functions than declarative memory. Results suggest that dysregulation of the HPA axis may play a role in the development of cognitive deficits in early psychosis, particularly in tasks more reliant on frontal than parietal regions. The effects of sex and symptoms will be explored. Future research utilizing psychosocial stressors may be necessary to fully test the "inverted U" hypothesis.

S92. Neuroanatomical correlates of socioeconomic status in schizophrenia and its implications for cognition

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Background: The role of socioeconomic status (SES) during development has been widely investigated and its long-term effects on people's wellbeing comprise cognitive, socio-emotional and health factors. Although early-life SES may be related to adult SES, status changes can occur at any age. Regarding mental disabilities, two hypotheses have been investigated thoroughly: 'causation' and 'selection'. The first hypothesis proposes that being raised in a low-SES family predisposes people to mental disability, whereas the selection hypothesis defends that biologically determined mental illnesses cause individuals to decline into low-SES groups. The results published so far regarding this question are controversial. Moreover, it is still unknown whether SES has an effect on cognition and little is known about its neuroanatomical correlates in schizophrenia.
The present research plan is therefore interested in a better understanding of the role of SES in a group of patients presenting schizophrenia with a high risk of disability. Moreover, we aim to investigate whether SES in this population influences brain structure and function.
Methods: Eighty-seven participants were recruited from the two sites of the Bipolar-Schizophrenia Network on Intermediate Phenotypes study (B-SNIP) (healthy controls = 20; patients with schizophrenia = 39; relatives of schizophrenia patients = 28) and cognitively assessed, including verbal memory skills (Hopkins Verbal Learning Test, HVLT), executive functions (EFs) (Wisconsin Card Sorting Test, WCST) and visual memory abilities (Brief Visuospatial Memory test, BVMT). For the HVLT and BVMT, two composite measures ((score1+score2)/2) were computed for each test adding learning and delay recall scores. For EFs another composite measure was calculated with categories and perseveration errors form the WCST. Socioeconomic variables, such as occupation/work and educational level were collected and codified following the Two Factor Index of Social Position proposed by Hollingshead (Hollingshead, 1957). Moreover, all participants underwent and MRI study on a 3 T Philips scanner located at the Johns Hopkins Hospital (Baltimore, MD, United States). Diffusion images were acquired and using state of the art neuroimaging techniques (DTI implemented in FSL) we obtained measures of white matter (WM) microstructure such as fractional anisotropy (FA). Socioeconomic status variables were correlated with FA for all studied groups. Those results that achieved statistical significant (corrected for multiple comparisons, FWE $P < 0.05$) were saved in a mask and this output was correlated with the different neuropsychological measures collected (HVLT, WCST, BVMT).
Results: White matter microstructure, and specifically FA was significantly correlated with socioeconomic variables, showing lower FA in those with disadvantageous socioeconomic backgrounds in schizophrenia. Healthy controls and relatives of schizophrenia patients did not show a statistically significant correlation between FA and SES. Moreover, the decrement of FA in those areas related to SES in schizophrenic patients, correlated with a worst performance in EFs (WCST) and verbal memory skills (HVLT). No results were found related to visual memory (BMVT).

Discussion: To sum up, our results suggest that SES is affecting the relationship between cognition and cerebral changes, specifically those related to WM alterations, in patients with schizophrenia. In schizophrenia, the higher the SES, the greater the FA of several cerebral regions. Moreover, these cerebral regions affected by SES are related to some specific cognitive domains, such as verbal memory and EFs.

S93. Clinical usefulness of the screen for cognitive impairment in psychiatry (SCIP) in patients with schizophrenia before and after cognitive remediation

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Background: Patients with schizophrenia are impaired in cognitive function including attention, memory and executive function. Treatment with antipsychotics has been shown to improve cognitive dysfunction, specifically in information processing, verbal learning and memory. Additional non-pharmacological interventions such as cognitive remediation have been proven effective in improving attention, verbal learning and information processing. Our study compares patients with schizophrenia with patients with major depressive disorder (MDD) and healthy controls. Cognitive assessment was performed by means of the Screen for Cognitive Impairment in Psychiatry (SCIP), a brief (10-15 minutes) cognitive test developed to assess cognition independently of the psychiatric diagnosis of the patient. After the acute episode all suitable patients admitted to a department with a defined epidemiological catchment area were offered a combination treatment with psychotropic drugs and cognitive remediation. We wanted to examine the feasibility of using the SCIP to detect cognitive dysfunction and its possible improvement.
Methods: 90 patients with schizophrenia (diagnosis according to the ICD-10 research criteria) were included as well as 90 patients with MMD and 90 healthy controls. A German version of the SCIP was first validated and then used to compare cognitive dysfunction in the three groups. Using the alternative forms of the scale which are available to facilitate repeated testing, 50 patients with schizophrenia (and 50 patients with MDD) were tested before and after a combination therapy with drugs (schizophrenia: atypical antipsychotics, MDD: second-generation antidepressants) and cognitive remediation (COGPACK).
Results: In all five domains of the SCIP (immediate and delayed verbal learning, working memory, verbal fluency and processing speed) patients with schizophrenia showed significant cognitive impairment compared to healthy controls. Patients with MDD showed an intermediate degree of impairment. In addition, the SCIP was able to detect an improvement in cognitive function after a combination treatment including COGPACK.
Discussion: Our open, non-randomised pilot study shows the practicality of using the SCIP as brief test to assess cognitive dysfunction. The SCIP in its German version is able to detect cognitive dysfunction and effects of therapy in patients with schizophrenia (and MDD). Using the SCIP might be helpful to specify indications for cognitive remediation in clinical routine. Further studies are needed to assess the validity of the SCIP in predicting prognosis in psychiatric disease.

S94. An investigation of semantic memory in first-episode psychosis

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Background: Disordered associative or semantic memory has been shown to be central to cognitive deficits in chronic schizophrenia. The aim of this current research project was to ascertain whether semantic memory deficits are present at the onset of schizophrenia, or whether the disease process results in progressive loss of semantic information. If they are present early in the illness it may help explain the thought and language difficulties, if they are not present it suggests other aspects of the illness, for example, isolation and long hospitalisations are detrimental to this cognitive ability.
Methods: Tasks developed to test semantic processing were administered to a patient group with first-onset psychosis (FEP) and a group of healthy controls. These tasks have all shown to be impaired in chronic patients (Rossell & David, 2006). The measures were semantic fluency, semantic priming, categorization, word definitions and whether accurate word associations can be detected.
Results: Preliminary results demonstrate reduced performance in first episode patients on the majority of the semantic memory measures (d's = 0.75 - 1.5). Only categorisation was not impaired (d = 0.4).
Discussion: The results to date suggest that semantic memory problems are present at the onset of the illness. These results have implications for interventions in schizophrenia, that is, cognitive remediation and occupational therapy will need to focus on learning semantic appropriate information. Helping individuals build logical and sensible information hierarchies, and assisting them with extracting the relevant semantic cues from experiences, will be important.
References: Rossell, S.L & David, A.S. (2006). Are semantic processing deficits in schizophrenia an access or storage problem? Schizophrenia Research, 82, 121-134.

S95. Learning to trust: trust and attachment in early psychosis

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Background: Distrust and social dysfunction are characteristic in psychosis and may arise from attachment insecurity, which is elevated in the illness. The relationship between trust and attachment in the early illness stages is unknown, yet could help to understand interpersonal difficulties and disease progression. This study aimed to investigate whether trust is reduced in patients with early psychosis and whether this is accounted for by attachment insecurity.
Methods: We used two trust games with a cooperative and unfair game partner in a sample of 39 adolescents with early psychosis and 100 healthy controls to study the development of social behaviour during 20 consecutive real-time social interactions. Attachment insecurity (anxiety and avoidance) was assessed with the Psychosis Attachment Measure and symptoms were assessed with the Positive and Negative Syndrome Scale. The association between group status and trusting behaviour (amount invested) and the moderating effect of attachment insecurity were analyzed by means of multilevel regression analyses.
Results: Patients had higher levels of attachment anxiety, but the groups did not differ in attachment avoidance. Basic trust was lower in patients than controls, as indicated by lower initial investments towards the unknown other. During cooperation patients increased their trust towards levels of controls, i.e. they were able to learn and to override initial suspiciousness. Patients decreased their trust less than controls during unfair interactions. Avoidant attachment was unrelated to trusting behaviour. Anxious attachment was associated with higher basic trust and higher trust during unfair interactions and predicted trust independent of illness status.
Discussion: Patients with early psychosis have reduced basic trust but adapt their trust in response to others' positive social signals. This suggests that the early illness stages could present a window of opportunity for interventions that aim to keep the behavioural flexibility towards others intact. While attachment anxiety seems to be important for trusting behaviour, it does not account for the differences in trust between patients and controls. Worries about the acceptance by others and low-self-esteem are associated with psychosis and attachment anxiety and may explain behaviour that is focused on conciliation, rather than self-protection.

S96. Implicit mentalizing in schizophrenia: a multivariate fmri study and association with genetic risk variants

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Background: Refining the clinical, cognitive, and imaging understanding of schizophrenia will aid the search for reliable intermediate biomarkers or endophenotypes. Theory of mind or social cognition is often impaired in schizophrenia with deficits seen before the onset of psychosis and following treatment. In the GWAS era, understanding the functional characteristics of risk variants will provide vital clues into the intermediate biological pathways leading to schizophrenia.
Methods: Using an established measure of mentalizing, the Triangles Task, a novel multivariate analysis (Partial Least Squares) based on 17 healthy controls and 29 patients with schizophrenia was employed to identify associated network level differences of potential interest. Behavioural measures as well as network level substrates activated during the task were analyzed for differences between patients and controls. Genetic risk, indexed by polygenic risk scores and rare mutation burden, are currently being explored for association in patients.
Results: Behavioural performance was impaired for patients and this was reflected in altered connectivity in key mentalizing regions such as the ventral medial prefrontal cortex (vmPFC) and temporoparietal junction bilaterally. Genetic risk, indexed by polygenic risk scores and rare mutation burden, are currently being explored for association with large, rare deletions associated with vmPFC connectivity.
Discussion: Social cognition may be a vital intermediate phenotype between genetic risk variants and clinical diagnosis. Multivariate statistical approaches to functional neuroimaging will also provide new and improved methods for discovering neural networks associated with cognition.

S97. Cognitive insight in schizophrenia: study about 30 Tunisian patients

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Background: Cognitive impairments are frequent in schizophrenia and the cognitive remediation is an important aspect of the treatment of the disease. To treat these disorders, it is important to evaluate their recognition by the patient called the "cognitive insight". This concept is derived from the concept of metacognition defined by Flavell as "knowledge" that one has its own cognitive processes, its products and everything that touches it. Metacognition is defined as the evaluation and regulation of its own cognitive processes. The aim of this study was to assess the cognitive impairment insight and its relationship with clinical and therapeutic features in patients with schizophrenia.
Methods: We conducted a transversal study carried out on 30 outpatients with schizophrenia in remission (total score in Positive and Negative Syndrome Scale < 60, medication not changed from at least 6 months) followed in the psychiatry Department of Monastir hospital (Tunisia). Patients have benefited of sociodemographic, psychometric, neurocognitive and functioning assessment. The neurocognitive assessment was made by the progressive matrix of Raven for the evaluation of the general intelligence, the dual task of Baddeley for the evaluation of the working memory, the Stroop test for the evaluation of the cognitive inhibition and the selective attention, and the verbal fluency test for the evaluation of the lexicon, semantic memory and cognitive flexibility capacity, an important function of executive functioning. The assessment of the cognitive insight was made by the MIC-CR (Measure of insight into cognition-clinician rated) translated into Tunisian dialect. Lower scores reflect better insight. The attribution of the cognitive disorders to the disease is also analyzed by the MIC-CR. The psychometric assessment was made by the PANSS (Positive and Negative Syndrome Scale), CGI (Clinical Global Impressions), GAF (Global Assessment of Functioning), and CDS (Calgary Depression Scale).
Results: The average age of our patients was 33.4 ± 6.9. The average IQ was 90.9 ± 9.2. Our patients presented essentially an alteration of working memory. Fifty per cent of our patients had a partial insight of the cognitive impairments and 40% had a poor insight. Concerning the relation between the cognitive insight and the clinical features, a poor insight of cognitive disorders was associated to a longer evolution duration of the illness ($P = 0.04$), to the disorganized type of schizophrenia ($P = 0.005$), to the severity of the illness in the CGI score ($P = 0.044$), and to lower CDS scores ($P = 0.01$). An attribution of the cognitive disorders to the disease was associated to the number of schizophrenic relapses ($P = 0.011$). Concerning the relation between cognitive insight and therapeutic features, a poor insight of cognitive disorders was associated to first generation antipsychotic use ($P = 0.011$) and to higher antipsychotic doses ($P = 0.045$).
Discussion: Several studies established that there is a poor cognitive insight in patients with schizophrenia. In literature, the poor cognitive insight was associated with the dimension of disorganization; better cognitive insight was associated with better therapeutic compliance but also with more depressive complications.
Cognitive disorders are an important aspect in the treatment of schizophrenia. In this context, the insight of these disorders seems to be an important factor to consider. The cognitive insight is influenced by several clinical and therapeutic characteristics of the patient to be taken into account in the management of the illness.

S98. Executive dysfunction in psychosis following traumatic brain injury

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Background: Executive dysfunction is well established in patients with traumatic brain injury, and in schizophrenia. However, assessments of executive function in psychosis following traumatic brain injury (PFTBI) are limited, inconsistent, and often do not reflect the prominent deficits demonstrated in TBI and schizophrenia. This research represents the first systematic and standardized measurement of executive function in a PFTBI cohort, and comparison with healthy and single-diagnosis controls.
Methods: Patients with PFTBI ($n = 10$) were recruited from the Royal Talbot Hospital (Kew, Australia) and matched on demographic, injury, and illness variables with traumatic brain injured patients without psychosis ($n = 10$), schizophrenia patients ($n = 23$), and healthy individuals ($n = 23$). All participants completed identical measures of executive function, including: the Stroop Task, the Trail Making Test, and the attention subtest of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Statistical comparisons were made using univariate Analysis of Variance and Student-Newman-Keuls post hoc tests.
Results: Significant executive dysfunction was shown by patients with PFTBI on all measures. PFTBI patients further demonstrated the poorest performance relative to all three comparison cohorts.
Discussion: These data present novel evidence of substantially impaired executive function in dually-diagnosed PFTBI patients, both relative to healthy controls, and the impairments of their brain-injured, and psychotic, counterparts. We speculate that PFTBI executive deficits are underpinned by exaggerated structural and functional disconnectivity established in both TBI, and schizophrenia, particularly with respect to network connections in the dorsolateral and ventromedial prefrontal cortices.

S99. Neurological soft signs in chronic schizophrenia

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Background: Neurological soft signs (NSS) are frequently found in schizophrenia. While a number of studies have established the course of NSS in the early phases of the disease, little is known about the

course of NSS in older patients with chronic schizophrenia. To prepare for a longitudinal study, we investigated NSS in younger, middle aged, and older patients with chronic schizophrenia.
Methods: NSS and psychopathological symptoms were investigated in 90 patients with chronic schizophrenia recruited in the psychiatric departments of two major hospitals and in a nursing home. 60 healthy volunteer carefully matched for age and gender served as a control group. NSS were examined using the Heidelberg scale, patients and controls were assigned to three age groups (18-29 ys, 30-49 ys, 50 ys and above).
Results: When compared with the healthy controls, the patients with schizophrenia showed significantly ($P < 0.05$) higher NSS scores. In both groups, NSS scores significantly increased with age. This effects was more pronounced in the patient group as indicated by a significant interaction diagnosis*age.
Discussion: Our results facilitate the hypothesis that NSS in schizophrenia increase with chronicity of the disorder, an effect which may correspond to ongoing brain changes. This hypothesis conforms with recent neuroimaging studies (Kong *et al.*, 2012); moreover, progressive brain changes may add an additional burden on the poor general health condition patients frequently show.

S100. Does cognitive performance map to categorical diagnoses of schizophrenia, schizoaffective disorder and bipolar disorder? A discriminant functions analysis

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Background: Despite known overlaps in the pattern of cognitive impairments in individuals with bipolar disorder (BD), schizophrenia (SZ) and schizoaffective disorder (SZA), few studies have examined the extent to which cognitive performance validates traditional diagnostic boundaries in these groups.
Methods: Individuals with SZ ($n = 49$), SZA ($n = 33$) and BD ($n = 35$) completed a battery of cognitive tests measuring the domains of processing speed, immediate memory, semantic memory, learning, working memory, executive function and sustained attention.
Results: A discriminant functions analysis revealed a significant function comprising semantic memory, immediate memory and processing speed that maximally separated patients with SZ from those with BD. Initial classification scores on the basis of this function showed modest diagnostic accuracy, owing in part to the misclassification of SZA patients as having SZ. When SZA patients were removed from the model, a second cross-validated classifier yielded slightly improved diagnostic accuracy and a single function solution, of which semantic memory loaded most heavily.
Discussion: A cluster of non-executive cognitive processes appears to have some validity in mapping onto traditional nosological boundaries. However, since semantic memory performance was the primary driver of the discrimination between BD and SZ, it is possible that performance differences between the disorders in this cognitive domain in particular, index separate underlying aetiologies.

S101. Change in verbal memory performance in schizophrenia patients and their siblings

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Background: Deficits in verbal memory (VM) are among the most prominent cognitive difficulties observed in schizophrenia. Literature confirms that first-degree relatives share similar but attenuated VM impairments with schizophrenia patients, suggesting a genetic susceptibility for VM deficit. Specifically, studies show that siblings of schizophrenia patients perform worse than controls on VM, in particular on immediate and delayed recall measures. Here, we investigate the longitudinal course of VM deficits in patients and first-degree relatives, i.e. siblings and parents.
Methods: This study is part of the Genetic Risk and Outcome of Psychoses (GROUP) study, a naturalistic longitudinal cohort study with assessments at baseline, after three and six years of follow-up. A total of 3.542 participants ($n = 1045$ patients; $n = 1921$ first-degree relatives [897 parents and 1.024 siblings]; and $n = 576$ healthy controls) were assessed, at least on one time point, on measures of VM using the 15 words learning test (15-WLT). Parents were only assessed at baseline. Demographic and clinical information was available at all relevant time points. ANOVAs and linear mixed model analyses (lme) were used to compare change over time in VM performance across the three time points between the groups, taken familial relatedness into account.
Results: At baseline, patients performed significantly worse as compared with healthy controls and their parents and siblings on immediate recall. On delayed recall both siblings and healthy controls performed significantly better than patients, which perform more similar to parents, but not differed significantly from healthy controls and siblings. Analyses of change in performance over time showed that there were significant interactions with group for immediate and delayed recall measures. The performance of patients, siblings, and controls improved over time, but the improvement in siblings and healthy controls was significantly more pronounced relative to patients.
Discussion: Our results confirm that immediate and delayed VM impairments reflect fundamental features of the disease, as patients' performance is below that of their parents and siblings as well as that of controls. Despite the finding that patients, their siblings and control perform better over time, the increase is performance is more pronounced in siblings and controls. The relationship with IQ and clinical variables will be discussed.

S102. Understanding the progression of semantic dysfunction in schizophrenia: insights using the schizotypy analogue

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Background: Semantic memory (SM) dysfunction is an established phenomenon in schizophrenia and has been associated with a number of symptoms. However, the nature and progression of SM dysfunction is still being debated, notably if it is more of an access or storage problem. SM studies in schizophrenia have been hampered by illness-related factors (e.g. length of illness, age of onset, and medication dose) that could be unduly affecting observations. The schizotypy model allows the circumvention of these issues by examining psychosis proneness in a healthy population. This study sought to examine SM performance in a schizotypy sample for two reasons: (1) to expand on previous work to better characterise SM performance in relation to individuals with higher psychosis proneness, and (2) to determine if the issue is more access- or storage-related to inform understanding of the trajectory of SM deficits along the schizophrenia spectrum.
Methods: 60 individuals with no history of mental illness (M = 22.92, SD = 2.70), were administered three semantic tasks: (1) the Boston Naming Test, (2) a category fluency task, and (3) a semantic priming task at two stimulus onset asynchronies (SOA) to examine both automatic and controlled processing. Schizotypy was assessed with the O-LIFE and premorbid IQ was estimated using the WTAR.

Results: Pearson's correlations revealed that increasing CogDis was related to both reduced fluency productivity (r = -.30, $P = .021$) and a trending reduced automatic priming effect (r = -.23, $P = .082$). A hierarchical regression, controlling for premorbid IQ, was conducted to examine the contribution of CogDis to fluency. CogDis significantly predicted fluency productivity, β = -.28, t(57) = -2.24, $P = .029$, accounting for 7.6% of the variance, F(1,57) = 5.03, $P = .029$.
Discussion: This study contributes to existing evidence that there are subtle SM impairments in non-clinical individuals prone to schizophrenia, though not in all SM domains. Particularly, schizotypy appears to significantly influence the ability to generate category-appropriate words. The pattern of findings appear to align with notions of an access-type SM problem in schizotypy. Regarding the question of trajectory, it may be that SM dysfunction in schizophrenia begins as pre-clinical access issues which potentially then lead to storage issues later after diagnosis. This is plausible given the dynamic nature of SM and predominant evidence that storage issues are characteristic of the later illness stage.

S103. Building a neurocognitive profile of auditory verbal hallucinations in schizophrenia

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Background: Auditory verbal hallucinations (AVH) in schizophrenia have been related to a number of neurocognitive domains such as attention, working memory and inhibition. However, to date, there has not yet been a comprehensive examination of general neurocognition in relation to AVH in a single sample. The contribution of neurocognition to AVH can be understood by comparing performance on these tasks in patients with and without the presence of AVH. This study thus seeks to examine and compare neurocognitive performance between four groups: current voice hearers (State), previous but not current voice hearers (Trait), non-hearers (Never) and healthy controls (HC).
Methods: 121 patients with schizophrenia/schizoaffective disorder were recruited and split into 3 groups: state ($n = 48$), trait ($n = 27$), and never (46) voice hearers using the SCID-PANSS. 121 HCs were also recruited. All participants were administered the MATRICS Consensus Cognitive Battery (MCCB) and the D-KEFS Stroop to assess 8 general neurocognitive domains: Speed of Processing, Attention, Working Memory, Verbal Learning, Visual Learning, Reasoning/Problem Solving, Social Cognition and Inhibition. z-scores were calculated based on mean HC performance, and groups compared using one-way ANOVAs on all eight domains.
Results: No significant differences were observed between the patient groups on all 7 domains of the MCCB. All patients groups performed significantly more poorly than HCs across most of the MCCB domains except Social Cognition. State hallucinators were performed significantly poorer on the Inhibition condition of the D-KEFS Stroop compared to Never hallucinators ($P = .005$), and a trend towards significance with the Trait hallucinators ($P = .064$). Inhibition errors did not differ between the groups ($P > .05$).
Discussion: Preliminary indications are that inhibition is reduced in the presence of AVHs. This aligns with the proposition that AVHs may be associated with reduced executive control. No significant differences were observed for the other neurocognitive domains. This is the first study to investigate AVH in schizophrenia between current, previous and never voice hearers and so replication of this finding is necessary. Recruitment is ongoing to enlarge the sample for subsequent analyses.

S104. Music & emotions in schizophrenia patients

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Background: Eerola et. al (2009) provide an acoustic approach for computing dimensional emotion ratings (valence, arousal) for a given piece of music with regression models using features extracted directly from the audio file. In the present study we tested if the computed ratings have an identifiable neural substrate within schizophrenia patients and healthy controls. To assess this we used electroencephalography recordings from 8 schizophrenia patients and 8 healthy controls. All participants listened to 3 different classical music pieces. Based on the regression model of Erola *et al.* we computed the emotional arousal and emotional valence ratings over time for these songs. It was the aim of the study to explore possible neuronal correlates of the computed emotional ratings.
Methods: To quantify neural tuning properties, we fit linear regression based models that describe the temporal tuning between individual electrodes (filtered in δ,θ, α, β and low γ frequency ranges) and the emotional ratings (valance, arousal). To investigate potential differences in anatomical locations we calculated an ANOVA using ‚electrode location' and ‚frequency' as factors. Using this procedure we were able to examine the degree to which a specific anatomical region was tuned to the emotional ratings.
Results: Results within the schizophrenia patients and healthy controls showed delta activation within the mid frontal line and an asymmetric posterior alpha activation within high emotional arousal. Within emotional valence healthy controls show a significant asymmetrical frontal alpha, which did not occur within patients.
Discussion: These initial findings suggest that computed arousal ratings have a complex neural substrate with distinct neuroanatomical regions responding to different frequency spectra. Schizophrenia patients seem to be prone to changes in arousal during music. However they lacking sensitivity for changes in valence.

S105. Cigarette smoking and cognitive functioning in schizophrenia

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Background: Persons with schizophrenia have a high prevalence of smoking, more than three times that of persons in the general population. Smoking has adverse effects in schizophrenia including adding to the risk of co-morbid medical illnesses and premature mortality. Previous studies of the association between smoking and cognitive functioning in schizophrenia are limited and have not examined the association when adjusting for biomarkers which have been associated with cognitive functioning in this population.
Methods: Participants were individuals with schizophrenia, bipolar disorder, or non psychiatric controls who were enrolled in the period January 1999 – October 2015. At time of the study visit patients were asked if they were a current cigarette smoker and, if yes, the amount of cigarettes smoked per day. All participants were assessed with a cognitive battery, the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). All patients had a blood sample drawn, from which were measured antibodies to herpes simplex virus type 1 (HSV-1) and C-reactive protein (CRP), markers which have been associated with cognitive functioning. Patients were also assessed with the Positive and Negative Syndrome Scale (PANSS). Within each diagnostic group, linear regression analyses were performed to determine the association between cognitive score, smoking status, and HSV-1 seropositivity, and the combination of these risk factors. We also calculated the odds of having a total cognitive score in the lowest quartile and the highest quartile of cognitive performance based on smoking status.

Results: The sample consisted of $N = 1790$ individuals, $n = 759$ with schizophrenia, $n = 484$ with bipolar disorder, and 547 non-psychiatric controls. The mean age of each group was 39.6 (±12.0), 35.7 (±13.0), and 32.6 years (±11.4), respectively. The prevalence of current smoking in each group was 62%, 37%, and 18%, respectively. Within schizophrenia, there was a significant inverse effect of smoking on total cognitive score adjusting for HSV-1 status, age, gender, race, illness onset, illness duration, and total PANSS symptom score (coefficient = -2.81, $P = .003$). The effect of smoking on cognitive functioning was not significant in the bipolar disorder group or in the control group ($P > .05$). Within the schizophrenia group, the combination of smoking and HSV-1 risk factors yielded an additive effect (coefficient = -6.38, $P < .001$). The association between smoking and worse cognition remained significant when the covariates, level of CRP and years education, were added (coefficient = -2.98, $P = 017$). Smoking was significantly and inversely associated with each of the RBANS scale scores except for the Language scale. There was not an association between amount of cigarettes smoked per day and cognitive performance. Cigarette smoking was associated with significantly reduced odds of being in the top quartile of cognitive performance (OR = 0.547, 95% CI 0.38, 0.79, $P = .001$) but not increased odds of being in the lowest quartile (OR = 1.20, 95% CI 0.82, 1.74, $P = 0.344$).
Discussion: Despite the transient benefits of nicotine on some aspects of cognitive performance, it appears that long-term exposure to nicotine via smoking has a negative effect on cognitive functioning in schizophrenia. This effect is independent of other risk factors including HSV-1 seropositivity and elevated levels of CRP. The mechanism involved may be related to the long term health effects of smoking including the adverse impacts of smoking on circulatory and respiratory systems. These data add further urgency to promoting smoking cessation in individuals with schizophrenia.

S106. High prevalence of obstructive sleep apnoea in patients taking clozapine compared to age matched controls

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Background: Sleep problems characterized by increased sleep latency; reduced sleep efficiency; circadian rhythm disturbances; and changes in sleep architecture are recognized as a feature of schizophrenia. Obstructive Sleep Apnea (OSA) is not well studied in schizophrenia. OSA is characterised by periods of functional obstruction of the upper airway during sleep, resulting in a decrease in arterial oxygen saturation and transient arousal. It is more common in those who are obese, smoke, are male, with increased age, consuming alcohol, and using hypnotic medications. Sleep apnoea is associated with increased cardiovascular risk factors, thus comorbid OSA may be an additive and modifiable risk factor for cardiovascular disease in people with schizophrenia. Symptoms of sleep apnoea include: non-rejuvenating sleep, daytime sleepiness, cognitive impairment, depression, somatic complaints, poor quality of life, and morning headaches. Negative symptoms of Schizophrenia may mask the symptoms of sleep apnoea in people with schizophrenia. High rates of OSA risk factors occur in people with schizophrenia, and prevalence estimates in selected populations vary between 13.5% and 52%, however the literature is heterogeneous and many studies had methodological flaws. These rates are higher than the general population prevalence of OSA of 2-4%.
Methods: The ASSET (assessing sleep in schizophrenia and evaluating treatment) Pilot study is currently performing Polysomnography, the gold standard for diagnosis of OSA, on participants recruited from a Clozapine clinic in the northern regions of Adelaide. This data has been matched with a representative sample of men (aged 41-88) from the MAILES (the Men Androgen Inflammation Lifestyle Environment Stress study 2009). MAILES included 2563 men in a SA representative cohort, 837 of whom were enrolled as a random sub-sample and underwent polysomnography.
Comparison of age and BMI using Mann-Whitney-Wilcox non-parametric tests, and unadjusted comparison of prevalence of severe OSA using Fisher exact test were undertaken. Propensity score matching was used to match (up to) 50 MAILES individuals to each member of the schizophrenic cohort, matching by either age or age and BMI. Conditional logistic regression was used to estimate the odds ratio between the two cohorts, stratifying by matching.
Results: 23 patients (male $N = 19$) with schizophrenia have enrolled in the ASSET study. 13 had no OSA (AHI 0-10.9), 3 had mild OSA (AHI 11-29.9), and 7 had severe OSA (AHI > 30).
MAILES median age was 59, median BMI 28, and prevalence of severe OSA 12.3%; 95% CI [10.2%, 14.7%] ($N = 103$). The ASSET median age was 42, median BMI 35, and prevalence of severe OSA 31.6%; 95% CI [12.6%, 56.6%] ($N = 6$). The MAILES cohort is older ($P < 0.001$) and less obese ($P < 0.001$). The unadjusted comparison of OSA indicates a significantly higher rate of OSA in the ASSET subjects ($P = 0.02$).
When matching by age, 13 of the 19 male ASSET participants could be matched. In the matched subgroups the prevalence of severe OSA was: ASSET 30.8%, and MAILES 11.0%. Conditional regression indicated that the odds of severe OSA were increased in the ASSET population by a factor (OR) 3.7 (95%CI = [1.1, 12.6]; $P = 0.03$).
When matching for BMI, 14 of the 19 ASSET participants were matched. In the matched subgroups the prevalence of severe OSA was: ASSET 21.4%, and MAILES 11.5%. In the conditional regression, the increase in odds of severe OSA in the ASSET population was not as large as when matching only by age, OR = 2.2 (95%CI = [0.6, 8.7]; $P = 0.24$).
Discussion: In an age-matched cohort OSA appears to be elevated in the ASSET population. Elevated BMI may be the cause of the increased OSA, however the dataset is too small to determine whether obesity explains all or part of the increase.

S107. High metabolic risk factors do not subside by routine outcome monitoring; data from the Phamous project

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Background: People with psychotic disorders have an increased metabolic risk and a shortened life expectancy compared to the general population. Ten years ago, a large study showed that many patients had untreated metabolic disorders. Since then, guidelines urge monitoring metabolic health. In this study we examine the course of metabolic disorders over time in people with psychotic disorders, and investigate whether treatment rates have improved.
Methods: Metabolic parameters were assessed in an observational cohort of 1259 patients with psychotic disorders, in four Dutch mental health institutions. Patients participated in three yearly screenings in which health status was routinely assessed and the use of pharmacologic treatment for hypertension, dyslipidemia and hyperglycemia was recorded.
Results: Prevalence of the metabolic syndrome, as defined by the NCEP criteria, was > 50% at each assessment. Based on the European Society of Cardiology (ESC) guidelines > 60% of the patients would need pharmacotherapy for their metabolic disorders at any assessment. Treatment rates with antihypertensive (from 31 to 38%, $P < .001$) and antihyperglycemic (from 32 to 44%, $P = .027$) pharmacotherapy increased during the assessments, but over half of the patients were not treated for their metabolic disorders while being monitored for three years or longer. Older patients were more likely to receive treatment for their metabolic symptoms. Patients who received treatment had lower blood pressure, cholesterol and triglyceride concentrations than patients not receiving the recommended treatment.
Discussion: Metabolic risk factors are still seriously undertreated in people with psychotic disorders. Better adherence to and better implementation of guidelines about monitoring and treating metabolic disorders in psychiatry is crucial.

S108. The effectiveness of short-term group schema cognitive behavioral therapy (SCBT-g) for people with psychotic disorders and co-morbid personality problems

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Background: There is a myth that psychotherapy cannot be done with patients who have a psychotic disorder. However there is no scientific evidence for this assumption. Schema therapy has proven to be an effective treatment for patients with borderline personality disorder. However, little is known of its merits in patients with psychotic disorder and co-morbid personality problems. This pilot study investigated whether short-term schema cognitive–behavioural group therapy [SCBT-g]) was associated with changes in symptom severity, schemas, modes and personality problems.
Methods: Twenty patients with a psychotic disorder and co-morbid personality problems who attended short-term schema cognitive-behavioral therapy (SCBT-g) were included. Besides some minor adjustments the original protocol developed by Vreeswijk and Broersen (2007) has been used. Patients completed the Symptom Checklist 90 (SCL-90), the Schema Questionnaire (YSQ), the Schema Mode Inventory (SMI) and the Severity Indices of Personality Problems (SIPP-118) at baseline and after the first follow-up session. A pre- and post-test was done to investigate changes in psychopathology, personality traits, schemas and modes.
Results: Outcome measurements showed significant reduction in quite a number of schemas and modes and an increase in healthy modes. Also reduction of symptom severity, especially interpersonal sensitivity, and reduction of different domains and facets of personality problems were found.
Discussion: In this pilot study, SCBT-g was effective for people with psychotic disorders and co-morbid personality problems, with reduced symptom, schema and mode severity and a reduction in personality problems. Schema therapy might therefore have great potential for the stability of these patients, as the psychotic vulnerability is perhaps less easily triggered with better personality functioning. Clinicians should be aware of co-morbid personality problems in patients with psychotic disorders and psychotherapy can be given!

S109. The bias effect of CNVs conferring risk for both autism and schizophrenia

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Background: A large number of genetic studies suggest that autism and schizophrenia spectrum disorders (ASD and SSD, respectively) are in part mediated by overlapping copy number variants (CNVs) (a form of structural variations or alterations of the DNA of a genome). It has been proposed that these shared risks for both ASD and SSD can be used to explain shared phenotypes in both disorders. A major challenge posed by these shared CNVs is the notion that the same CNV locus can confer risk to two distinct conditions. Here we introduce a novel approach to reconcile such conceptual difficulties by indexing the relationship between ASD and SSD in terms of bias and additive (sum) effects.
Methods: The analysis is based on the social functioning and CNV data reported in the supplementary material accompanying Stefansson *et al.* (Nature 505, 361-366: 2014). The data consist of the ASD and SSD risk ratios of 10 CNVs in 167 healthy carriers and their pooled social functioning scores measured with the Global Assessment of Functioning Scale. To estimate the relative risk associated with each CNV for either ASD or SSD, we first converted their estimated odds ratios for risk to either ASD or SSD into Z scores. We then derived the bias score for each CNV by subtracting the CNV's risk for ASD from its risk for SSD, and the sum score by adding the risks. The CNVs impairment effect on social functioning was estimated in a backward regression model, with the following initial predictors: (1) CNV-risk-bias for ASD or SSD, (2) the sum of the risks for ASD and SSD, (3) the interaction term of the Bias x Sum of risks, (4) quadratic term of the bias, and (5) the quadratic term of the sum of the risks, while controlling for the number of individuals carrying each CNV.
Results: The overall model is significant ($F(3,6) = 5.45$, $P = .038$, Radj. $2 = .597$), explaining 59.7% of the variance, and reveals that the CNVs' impairment effect on social functioning is predicted by the quadratic term of the CNV-risk-bias ($\beta(\pm SE) = .646$ (.781), $t = 3.62$, $P = .011$). The results suggest that impairment level is associated with the relative risk these CNVs confer for ASD or SSD, whereby CNVs that equally confer risk for either disorder (e.g., 2p16.3 (NRXN1) deletion, 22q11.21 duplication) have the least impairing effect on social functioning, whereas CNVs that predispose risk mainly for SSD (e.g., 17p12 deletion) or mainly for ASD (e.g., 16p11.2 deletion) have the most impairing effect on social functioning.
Discussion: CNVs that equally predispose individuals to ASD or SSD generally appear to confer a smaller impairment effect on social functioning compared to CNVs that strongly predispose individuals to one disorder or the other. This finding is consistent with the notion that social functioning and related abilities are associated with the relative expression of autistic and psychosis liability (Abu-Akel *et al.* 2015, Proc R Soc B), and advances the notion that such association might be mediated by the relative expressions of genes conferring risks for ASD and SSD. If confirmed, this would raise the important possibility that a balanced expression of risk factors associated with these disorders can induce an attenuating effect on cognitive and behavioral difficulties associated with these disorders. Future research is needed to uncover the mechanisms that underlie this attenuating effect.

S110. Depression and clinical high-risk states: clinical presentation of depressed vs. non-depressed participants in the NAPLS-2 cohort

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Background: The high degree of correlation between depressive and attenuated psychotic symptoms complicates the conceptualization of "clinical high-risk" (CHR) youth as primarily 'prodromal' to psychotic disorders, and introduces questions regarding the presentation and impact of depression among CHR populations. Although mood does not figure into diagnostic criteria for CHR states, the literature suggests that depressed mood is highly prevalent in CHR samples. Dysphoric mood appears to contribute uniquely to losses in social and role functioning, beyond impairments explained by positive and negative symptoms, and may also be associated with heightened risk for suicidal behavior. Thus depression appears to constitute a central clinical feature and risk factor within this already vulnerable population. Better comprehension of CHR mood disturbances may help to both establish a standard of care for this population and improve the field's understanding of CHR prognosis with regard to diagnostic and functional outcomes. To these ends, the proposed project aims to investigate the clinical presentation of depression within a large prospective CHR sample.
Methods: The current study utilizes baseline clinical data collected from participants at the time of admission to the second iteration of the North American Prodromal Longitudinal Study cohort (NAPLS-2). The NAPLS-2 sample comprises 746 help-seeking teens and young adults ages 12-35 meeting CHR criteria based on the Structured Interview for Psychosis Risk Syndromes (SIPS). Participants were recruited across the eight sites between January 2009 and December 2012. CHR participants could be included if they met DSM-IV criteria for any other non-psychotic disorders, as long as the disorder did not clearly account for the individual's prodromal symptoms.
Results: Sixty percent of CHR subjects had a lifetime diagnosis of a depressive disorder, and 42% met DSM-IV criteria for current depression at the time of their baseline assessment, making depression the most common comorbid condition within the sample (56% had a lifetime anxiety diagnosis, including PTSD and specific phobias; 22% were diagnosed with ADHD; and 20% had a lifetime

substance use disorder). Those with a lifetime diagnosis of depression were somewhat older and more likely to be female relative to those with no lifetime depression diagnosis. Individuals with depression also had greater exposure across multiple categories of psychiatric medications. Relative to never-depressed CHR subjects, those with depression had more severe positive, negative, disorganized, and general symptoms and greater impairments in social and role functioning, with depressed mood contributing uniquely to functional impairments beyond the impact of positive and negative psychosis-related symptoms. Depressed and non-depressed participants had similar rates of conversion to psychosis over time.
Discussion: Depression was the most common comorbid condition in the NAPLS-2 cohort. CHR participants with a history of depression (defined here as Major Depressive Disorder, Dysthymic Disorder, or Depression Not Otherwise Specified) presented with more prior medication exposure, greater clinical symptom severity, and more pronounced functional impairments relative to non-depressed CHR participants. In spite of these baseline differences, depression did not appear to confer added risk toward developing a full-blown psychotic disorder, nor was depressed mood at baseline protective against conversion to psychosis over time. This information will likely be useful to professionals treating CHR patients and formulating best practices for CHR populations in clinical settings.

S111. Hallucinations and trauma: a complex relation

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Background: Many studies reported a relationship between Auditory Verbal Hallucinations (AVH) and trauma. However, to demonstrate a possible causal association, factors that confound this association also need to be considered. Hence, we studied the relationship between voice hearers reporting trauma and traumatized patients reporting AVH adjusted for age, gender and diagnosis.
Methods: During a 3 months period all patients with consecutive referrals to a psychiatric Out-Patient Department (OPD) were assessed for psychiatric diagnosis (DSM-IV-TR), AVH (AVHRS: a structured 16-item interview) and trauma (TRAMAL; a self-report list consisting of 6 trauma items (bullying, blackmail, physical- and sexual abuse, threatening and murder) with scores on frequency, severity and offenders.
Descriptive statistics, Chi-square tests, Mann-Whitney U tests and logistic regression models were used to analyze data. For all tests, a two-tailed significance level of $P < 0.05$ was used.
Results: •153 (92%) of 166 patients were included in complete case analysis; majority were males (57.2%). Married were 59% of the men and 41% of the women. Diagnoses were: psychotic disorder: $n = 56$ (36%), affective disorder: $n = 43$ (12%), anxiety disorder: $n = 23$ (15%), drugs-related disorder: $n = 3$ (2%), other: $n = 18$ (12%), and no axis-I disorder = 13 (8%). Thirty-eight subjects (25%) had an axis-II diagnosis, majority were borderline personality disorders. Former psychiatric admission was reported by 48.2% of the Ss.
•No significant adjusted relationship was found between social adverse experiences (SAE) and voice hearing ($P = 0.36$); 83% of Ss who reported one to five past SAE had never heard voices against 78% of voice hearers who reported one to five past SAE.
•Of six traumas, a significant association was observed for sexual abuse only (OR = 2.08, 95%CI: 1.06-4.08; $P = 0.03$) and a trend for undeserved punishment and blackmail (OR = 1.86, 95%CI: 0.98-3.54; $P = .06$).
•No dose-relationship between the number of traumas and the number of voice hearers could be identified. Command hallucinations regarded suicide and assaulting others.
Discussion: Based on present findings in a relatively small sample we conclude that trauma assessment can be justified in case of AVH, as is the reverse. Our findings support the observation that trauma specificity and dose-effect are complex concepts and warrant further investigation.

S112. Unique and overlapping symptoms in schizophrenia spectrum and dissociative disorders in relation to models of psychopathology: a systematic review

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Background: Schizophrenia spectrum disorders and dissociative disorders are described in the DSM-5 and ICD-10 as two categorically distinct diagnostic categories. However, several studies indicate high levels of co-occurrence between these diagnostic groups, which might be explained by overlapping symptoms. The aim of this systematic review is to provide a comprehensive overview of the research concerning overlap and differences in symptoms between schizophrenia spectrum and dissociative disorders.
Methods: The PubMed, PsycINFO and Web of Science databases were searched for relevant literature.
Results: The literature contained a large body of evidence showing the presence of symptoms of dissociation in schizophrenia spectrum disorders. Although there are quantitative differences between diagnoses, overlapping symptoms are not limited to certain domains of dissociation, nor to non-pathological forms of dissociation. In addition, dissociation seems to be related to a history of trauma in schizophrenia spectrum disorders, as is also seen in dissociative disorders. There is also evidence showing that positive and negative symptoms typically associated with schizophrenia may be present in dissociative disorders.
Discussion: These results seem to be more consistent with a combination of the dimensional model and network structure model of psychopathology than with categorical models of psychopathology. However, other factors, such as misdiagnosis, item overlap and construct overlap might also play a role.

S113. Does age of first cannabis use and frequency of use influence age of first-episode psychosis (FEP)? A comparison between north and south of Europe

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Background: Cannabis is one of the most commonly used drugs among young people across Europe (EMCDDA data 2014), Moreover, it is one of the most abused illicit drugs among patients suffering from schizophrenia (Linszen *et al.*, 1994) and, particularly, in patients at their first episode of psychosis (Donoghue *et al.*, 2011). Furthermore, patients suffering from psychosis with a history of cannabis use have an earlier age of onset of psychosis (AOP) than those who never used it (Di Forti *et al.*, 2013).
We aim to investigate if the reported association between use of cannabis and AOP is consistent across to European samples with expected differences in pattern of cannabis use (i.e. age at first use, frequency of use)
Methods: Cannabis is one of the most commonly used drugs among young people across Europe (EMCDDA data 2014), Moreover, it is one of the most abused illicit drugs among patients suffering from schizophrenia (Linszen *et al.*, 1994) and, particularly, in patients at their first episode of psychosis (Donoghue *et al.*, 2011). Furthermore, patients suffering from psychosis with a history of cannabis use have an earlier age of onset of psychosis (AOP) than those who never used it (Di Forti *et al.*, 2013).
We aim to investigate if the reported association between use of cannabis and AOP is consistent across to European samples with expected differences in pattern of cannabis use (i.e. age at first use, frequency of use)
Results: In the total sample, $N = 935$, comparing FEP who were cannabis users with never users, we found a significant difference in mean AOP (cannabis users: 28.30 (9.05) vs. non-users: 34.94 (12.5), t = -

9.32, $P < 0.001$). Moreover, 58% of cannabis users started at age ≤16 years old, with mean age of onset of Psychotic Disorder (25.47, sd = 7.03), compared with those who started later (M = 25.47, sd = 10.05) (t = -9.42, $P < 0.001$). When the sample was split in NE and SE groups, we found that NE sample the mean AOP in cannabis users was 28.12 (±8.42) and 34.18 (±12.68) non-users (t = -4.65, $P < 0.001$). In SE sample the mean AOP in cannabis users is 29.02 (±9.62) and in never users is 35.55 (±11.61) (t = -5.75, $P < 0.001$). All predictors are statistically significant (in NE sample age first use β = .31, t = 5.16, $P = .000$, frequency β = -1.80, t = -2.93, $P < 0.001$; in SE sample age first use β = 0.41, t = 6.67, $P = .000$, frequency β = -2.87, t = -4.66, $P < 0.001$). In SE, the percentage of variance explained in a regression model is 31% (R2adj = .30) vs 16% (R2adj = .15) of NE.
Discussion: Our results support the association between cannabis use and younger AOP in both samples, but were not observed significant difference across Europe. Linear regression model on predictors (age of first use, frequency of use) analyzed in the NE and the SE clinical samples confirmed relationship of causality with dependent variable (AOP), with a higher percentage of explained variance in sample of SE than NE.

S114. Long-term effects of adolescent THC on the adult brain: an vivo MRI / 1H-MRS study with ex vivo and post-mortem confirmation

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Background: Adolescence is a period of vulnerability with regard to the emergence of psychotic disorders (Keshavan *et al.*, Lancet Psychiatry, 2014) especially in boys (Häfner *et al.*, Schiz. Bull. 1998). Cannabis use during adolescence may be a contributing factor; high odds ratios are reported for schizophrenia in a prospective study of men (Manrique-Garcia *et al.*, Psychol. Med. 2012) comparing frequent cannabis users (>50 occasions by those aged 18-19 years) with nonusers. However, the neurobiology of this association remains unclear. To develop a model to explore this, we examined the long-term impact of adolescent exposure to delta-9-tetrahydrocannbidiol (Δ9-THC) on the rat brain, using small animal magnetic resonance imaging and spectroscopy. We hypothesized that Δ9-THC exposure would result in volumetric reductions and/or metabolic alterations particularly in schizophrenia-relevant brain regions such as the prefrontal cortex and hippocampus.
Methods: Male Sprague-Dawley rats were treated with either constant (1 mg/kg i.p.; $n = 10$) or escalating (2.5; 5; 10 mg/kg; i.p.; $n = 10$) doses of Δ9-THC during adolescence, (P35-45). Control animals ($n = 10$) received drug vehicle. All animals were then left undisturbed until adulthood (P80), at which point 1H-magnetic resonance spectra (1H-MRS) were acquired using a PRESS sequence from the left anterior hippocampus using a 7 T small animal MRI system (Agilent Technologies, USA). The animals were then sacrificed by anaesthetic overdose and perfusion-fixed prior to high resolution ex vivo 3D MRI. The MRI data were then analysed for group level differences using unbiased voxel-wise tensor based morphometry (TBM), corrected for multiple comparisons (q = 0.05). Hippocampal MR spectra were analysed using LC-model (Provencher *et al.*, MRM 1993) and the data normalized to levels of creatine. Fixed brain tissues were then dissected and serial tissue sections (1 in 12, 40 µm-thick) processed for Nissl staining and volume assessment using the Cavalieri estimator probe.
Results: Brain-wide TBM analysis revealed that adolescent Δ9-THC exposure did not result in any significant changes (q = 0.05 FDR corrected) in the macroscopic volume of the rat brain, irrespective of the dose of Δ9-THC administered. Clusters of decreased voxels were observed at trend-level ($P < 0.01$ uncorrected) in the cerebellum. Constraining the analysis to a priori regions of interest, (anterior cingulate cortex [ACC], hippocampus) did not change these results and revealed the same trends in the cerebellum. Post-mortem stereology based-volume measurement confirmed the absence of any volume decreases in the ACC and hippocampus following adolescent exposure to Δ9-THC. In contrast, in vivo MRS revealed a dose-dependent decrease in myo-inositol: cr and metabolic decoupling of N-acetyl-aspartate: cr (a marker of neural health/activity) and glutamate: cr.
Discussion: These data resonate with recent findings in humans that suggest adolescent or adult THC exposure does not lead to alterations in the macroscopic structure of the brain, unless combined with high polygenic risk for schizophrenia (French *et al.*, JAMA Psychiatry 2015) or co-morbid alcohol use (Weiland *et al.* J Neurosci. 2015). In contrast, we provide preliminary evidence that adolescent Δ9-THC exposure does have long-term effects on hippocampus function, which map onto findings in some patients with schizophrenia (Kraguljac *et al.*, Neuropsychopharm. 2012). These data highlight the power of rodent models to back-translate and dissect the mechanisms underlying clinical neuroimaging observations and provide new leads to link cannabis use during adolescence and increased risk for psychiatric disorders in adulthood.

S115. Nicotine dependence in patients with schizophrenia: relationships to psychopathology, insight and severity of illness

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Background: Nicotine dependence is common in patients with schizophrenia. One meta-analysis has reported the prevalence of cigarette smoking among patients with schizophrenia three times higher than the prevalence in the general population. Reasons for the increased prevalence of cigarette smoking in schizophrenia are unclear. Studies examining the association between psychopathology and nicotine dependence in this population have found conflicting results, with some studies suggesting increased positive and negative symptoms, some suggesting no difference. This study aims to examine the relationships between psychopathology, insight, severity of illness and nicotine dependence in patients with schizophrenia.
Methods: In this cross-sectional study, 62 smoking outpatients with DSM-IV diagnosis of schizophrenia were recruited from Bakirkoy Research and Training Hospital, Psychotic Disorders Center. Positive and Negative Syndrome Scale (PANSS), Schedule for Assessment of Insight (SAI), Clinical Global Impression Severity of Illness (CGI-S) were used to evaluate psychopathologic variables. The demographic data including age, gender, duration of education, duration of illness, numbers of antipsychotic drugs used, the amount of cigarettes per day and duration of smoking were also obtained. Nicotine dependence was measured using the Fagerstrom Test for Nicotine Dependence (FTND) which is a six-item questionnaire scoring between 0 and 10. Participants were classified with high dependence (FTND >6, heavy smokers) or mild–moderate dependence (FTND <6, non-heavy smokers). We compared heavy smokers and non-heavy smokers on measures of demographics, psychopathology, insight, and symptom severity.
Results: The heavy ($n = 26$) and non-heavy ($n = 36$) smoker groups were not significantly different from one another with respect to gender, duration of education and number of antipsyhotics. The heavy smokers were older than the non-heavy smokers (45.92 ± 9.24 and 40.0 ± 7.67, respectively, $P = 0.011$). The duration of illness was longer in heavy smokers (21.57 ± 8.30; 17.55 ± 8.03, $P = 0.038$). PANNS positive (12.0 ± 4.80; 9.05 ± 3.52, $P = 0.004$), negative (17.8 ± 5.70; 13.47 ± 4.06, $P = 0.002$), general psychopathology (29.92 ± 7.38; 24.88 ± 6.27, $P = 0.008.9$) scores, CGI-S scores (1.92 ± 0.89; 1.27 ± 0.84, $P = 0.005$), amount of cigarettes per day (38.65 ± 9.44; 18.22 ± 7.98, $P < 0.0001$) were higher in heavy smokers. SAI scores (12.88 ± 4.11; 15.80 ± 3.77, $P = 0.000$) were higher in non-heavy smokers. Mean duration of smoking was longer in the heavy-smokers group (24.57 ± 8.53; 17.38 ± 6.17, $P = 0.000$).
Discussion: Our findings suggest that smoking with high dependence is associated with not only severe psychopathology but also with poorer insight and higher severity of illness than mild-moderate dependence in patients with schizophrenia.

S116. The impact of cannabis use in psychosis: reflections and analysis of motivational interviewing/cognitive behaviour therapy trials in established psychosis

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Background: Substance use disorders are common among people with psychosis and are associated with poorer prognoses. Cannabis use has been identified as a potent predictor of earlier onset psychosis, but there are inconsistent findings as to whether cannabis use has a negative impact on clinical outcomes for people with established psychosis. In this paper we investigate the relationship between cannabis use and outcomes, including whether change in cannabis use affects symptoms and functioning, in a large group of first episode and established psychosis samples with co-occurring cannabis use. By combining data from several important randomised controlled trials in psychosis samples conducted in both Australia and the UK, participants whose substance use included cannabis were compared on baseline demographic, clinical, functioning and substance use variables.
Methods: Longitudinal design, repeated measures of substance use and psychopathology will be used to estimate the effects of cannabis dose on later clinical outcomes and whether change in cannabis use is associated with change in outcomes. We examine whether our findings differ across the life-course of psychosis by comparing results across psychosis trials conducted in the UK and Australia, while adjusting for a range of confounds.
Results: We found that cannabis has no direct impact on a range of outcome variables, including positive psychotic symptoms, negative symptoms, general psychotic symptoms, hospital admissions and relapse across the phase of illness. Furthermore, there was no evidence of durable symptomatic improvements from either cutting down or abstaining from cannabis use.
Discussion: These findings call into question the utility of targeting cannabis use and its impact on psychotic symptoms directly as the 3 trials we analysed in our data set, both individually and as pooled samples, showed no significant association between change in cannabis use and psychotic symptomatology. We discuss the implications of the results for the treatment of people with co-occurring cannabis use including models of psychological intervention, and suggest approaches for designing future cannabis and psychosis treatment trials.

S117. Youth offending, the narrow line between substance abuse and psychosis

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Background: The youth criminal phenomenon does not appear as a watertight compartment, but is subject to the influences of environment modifying its genesis and realization. In our region (Balearic Island) we have reported nearly 1150 judicial measures in minors aged from 14 to 17 years. From these measurements, a significant number of cases have therapeutic internment regime.
According to a investigation financed by Spanish Observatory on Drugs and Drug Abuse called "Prevention of drug abuse in juvenile detention centers" (2013), 81% of juveniles convicted men have a high consumption of substances.
Methods: We conducted an observational study of the psychiatric evolution of the cases that performed monitoring of therapeutic internment measures. The PubMed and Embase databases were searched for relevant medical literature regarding the use of psychotropic drugs in young offenders with substance abuse whom are ultra high risk for psychosis. The database search, updated to October 2015, used the generic name of antipsychotic in combination with the terms (young/juvenile offenders, substance abuse).
Results: We have observed that cannabis and the synthetic presentation "Spice" are the most common illegal drug used by juveniles placed in youth corrections facilities in our region. Most of these adolescents experiment paranoid delusions, confusion or agitation during the exposure.
In our case, 5 new-onset psychosis were observed and needed psychopharmacology management with LAI antipsychotic.
• In our patients we have seen a global clinical and behavioral improvement after introducing Paliperidone LAI in doses between 75-150 mg/ 28d.
• The substance abuse had decrease and the psychotic phenomenons are less frequent.
Discussion: The relationship between drugs and delinquency has been widely analyzed in different studies and researches. However, the literature about dealing with juvenile offenders with mental health issues is limited. It is expected that juvenile detention centers and juvenile institutions provide mental health services to their residents. It is well known the high prevalence of young offenders in therapeutic internment regime with substance abuse and high-risk mental states of developing psychosis. We have observed that early pharmacological intervention with antipsychotics had reported good results improving the course and prognosis of the disease. In our experience Paliperidone LAI is an attractive option because psychotic symptoms gradually subsided and the significant improvement in functioning.

S118. Strong association between severe nicotine dependence and depression in smokers with schizophrenia. Results from the face-sz dataset

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Background: Subjects with schizophrenia (SZ) smoke more heavily than the general healthy population. It has been hypothesized that SZ subjects may smoke to alleviate some psychiatric symptoms, especially cognitive, negative and mood symptoms. This is called the "self medication hypothesis". However, recent epidemiological and genetic findings have suggested that tobacco smoking is a risk factor for schizophrenia. In light of these new results, evaluating whether smoking is associated with more severe clinical characteristics in schizophrenia is crucial because it could be used to develop more effective smoking cessation strategies for this population. It could also provide additional support for a potential causal role of smoking in the development of schizophrenia and for prevention in adolescents. The objective of the present study was to determine whether nicotine (NIC) dependence was associated with more severe clinical characteristics in stable SZ patients.
Methods: 240 SZ smokers (mean age = 31.9 years, 80.4% male gender) were systematically included in the network of FondaMental Expert Center for Schizophrenia and assessed with the Structured Clinical Interview for DSM-IV Axis I Disorders and validated scales for psychotic symptomatology. Severe NIC dependence was defined by a Fagerstrom questionnaire score ≥ 7. Depression was defined by a Calgary scale score ≥ 6. Ongoing psychotropic treatment was recorded.
Results: In crude analysis, SZ smokers with severe NIC dependence were more frequently depressed ($P = 0.006$), more frequently treated by antidepressant ($P = 0.045$), and had more frequently a history of childhood trauma ($P = 0.037$). None of the patients received bupropion, one of the antidepressant treatments for tobacco cessation with associated depression. In multivariate analysis, severe nicotine dependence remained associated with depression (OR = 2.442; 95% CI 1.069-5.577, $P = 0.034$) and childhood trauma (OR = 1.036; 95%CI 1.004-1.069, $P = 0.028$), independently of socio-demographic characteristics, SZ severity, treatments and alcohol or cannabis consumption.
Discussion: Our first major finding is that severe NIC dependence was associated with major depression in SZ patients independently of socio-demographic and clinical characteristics and treatments. A recent systematic review of 15 longitudinal studies on the association between depression and smoking has concluded that smoking may actually be a causal factor in the development and exacerbation of depressive symptoms in healthy subjects. Our current findings extend this assumption to schizophrenia. This could have important implications for clinical practice and encourage effort to develop smoking cessation strategies for SZ patients.

Our second major finding is that severe NIC dependence and SZ share childhood trauma as an important common risk factor. This was not demonstrated to date in previous studies. Since heavy smoking was suggested as a risk factor for SZ onset, further studies should determine if NIC dependence is a mediation factor between childhood trauma and SZ.
Altogether, our findings emphasize the need to consider tobacco smoking and major depression as crucial issues in SZ patients. This vulnerable though undertreated group should benefit from personalized strategies for smoking cessation interventions.

S119. The nature of the relationship of psychomotor slowing with negative symptomatology in schizophrenia

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Background: Psychomotor slowing is an important feature of schizophrenia and the relation with negative symptoms is not fully understood. This study aims, first, to investigate the association between negative symptoms and psychomotor slowing. Second, we want to investigate whether fine motor slowing reflects clinically observable gross motor slowing.
Methods: In 53 stabilised adult patients with schizophrenia, negative symptoms were assessed using the Positive and Negative Syndrome Scale negative subscale (PANSS-N) with two calculated factors entering the analysis: an expressivity factor and a volitional factor. Psychomotor slowing was assessed by using a modified version of the Salpeˆtrie`re Retardation Rating Scale, the Finger Tapping Test, and a writing task measuring fine psychomotor slowing.
Results: Medication status: All participating patients received antipsychotic medication at the time of testing. Mean chlorpromazine equivalent dose was 466.4 mg (SDô◦ 395.9 mg). Some patients additionally received an anticholinergic agent (nô◦ 8, 15.1%), mood stabilisers (nô◦ 10, 18.9%), SSRI (nô◦ 8, 15.1%), or tricyclic antidepressants (nô◦ 2, 3.8%).
Overall psychomotor performance: The GLM multivariate analysis yielded an overall significant difference when all psychomotor measures were entered, Fô◦ 6.489, pB.001. Highly significant group differences emerged for FCT-IT and FCT-ET but not for FCT-REIN, whereas group comparison for FTT-d performance almost reached significance (see Table 2).
Associations between psychomotor symptoms and clinical symptoms: In the patient group, the score on the SRRS, measuring clinically observable psychomotor slowing, was correlated to the score for negative symptoms on the PANSS-N, rô◦ .671, pB.001. However, SRRS did not correlate with the FCT measures (FCT-IT r ô◦ .238, p ô◦ .107; FCT-ET r ô◦ .057, p ô◦ .703; FCT-REIN r ô◦ .100, pô◦ .506) or FTT-d, rô◦ ô◦ .116, pô◦ .419, suggesting that the clinical assessment of gross motor slowing seems unrelated to fine motor slowing as measured by psychomotor tasks. In contrast, FTT-nd correlated moderately to SRRS, rô◦ ô◦ .314, pB.05.
In order to determine which processes involved in psychomotor slowing are affected by negative symptomatology, the correlation with the three FCT measures was examined. Interestingly, negative symptomatology (PANSS-N) was significantly correlated to FCT-IT, rô◦ .334, pB.05, but not to the other FCT-measures (FCT-ETrô◦ .197, pô◦ .185; FCT-REIN, rô◦ .090, pô◦ .546), which seems to indicate that high negative symptomatology is reflected in motor initiation but not in execution or planning difficulties.
In consecutive analyses, we further explored this association by investigating the link between FCT-IT and the two negative symptom factors: expressivity deficits and avolition as evaluated by PANSS-exp and PANSS-ap, respectively.
Interestingly, only PANSS-ap was associated with FCT-IT, rô◦ ô◦ .407, pô◦ .005, whereas PANSS-exp, rô◦ .060,pô◦ .689, was not. Correction for age and extrapyramidal symptoms yielded the same association between FCT-IT and PANSS-ap, r ô◦ .345, pô◦ .032 (Table 3).
Another finding of interest was that clinically observable psychomotor slowing as assessed by the SRRS correlated to both PANSS-exp, rô◦ .694, pB.001, and PANSS- ap, rô◦ .552, pB.001. Again, results remained significant when correcting for age and extrapyramidal symptoms (Table 3).
Discussion: These findings indicate that higher values of negative symptomatology*more specifically the volitional deficit cluster*affect motor initiation, indicating a heterogeneity in the PANSS-N factorial structure, and that gross and fine psychomotor functioning are affected independently.

S120. Tackling mental health stigma and discrimination by changing the name: the case against schizophrenia

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Background: Over recent years the term schizophrenia is being increasingly contested by researchers, clinicians, patients and family members. According to researchers and clinicians, the term schizophrenia is misleading: "split brain" (the literal meaning of "schizophrenia") has nothing to do with this disorder (Kingdon *et al.*, 2013); moreover, 'schizophrenia' does not provide any information about the fundamental nature (eg, pathophysiology) and psychopathological structure of the disorder (Boyle, 2004); finally, the term is of limited clinical utility, since it does not provide specific information on treatment needs, course and outcome (due to large heterogeneity of the condition defined by the term) (van Os, 2009). According to patients and their families 'schizophrenia' is a potentially harmful term, since it has a strongly negative connotation, which in turn leads to a negative self-image in persons affected by the condition; as such, the term 'schizophrenia' represents an obstacle for seeking care, a barrier to recovery, and an obstruction to the possibility for patients to find a meaning in what has happened them. No wonder if professionals and mental health users and around the world have started calling for a change of the schizophrenia name. The debate on renaming schizophrenia was prompted by the decision of the Japanese Society of Psychiatry and Neurology in 2002 to change the name from "mind-split-disease" to "integration dysregulation syndrome". This paper aims to review the literature published so far on the issue of renaming schizophrenia, in order to facilitate the examination to carefully weigh the pros and cons of the proposed changes.
Methods: A literature search was performed on PUBMED and PSYCHINFO using as MeSH terms "Schizophrenia" OR "Psychotic disorders" AND "Terminology as Topic". The search was conducted on all papers published until April 2014 in the English language: 47 papers were found, encompassing editorials, research papers, commentaries to editorials, letters, forum papers and narrative reviews.
Results: The debate on renaming schizophrenia should not be driven only by opinions, since some promising evidence already exists. This evidence is drawn from large scale (nationwide) "social experiments" and comes from the countries (ie, Japan and South Korea) where the name change had taken place. The first lesson from the Asian experiences is that a change is possible; the second is that the change may be beneficial for mental health users and their carers and professionals alike. An early effect of renaming would increase the percentage of patients informed about their diagnosis, prognosis and available interventions. This would facilitate help seeking and service uptake by patients and it would be most beneficial for the provision of psychosocial interventions, as better informed patients have generally a more positive attitude towards care and a more active involvement in their own care programs.
Discussion: Renaming schizophrenia is not just a matter of semantics, it is rather an attempt to change the iatrogenic stigma caused by the use of stigma-inducing term. This change will, however, not be useful unless accompanied by parallel changes into the legislation, services and education of professionals and of the public. What needs to be changed is the public perception of what is currently known as "schizophrenia". Simple relabeling is not likely by itself to address the problem of stigma, which arises out of background assumptions about the nature of mental disorders. Nevertheless, renaming may be a welcome initial step.

S121. Conversion into overt psychosis in individuals at ultra-high risk for psychosis: possible roles of schizotypy and basic symptoms

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Background: The aim of this study was to examine the potential links between multi-dimensional schizotypy, basic symptoms and emerging psychosis as defined by positive symptoms in individuals at ultra-high risk (UHR) for psychosis.
Methods: Sixty-two individuals (M = 37, F = 25) at UHR, diagnosed by SIPS, and 55 healthy controls (M = 26, F = 29) were invited for baseline assessments. For multi-dimensional schizotypy assessments, Chapman's perceptual aberration scale, magical ideation scale, revised physical and social anhedonia scales, schizotypal ambivalence scales, and Eysenck's impulsiveness scale were used. Basic symptoms were assessed by using the schizophrenia-specific items of the Frankfurt complaints questionnaire.
Results: Individuals at UHR were found to be higher schizotypy scores and basic symptoms at baseline. The conversion rate of overt psychosis was 36.8% during 4 years of follow-up. Cox-regression hazards ratio analysis showed that the basic symptoms at baseline [Exp(B) = 1.375, $P = 0.020$] was a significant predictor of conversion into overt psychosis in individuals at UHR.
Discussion: The addition of the self-reported basic symptoms may be useful for a risk enhancement or stratification strategy in individuals at ultra-high risk for psychosis.

S122. Is disorganized schizophrenia a risk factor for treatment resistance in schizophrenia? New evidence for a traditional subtype

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Background: Approximately 30% of patients do not respond properly to antipsychotic treatment and are considered treatment-resistant schizophrenia (TRS). Based upon several lines of evidence there is a consensus that clozapine is the best antipsychotics for TRS. The schizophrenia subtypes were removed from DSM-5 due to their uncertain clinical utility. However, disorganized schizophrenia seems to be associated with worse outcome. Our objective is to investigate if disorganized schizophrenia is a risk factor for TRS.
Methods: Two independent samples of inpatients ($n = 185$) and outpatients ($n = 196$) were assessed with the Positive and Negative Syndrome Scale (PANSS), the Clinical Global Impressions-Severity Scale (CGI-S) and the Global Assessment of Functioning Scale (GAF). Diagnosis was confirmed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). Patients were considered TRS if they fulfilled the criteria of the Schizophrenia Algorithm of the International Psychopharmacology Algorithm Project (IPAP). In the inpatient sample, non-response to antipsychotics was defined as the absence of a reduction of at least 40% in total PANSS scores. In the outpatient sample, non-response was decided in a consensus of at least two expertise clinicians according to the above mentioned IPAP criteria. Patients were classified as disorganized or non-disorganized (paranoid, catatonic, undifferentiated or residual) schizophrenia according to SCID-I. The percentages of TRS, mean scores of the total PANSS, CGI-S, GAF and age of onset were compared between the two groups. Statistical analyses were performed with SPSS 21.0.
Results: TRS was more common in disorganized schizophrenia in the inpatient sample (73.8% vs 22.4%, $P < 0.001$) and in the outpatient sample (68.2% vs 28.2%, $P < 0.001$) in comparison to non-disorganized schizophrenia. Disorganized schizophrenia also presented worse scores on PANSS, CGI-S and GAF in the acute phase (inpatient sample) and in the stable phase (outpatient sample), (all, with $P < 0.001$). As expected, disorganized schizophrenia presented a significant lower age of onset in both samples ($P < 0.001$).
Discussion: Considering that around 70% of disorganized schizophrenia patients were TRS, it seems reasonable the authors propose that patients with the disorganized subtype may benefit from clozapine as a second line agent and that this protocol should be tested in future studies.

S123. Clinical network analysis: insight in variation in symptom severity and clustering to improve schizophrenia care; a case report

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Background: In daily life, symptoms of patients diagnosed with a psychotic disorder vary over time. In one patient, Experience Sampling Method (ESM) data were used to study associations between the previous and the current assessment (networks) and differences in those networks, depending on symptom severity.
Methods: The one-year prospective follow up included 10 assessments per day for 4 days per week. Five a priory-selected symptoms were analysed: hearing voices, down, relaxed, paranoia and loss of control. First, explorative graphs were plotted. Second, regression analysis was performed including current level of one symptom as the dependent variable and all included symptoms at the previous assessment (lag) as the independent variables. Resulting regression coefficients were printed in graphs representing network analyses. Two levels of symptom severity were defined: stabile state and relapse state during which symptoms were aggravated defined by increased dosage of clozapine. Network graphs were generated for both levels of severity, separately.
Results: The explorative graphs showed day-to-day variations in hearing voices, paranoia, down, loss of control and relaxed mood. In stable state, paranoia and down acted in a two-sided positive loop, but neither was connected with hearing voices or loss of control. In relapse state, the connections between symptoms were stronger.
Discussion: Long term ESM assessment in one patient was feasible and the graphical representations of symptoms provided information that could be used in treatment. In this patient, depressive and paranoid symptoms were strongly connected. In addition, relapse was characterised by an increase in symptom clustering.

S124. Affective features and gender in psychosis: duration of illness makes a difference

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Background: Gender differences in schizophrenia are generally accepted: Men show earlier age of onset, more negative symptoms, less affective symptoms, and worse prognosis. Also, some studies showed more prominent gender differences in later than earlier disease stages.
Our Aim: 1.To test gender differences in clinical presentation and functioning in our sample. 2. To test whether duration of illness moderates these differences.
Methods: Gender differences in 262, inpatients and outpatients, affected by schizophrenia ($n = 225$) and schizoaffective disorder ($n = 37$) were compared. Symptoms were evaluated through Positive and Negative Syndrome Scale (PANSS) and its five Lindenmayer factors; functioning was measured by Global Functioning Assessment (GAF). Premorbid Intelligence Quotient (IQ) is estimated by verbal subscale of WAIS. Univariate analysis is made by t-student test, and non parametrical test (U Mann-Whitney) when necessary. A moderation analysis with simple slopes and Johnson-Neyman Technique methods is undertaken using PROCESS application.
Results: - Female patients showed later age of onset and higher Positive and Affective factors score. No statistically significant differences were found in GAF, IQ, total PANSS, and Negative, Disorganized, and Excitement factors.

- A moderating effect of duration of illness in affective symptoms was present, with statistical significance in patients with more than 17,7 years of evolution: more chronic females showed more affective symptoms (Predicting Model of Affective Factor: Duration x Gender: B = 0,1 (0,04); $P = 0{,}015$).
- This interaction, in turn, was not moderated by diagnosis (third order interaction is not significant when added to the model, Duration x Diagnose x Gender).
- This interaction, in turn, was not moderated by diagnosis.
- Duration had no moderation effect on gender differences in other Lindenmayer's factors, neither in total PANSS, IQ and GAF (table 1).

Discussion: - Our data support the common finding of earlier age of onset in males1.
- There are gender differences in positive and affective symptoms.
- Time of evolution had a moderating effect on gender differences in affective symptoms.

S125. Self-evaluation of negative symptoms (SNS): a novel tool to assess negative symptoms

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Background: Many patients with schizophrenia have negative symptoms, but their evaluation is a challenge. Thus, standardized assessments are needed to facilitate identification of these symptoms. Many tools have been developed, but most are based on observer ratings. Self-evaluation can provide an additional outcome measure and allow patients to be more engaged in their treatment. The aim of the present study was to present a novel tool, Self-evaluation of Negative Symptoms (SNS), and demonstrate its validity.
Methods: Forty-nine patients with schizophrenia and schizoaffective disorders according to DSM-5 were evaluated in order to demonstrate three components of the scale's validity: face and content validities and reliability.
Results: Cronbach's coefficient ($\alpha = 0.867$) showed good internal consistency. Factor analysis extracted two factors (apathy and emotional) that accounted for 75.2% of the variance. The SNS significantly correlated with the Scale of Assessment of Negative Symptoms ($r = 0.628$) and the Clinician Global Impression on the severity of negative symptoms ($r = 0.599$), supporting good convergent validity. SNS scores did not correlate with level of insight ($r = -0.008$), Parkinsonism ($r = 0.175$), or BPRS positive subscores ($r = 0.253$), which indicates good discriminant validity. The intra-subject reliability of the SNS revealed excellent intraclass correlation coefficients ($ICC = 0.942$).
Discussion: Taken together, the results show that the SNS has good psychometric properties and satisfactory acceptance by patients. The study also demonstrates the ability of patients with schizophrenia to accurately report their own experiences. Self-assessments of negative symptoms should be more widely employed in clinical practice because they may allow patients with schizophrenia to develop appropriate coping strategies.

S126. Cultural influences on schizotypy among British and Trinidadian adults: a latent mean comparison and event-related potential study

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Background: Schizotypy is a dimension of personality characterised by thought processes and psychological experiences which are associated with psychosis and the paranormal (e.g., paranoia, magical thinking and cognitive disorganisation). Recent psychometric research has focused on defining the latent structure of schizotypy. Despite this, there has been limited work between samples varying in culture and ethnicity, limiting cross-cultural comparisons. High schizotypal levels are associated with similar biological, cognitive and phenomenological abnormalities common in those with schizophrenia. Change of the auditory evoked P300 potential is among the most reliable biological markers of schizophrenia, with recent studies extending this to schizotypal research. The aim of this study was to explore schizotypy within an ethnic and cultural framework, investigating latent mean comparisons of schizotypal factors with P300 potential.
Methods: Participants from a White British sub-sample ($n = 351$) resident in the UK, and from an African Caribbean sub-sample ($n = 284$) resident in Trinidad, completed the Schizotypal Personality Questionnaire. Event-related Potentials (ERPs) were examined from 10 of the British sub-sample (5 high and 5 low) and 12 of the Trinidadian sub-sample (7 high and 5 low). This represented participants within the top and bottom 25% of respondents. ERPs were recorded at Fz, Cz, and Pz, during an auditory oddball task.
Results: The findings from the Trinidadian sample, at a descriptive level, suggest an attenuated P300 amplitude for the high schizotypal sub-sample. Between-group differences for sex and ethnicity were investigated using multivariate analysis of variance in relation to the SPQ 4-factor structure (cognitive-perceptual, disorganised, paranoid, and negative domains). The British sub-sample had significantly higher scores across all domains than the Trinidadian group, and men scored significantly higher on the disorganised domain than women.
Discussion: With regards to the ERP element of this study, findings within the Trinidad sub-section suggest a profile of a reduced P300 amplitude for those rating high on schizotypy, which mirrors previous psychophysiological investigations into P300 and schizotypy. Men scored higher on the disorganised factor than women. While this is a consistent finding, previous research has found that men score higher on the negative factor and women score higher on the cognitive-perceptual factor, which were not established in the present study. However, this may have been influenced by the 4-factor structure, rather than a more traditional 3-factor. Finally, between-group analysis of the subgroups indicated that the White British group scored significantly higher the African Caribbean group on the four higher-order domains. The study indicates psychophysiological and behavioural differences between the two cultural samples that warrant further investigation of trait markers of the schizophrenia spectrum.

S127. Psychotic symptoms in patients with anxiety and depression – clinical correlates and implications for psychiatric service utilization

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Background: The co-occurrence of affective and psychotic symptoms is not uncommon, and predicts poorer course and outcome of psychopathology. Previous studies have shown that psychotic symptoms in people with depression or anxiety disorders are associated with poorer response to antidepressants (Perlis *et al.*, 2011), poorer illness course, greater likelihood of service use and drug use (Wigman *et al.*, 2012).
The current study aims to examine the demographic and clinical correlates of psychotic symptoms in patients with depression/anxiety and test the hypothesis that the co-occurrence of such symptoms is associated with poorer prognosis.
Methods: Data for this study was obtained from the Camden and Islington NHS Foundation Trust (C&I), a large mental health provider serving a geographic catchment of two London boroughs, and approximately 440,000 residents. The Clinical Record Interactive Search (CRIS) was developed to enable routinely collected electronic health records to be used in research and contains full but anonymised information from over 100,000 mental health service users. We identified 4,584 patients with a diagnosis of depressive or anxiety disorder (ICD-10 F3x, F4x) and no history of psychosis (F2x, F32.2, F33.3) or bipolar disorder. Psychotic symptoms were defined as moderate to severe hallucinations or delusions as recorded on the Health of the Nation Outcome Scale (HoNOS). HoNOS is a previously validated 12-item scale used by professionals to assess risk and vulnerability in individuals with mental health problems.
Results: Of the 4,584 patients who comprised the analytic sample, 611 (13.3%) were recorded as having moderate-severe psychotic symptoms. Analyses indicated that patients with depression/anxiety with psychotic symptoms, compared with those without psychotic symptoms, were more likely to be male, of non-white ethnic origin and from socially deprived areas (Table 1). Similarly, suicidal behaviour, substance abuse and use of antipsychotics were all more

prevalent in those with psychotic symptoms. Finally, we used Negative Binomial regression with log rank, adjusted for sex and ethnicity, to test the impact of psychotic symptoms in patients with depression/anxiety on psychiatric service utilization (defined for purposes of this study as number of admissions, number of involuntary admissions and total days of admission per year). There was a 3-4 fold increase in all three measures of service utilization among patients with depression/anxiety with psychotic symptoms compared with those without psychotic symptoms (Table 2).

Table 1. Demographic and clinical correlates of psychotic symptoms

	No psychotic symptoms	*Psychotic symptoms*	*OR (95% CI)*
Male	40.9%	45.7%	1.22 (1.02-1.44)
Single	58.8%	59.9%	1.05 (0.87-1.26)
Non-white	17.7%	28.9%	1.89 (1.55-2.30)
Social deprivation	24.4%	29.1%	1.27 (1.05-1.53)
Suicidal behaviour	11.0%	22.8%	2.40 (1.94-2.98)
Substance abuse	11.3%	17.9%	1.71 (1.36-2.15)
Use of antipsychotics	14.8%	50.7%	5.94 (4.96-7.12)

Table 2. Associations between psychotic symptoms and psychiatric service utilization

Number of admission p/year	*Number of involuntary admissions p/year Adjusted OR (95% CI)*	*Total admission days p/year*
3.70 (2.84-4.82)	4.45 (2.08-9.52)	3.34 (2.01-5.56)

Discussion: Patients with depression/anxiety with psychotic symptoms differ significantly from their counterparts without psychotic symptoms on demographic and clinical characteristics. Psychotic symptoms, even in the absence of a diagnosed psychotic disorder, are associated with a more severe form of psychopathology, poorer prognosis and more frequent and intensive use of psychiatric services.

S128. Schizotypal personality questionnaire-brief: factor structure analysis in general population in France

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Background: The study, in the general population, of schizotypal traits and its determinants has been recently proposed as a way toward the understanding of aetiology and pathophysiology of schizophrenia. To do that, self-report measures of psychometric schizotypy have been shown to be valid, inexpensive and non-invasive tools. A shorter version of the widely used Schizotypal Personality Questionnaire has been extensively investigated in different countries particularly in samples of students or clinical adolescents, but at our knowledge not in a French version. Few studies used a Likert-type scale format, which could be better able to allow partial endorsement and to detect more defended respondents than the forced choice format.
Methods: We examined factor structure and internal reliability of a French version of the Schizotypal Personality Questionnaire-Brief (SPQ-B), in a Likert format, in a representative sample of the general population of the city of Créteil, in France ($N = 233$). We investigated the dimensional structure of the French version of the SPQ-B with a Principal Components Analysis (PCA) followed by a promax rotation. Factor selection was based on Eigenvalues over 1.0 (Kaiser's criterion), Cattell's scree plot test, and interpretability of the factors. Items with loadings greater than 0.4 were retained for each dimension. We calculated Cronbach's Alpha for total SPQ-B and for each dimension.
Results: Our sample was constituted of 131 women and 102 men. The mean age was 52.7 ± 1.2 years. SPQ-B Likert total scores ranged from 22 to 84 points (mean = 43.6 ± 13). Factor analysis resulted in a 3-factor solution that explained 47.7% of the variance. Factor 1 (Disorganized; 10 items) includes items related to "odd behavior", "odd speech", as well as "social anxiety", one item of "constricted affect" and one item of "ideas of reference". Factor 2 (Interpersonal; 7 items) includes items related to "no close friends", "constricted affect", and three of the items of "suspiciousness". Factor 3 (Cognitive-perceptual; 5 items) includes items related to "ideas of reference", "magical thinking", "unusual perceptual experiences" and one item of "suspiciousness". Coefficient Alpha for the three subscales and total scale, respectively, were 0.81, 0.81, 0.77 and 0.88.
Discussion: Factor analysis of the French version of the SPQ-B in a Likert format confirmed the three-factor structure of schizotypy. Some differences with the original version do exist and were discussed. The SPQ-B and its subscales demonstrated good internal reliability.

S129. The relation between childhood trauma history and psychotic symptoms in patients with first episode psychosis

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Background: To identify the relation between childhood trauma on psychotic symptoms in 60 patients with first-episode.psychosis.
Methods: Sixty First Episode Psychosis patients and sixty normal controls were included into the study. Psychopathology was assessed by Positive and Negative Syndrome Scale (PANNS) at first admission. Childhood trauma was assessed by Childhood Trauma Questionnaire (CTQ) after discharge. CTQ evaluates emotional, physical and sexual abuse and physical and emotional neglect during childhood.
Results: We found significant relation between positive symptoms and history of childhood trauma. Childhood physical abuse (CPA) score correlated to PANSS conceptual disorganization score ($P = 0.023$). Childhood emotional neglect (CEN) score was correlated to PANSS delusions ($P = 0.006$) and hallucination ($P = 0.003$) of the patients score respectively. Also histories of childhood sexual abuse (CSA) was found in correlation with PANSS delusions ($P = 0.015$) and hallucination ($P = 0.002$) items of the patients respectively. There were significant gender differences between patients and controls, sexual abuse was significantly related to psychosis in women compared to men. PANSS-General Psychopathology Scale items somatic concern ($P = 0.029$), anxiety ($P = 0.042$), guilty ($P = 0.021$) and depression ($P = 0.019$) was found to be related with CPA.
Discussion: Our findings suggest that childhood trauma may be related to positive symptoms of first episode psychosis There is a high prevalence on psychotic symptoms of childhood trauma in patients with first-episode.psychosis.

S130. Trajectories of depression in a pragmatic, randomized trial

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Background: Depression is common in psychotic disorders with point prevalence figures in schizophrenia around 25%. Depression is associated with a poorer quality of life, increased rates of relapse and increased mortality related to suicide. Trajectory analyses highlight heterogeneity in treatment response, but have not been studied thoroughly concerning depression in pragmatic antipsychotic drug trials. We aimed to investigate different trajectories of treatment response defined by level and change in Calgary Depression Scale for Schizophrenia (CDSS) sum score in patients suffering from schizophrenia spectrum disorders.
Methods: 226 patients >18 years admitted to an acute psychiatric ward due to psychosis were consecutively included. The study design was pragmatic, thus entailing a clinically relevant representation. The Positive sum score from the Positive and Negative Syndrome Scale for

Schizophrenia (PANSS), a diagnosis within Schizophrenia spectrum versus non-spectrum psychoses, gender and being medication naive on baseline were entered into the models with CDSS sum score as the primary outcome. Visits were at baseline (T1), about 4 weeks (T2), 14 weeks (T3) and 27 weeks (T4). Latent Growth Curve (LGC) and Growth Mixture Models (GMM) were conducted with Mplus 7.4.
Results: One third of the 226 patients were female (32.7%). The mean age at the first measurement occasion was 34.1 (SD 13.5). About half the patients had not been medicated with antipsychotic drugs at an earlier point of time (44.2%).
A three class model showed best fit with data, with a high and a low-level class based on CDSS sum score (14.7% and 69.6%). The third small class (15.7%) started at a very high level and decreased to the low-level class at the second measurement. A multi-sample piecewise growth curve model of the total sample showed that the schizophrenia group started at a lower depression level (b = 5.44, p < .001) compared to the other diagnoses group (b = 7.84, p < .001), dropped to T2 (b = -0.62 per week, p < .001) and did not change any more. The other group of psychoses dropped to about five in T2 (b = -0.74 per week, p < .001), kept at this level to T3 and then reduced to T4 (b = -0.09, p < .001). Predictors of level and changes in CDSS: The final predictor model fitted data well ($\chi2 = 16.8$, df = 19, p = .60, CFI = 1.00, TLI = 1.03, RMSEA = .000, RMSEAc.i. = .000-.051, RMSEA close fit = .94). Changes in CDSS were associated with change in PANSS positive in all time intervals (b = 0.18, $P < 0.001$; 0.21, $P < 0.023$; 0.43, $P < 0.001$). Reduction in PANSS positive from T1 to T2 was strongest among medication-naive patients (-0.61, $P < 0.01$). Lower baseline-level of CDSS was associated with being diagnosed within schizophrenia-spectrum compared to other psychoses (b = -2.63, $P < 0.001$). Change in CDSS from baseline to T2 was associated with a schizophrenia spectrum-diagnosis with a lower reduction in the schizophrenia group (b = 0.64, 0 < 0.02). Change in CDSS was also associated with schizophrenia-spectrum in the interval T2-T3 (-0.25, $P < 0.003$).
Discussion: We found support for three distinct trajectories for change in CDSS. Clinically important, an early responding and a treatment refractory group were identified. Generally, medication-naive patients responded better. Patients with improvements in PANSS Positive score also had larger reductions in CDSS sum score. Schizophrenia spectrum patients generally scored lower on CDSS. We could not identify a post-psychotic depression group in the first 6 months of the trial.

S131. Introduction and validation of the questionnaire for psychotic experiences: a clinical tool to assess psychotic symptoms across diagnoses

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Background: Psychotic experiences are highly prevalent across many psychiatric, neurological and medical disorders, but also in non-clinical subjects. Yet, investigation of these symptoms is largely confined to the diagnostic boundaries of schizophrenia spectrum disorders. As a result, the majority of rating scales are specifically designed for these disorders, and not applicable for patients with alternate diagnoses. This has led to underdiagnosis and, consequently, undertreatment of psychotic symptoms in other diagnostic categories. To overcome this limitation, we developed a new clinical tool, the Questionnaire for Psychotic Experiences (QPE), applicable to all psychotic symptoms regardless of diagnosis.
Methods: Using input from international experts and consumer groups and by selecting items from existing questionnaires, we developed a 50-item structured interview to assess presence, severity and phenomenology of psychotic symptoms. The questionnaire was completed by 205 participants, including patients with schizophrenia spectrum disorders, hearing impairment, Parkinson's disease, Dementia with Lewy Bodies, Alzheimer's disease, Charles Bonnet syndrome, delirium and recent cardiac surgery. Structure and construct validity were assessed in this comprehensive sample.
Results: Average questionnaire completion time was 30 minutes. Principal Component Analyses (PCA) yielded four dimensions for both auditory and visual hallucination subscales, and two dimensions for the delusion subscale. The PCA models differed between diagnostic categories implying good discriminating quality between different types of psychotic experiences. Good construct validity was demonstrated.
Discussion: The QPE is the first instrument to reliably investigate psychotic symptoms transdiagnostically with good psychometric properties. It can be considered a valuable tool in both clinical and research settings.

S132. Searching across the diagnostic divide: towards a mechanistic understanding of disease progression through symptom and cognitive trajectories

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Background: Schizophrenia research is increasingly witness to a shift in focus from narrowly defined syndromes to broadly relevant notions of disability. Concurrently, case-control studies in chronically ill individuals are being eschewed by prospective and early, transdiagnostic cohorts, which are better equipped at disentangling mechanisms of change with the ultimate goal of disease prevention or delay. Here we present a series of prospective studies in adolescents and young adults with major mood and psychotic disorders to clarify how symptom and cognitive trajectories may explain functional changes associated with illness progression.
Methods: Two overlapping cohorts of adolescents and young adults were independently recruited from specialised youth mental health outpatient services. Individuals were assessed at two time-points, at least one year apart. In one study, various symptom and socio-cultural measures were administered to individuals with attenuated psychotic syndromes, whereas detailed neuropsychological testing, as well as clinical and functional assessments, were conducted on a separate cohort with established recent-onset disorders.
Results: Out of 696 participants (15-24 years old), 27% ($n = 120$) experienced remission of clinical depression at follow-up. Remission from depression was linked to reductions in self-reported disability compared with those who instead developed depression ($P < 0.001$), although disability still remained impaired by normative standards. In a smaller cohort of individuals (12-35 years old) diagnosed with schizophrenia-spectrum illnesses ($n = 35$), bipolar disorder ($n = 61$) and major depression ($n = 71$), symptom and cognitive changes did not differ between diagnoses. Three cognitive subgroups emerged through cluster analysis, characterised by improved memory or vigilance, and psychomotor slowing. Reductions in residual positive and negative symptoms were differentially observed in the improved memory and vigilance subgroups ($P < 0.05$). Importantly, cognitive improvers reported a reduction in disability ($P < 0.01$) and were more likely to be in paid employment at follow-up ($P < 0.01$), independently of any symptom changes. Whereas cognitive change was strongly linked to functional change, symptom improvement was uniquely associated with better quality of life at follow-up ($P < 0.05$). Preliminary path modelling further demonstrated that a latent cognitive functioning factor was the single, strongest predictor of functional outcome 12-to-36 months following time of initial presentation, while controlling for relevant clinical factors ($\beta = 0.33$, $P < 0.01$).
Discussion: Improvements in depressive, negative and positive symptoms were linked to improved quality of life, and in some cases, improved functional outcome. By comparison, improved memory and vigilance were more strongly associated with a reduction in overall disability and an increase in economic participation, suggesting that cognitive and brain changes in fronto-temporal systems may contribute to functional deterioration and disease progression in a subset of individuals with major mood or psychotic syndromes. By examining shared phenotypes across the psychiatric spectrum, it is becoming clearer that earlier, diagnostically constrained findings have

much greater relevance across disorders and illness stages than previously thought. Further, the current findings reinforce the emerging perception that the heterogeneity of syndromal presentations is likely the result of various combinations and permutations of shared phenotypes spanning arbitrarily defined nosological boundaries. Examination of phenotypes and trajectories in transdiagnostic, birth cohort and family studies is now warranted.

S133. Bayesian confirmatory factor analysis fails to confirm five-factor model of the positive and negative syndrome scale for schizophrenia (PANSS) in a representative Brazilian sample

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Background: Schizophrenia is marked by extensive clinical heterogeneity that causes several challenges for stablishing accurate diagnosis. The Positive and Negative Syndrome Scale (PANSS) is widely used as an instrument to assess symptomatology. The five-factor model is the most replicated model in studies analyzing the subjacent structure underlying symptoms profiles. However, there is no confirmatory factor analysis (CFA) study with good fit indexes. Since CFA hypothesizes that an item loads on only one factor (no items have cross-loadings), a Bayesian confirmatory factor analysis (BCFA) would be more appropriate to a dimensional expectative on schizophrenia. The aim of this study is to perform a Bayesian CFA on the PANSS in patients with schizophrenia.
Methods: The sample comprised 757 individuals with confirmed diagnosis of schizophrenia, schizoaffective disorder or schizophreniform disorder. The mean (SD) age was 34.58 (10.83) years and 64% were male. Age of onset and duration of illness means were 21.94 (7.93) and 12.63 (9.81), respectively. All patients were receiving antipsychotics. The model chosen was composed of the following factors: Negative, positive, disorganized, excited and depressed according to Wallwork and colleagues. We conducted a CFA with weighted least squares using a diagonal weight matrix with standard errors and mean- and variance-adjusted estimator with polychoric correlation matrix to explore the goodness of fit of the model. We assessed the fit of the model considering Comparative Fit Index (CFI) and Non-Normed Fit Index (NNFI) > 0.95, the Root Mean Square Errors of Approximation (RMSEA) < 0.06 and Weighted Root Mean Square Residual (WRMR) < 1.0. The Bayesian CFA use the estimator bayes and has only one fit index, which is the Posterior Predictive *P*-value (PPP) and it's confidence interval (CI) of 95%. PPP values near of 0.5 and a CI centred on zero suggests a good fit-index.
Results: The model proposed by Wallwork and colleagues and tested by CFA in our sample had the following fit indexes: RMSEA = 0.101 (90% CI: 0.096–0.106), CFI = 0.917 and NNFI = 0.902 and WRMR = 2.032. Since the model had poor fit indexes by CFA, a BCFA was performed. The PPP value was 0.001 and CI 43.248 - 168.026, which once again indicates a poor fit-index.
Discussion: Both CFA and Bayesian had poor fit indexes. Even a more flexible approach such as the Bayesian CFA failed. These results suggest that a dimensional approach (i.e. factor analysis) does not represent the true utility for the PANSS. Other strategies should be investigated to tackle the heterogeneity challenge on schizophrenia, such as combining subtyping and dimensionality with latent variables.

S134. Risk factors for aggression in first episode psychosis – a naturalistic database study in Singapore

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Background: There is an increase aggression among those with mental illness especially amongst those with a psychotic illness.
Methods: In this naturalistic database study, 794 patients accepted into Early Psychosis Intervention Programme(EPIP) services in Singapore were recruited. Diagnosis was made based on SCID 1 (Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), Axis I Disorders). Information about DUP and sociodemographic characteristics and aggression was collected from patients and relatives. Aggression towards others, was further categorized to level 1 (battery with no physical injury) and Level 2 (Battery with physical injury, sexual assaults, use of weapon). Positive and Negative Symptom Scale (PANSS) and Global Assessment of Functioning (GAF) Scale were used as tools to assess the severity of symptoms and functioning of the patient. The main reasons for presentation to services were examined. The proportion of individuals presenting with aggressive behaviour was determined and these individuals were compared to those who were not aggressive on a range of variables including sociodemographic, diagnoses and PANSS scores.
Results: Of the total sample of 794 patients, a total of 28.4% presented with aggression at first contact with services; of whom 65.3% were level 1 aggression and 34.7% were level 2 aggressions. 71.6% of the patients did not present with aggression at baseline. Amongst all the diagnoses that the patients had, there was a positive co relation with aggression (both level 1 and 2) between those with a diagnosis of Bipolar affective disorder, current phase manic with psychotic symptoms. Also those with longer DUP and those of Indian ethnicity had more level1 aggression, at first contact with services. There were no differences in gender, marital status, age and employment. The mean total PANSS scores did not differ significantly among the three groups. However, the scores on 'Hostility' was significantly higher in those with both level 1 and 2 aggression as compared to those without aggression at baseline.
Discussion: This study found a positive correlation between increased aggression at baseline and longer DUP, diagnoses of Bipolar affective disorder, certain ethnic groups and increased scores on, hostility.

S135. Social media in first episode psychosis: a linguistic analysis

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Background: Social media platforms have become tools for capturing data pertaining to thoughts, behaviors and emotions in the forms of explicit commentary, patterns and frequency of use, as well as in the intricacies of language. Analyzing user data through social media sites like Facebook, Twitter and Tumblr has proven successful in extracting signals for characterizing the onset of depression, predicting vulnerability to depression and predicting significant postpartum changes in emotion and behavior. We hope to asses and obtain signals for characterizing the presence of and onset of psychotic symptoms.
Methods: Participants with psychotic disorder, mood disorders and healthy controls were asked to give access to their Social Media by 'adding as friend' or 'following' them. Two year history of their Social Media activity and commentary was then extracted from Facebook, Twitter, Tumblr or Reddit. Text analyses were done that examined text coherence, content and structure. Data was analyzed using Language Inquiry and Word Count (LIWC).
Results: Participants with psychotic disorders differentiated themselves in the frequency of use of certain words, verbs and prepositions. Of the people the preliminary algorithms identify as psychotic, 87% of them have a mental illness, meanwhile correctly recognizing participants with psychotic disorders from participants with mood disorders and healthy controls 64% of the time. Of the people whom the model predicts as psychotic, 67% are actually psychotic.
Discussion: A psychosis specific signal may be apparent in the social media activity of individuals with psychotic disorders. Social media based language and pattern analysis holds the potential for gathering objective, non-invasive, easily accessed, indicators of psychotic symptoms.

S136. The factor structure of psychotic symptoms in early psychosis

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Background: Psychotic symptoms are often described as having a 3-factor structure comprised of negative, reality distortion and disorganisation domains. The factor structure may be more extensive than this, however, it is also likely to be hierarchical in nature and may not be evident in early psychosis. In particular the disorganisation domain is reported to be the most unstable of all the domains. Establishing the factor structure of symptom dimensions is important to inform the nosology of mental disorders and, indeed, the results of factor analysis has influenced the diagnostic criteria for certain DSM-V disorders. We aimed to report on the hierarchical nature and temporal stability of the factor structure of psychotic symptoms in early psychosis.
Methods: Participants were recruited after referral to the DETECT Early Intervention in Psychosis Service in Dublin, Ireland between February 2005 and July 2014. Participants were aged 16-65 years old and those with first episode affective or non-affective psychotic disorders were included in the study. Psychotic symptoms were evaluated at both time points with the Structure Assessment of Positive Symptoms (SAPS) and the Structured Assessment of Negative Symptoms (SANS); individual symptom items were excluded from analysis if they occurred at $<5\%$ prevalence in the whole sample. Diagnosis was established with the SCID-IV. Inter-rater reliability for the SAPS and SANS was excellent. Lower and higher order factors were established with Principal Components Analysis (PCA) and were subjected to the Schmid Leiman transformation to establish the relative contribution of higher vs. lower order factors to each symptom. Funding was provided for the study by the Health Research Board of Ireland and ethical approval was granted.
Results: A total of $n=623$ participants were evaluated at FEP presentation and of these $n=397$ were re-assessed at 1 year (i.e. 64% follow-up rate). In total 48 SAPS and SANS items were included in the FEP analysis and 27 items included in the 1 year analysis. At FEP presentation, 13 lower order and 6 higher order factors were evident. At 1 year assessment, 6 lower order and 4 higher order factors were evident. At both time points the majority of the variance in almost every symptom domain was explained by higher order factors. A negative domain was apparent at both FEP and 1 year. A disorganisation domain was apparent at FEP presentation but not at 1 year. A poorly-circumscribed reality distortion domain was apparent at FEP presentation and this was replaced by a well-circumscribed positive domain at 1 year.
Discussion: The factor structure of the SAPS and SANS is hierarchical and multi-dimensional in early psychosis. Psychotic symptom domains vary in temporal stability in early psychosis, with negative symptoms being most stable and positive/disorganised symptoms least stable. The factor structure of the SAPS and SANS becomes more parsimonious and easy to interpret clinically at 1 year, although this may be related to the fact that symptoms are less prevalent at 1 year than at presentation. Similar analyses should be extended to include symptom domains other than positive, negative and disorganised.

S137. The associations between paternal age, age at onset of psychosis in patients and schizotypal traits in general population

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Background: Advanced paternal age is associated with schizophrenia susceptibility in offspring and with younger age at the illness onset, independently of the variety of examined factors (maternal age, heredity, birth complications, etc.). Several factors were hypothesized to mediate this association, such as de novo mutations in paternal germ cells and selection into late fatherhood. However, little is known about the relation between paternal age and schizotypal traits in the general population. In order to resolve whether this association reflects a pathogenic process distributed dimensionally across the general population, we evaluated the association of paternal age with the age at the illness onset in patients, and with subclinical schizotypal traits in a representative sample of healthy adults from Serbia.
Methods: We examined 52 patients with schizophrenia-spectrum disorder (59.6% male, mean age 29.33 ± 5.96, illness duration 5.23 ± 4.73 years) and 51 healthy adults (45.1% male, mean age 29.80 ± 6.34 years). All participants were assessed using the socio-demographic questionnaire and The Family Interview for Genetic Studies (FIGS). The control group was additionally assessed with The Structured Interview for Schizotypy-Revised (SIS-R). Partial correlation analyses (adjusted for age, sex, heredity-FIGS) were used to explore the associations between paternal age, age at the illness onset and SIS-R items. Study was performed in collaboration with the EU-GEI research network.
Results: Patients did not differ from controls in terms of age and sex, but had lower IQ ($P=.00$) and less education ($P=.00$), as expected. Mean paternal ages were similar in both examined groups (patients 29.50 ± 5.09, controls 29.74 ± 5.04 years). In patients, paternal age showed significant negative correlation with the age at the illness onset ($r=-.33$, $P=.03$). In controls, when SIS-R scores were grouped into the positive and negative-disorganized dimensions, their associations with paternal age were missing. However, partial correlation analyses which included particular SIS-R items revealed significant associations with subclinical schizotypal traits: hypersensitivity ($r=-.36$, $P=.01$) and depersonalization ($r=.41$, $P=.01$), and a trend towards significance for the poverty of content of speech ($r=.26$, $P=.08$).
Discussion: Present research demonstrates that advanced paternal age substantially contributes to the schizophrenia risk by showing that the association between aforementioned feature and earlier age at the illness onset extends to the increased level of schizotypal traits in healthy population. Recent research linked older paternal age and schizophrenia risk with a molecular finding of longer telomere lengths, suggesting shared genetic susceptibility. In addition to genetic changes, altered epigenetic processes (such as parental imprinting) may also underlie this association. Our findings should encourage research concerning the largely unknown mechanisms underlying the association of advanced paternal age with subclinical schizotypy in the general population.

S138. Delusions in first-episode psychosis: factor analysis of twelve types of delusions and their demographic and clinical correlates

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Background: It is remarkable how, although delusions represent one of the core symptoms of schizophrenia and related psychotic disorders, very few studies have investigated distinct delusional themes. Studies to date have generally focused on delusions overall, regardless of their specific type. In this study, we made use of in-depth clinical research data from a large sample of hospitalized first-episode psychosis patients to test hypotheses related to delusional thought content. First, we conduct an exploratory factor analysis of the 12 delusions items of the Scale for the Assessment of Positive Symptoms (SAPS). Then, using the extracted factors obtained via factor analysis, we tested a priori and exploratory hypotheses. A priori hypothesis referred to the prevalence of delusional themes, the relation between persecutory delusions and demographic variables, and the linkage between depression and persecutory/grandiose delusions. Exploratory research questions pertained to the relationship between delusional themes and other symptom domains (i.e., hallucinations and negative symptoms), childhood adversity, religious affiliation, and substance abuse/dependence.
Methods: A total of 245 consecutively admitted patients with first-episode psychosis were assessed using the SAPS, Scale for the Assessment of Negative Symptoms (SANS), Positive and Negative

Syndrome Scale (PANSS), Structured Clinical Interview for DSM-IV Axis I Disorders (SCID), Childhood Trauma Questionnaire–Short Form (CTQ-SF), Trauma Experiences Checklist (TEC), Parental Nurturance, Parental Harsh Discipline, Violence Exposure, Friends' Delinquent Behavior, and School Connectedness Scale. After performing Principal Component Analysis (PCA), all hypothesis tests and exploratory analyses were carried out using chi-square tests, Mann-Whitney U tests, analysis of variance (ANOVA), and Pearson or Spearman correlations, as appropriate.
Results: PCA revealed five distinct components: Delusions of Influence (delusions of being controlled, mind reading, thought broadcasting, thought insertion, and thought withdrawal), Affective Delusions (grandiose and religious delusions), Paranoid Delusions (persecutory delusions and delusions of reference), Other Delusions (delusions of jealousy and of sin or guilt), and Somatic Delusions. The most prevalent type of delusion was Paranoid Delusions, and such delusions were more common at older ages of onset of psychosis. Delusions of Influence were significantly correlated with the severity of hallucinations and negative symptoms. We ascertained a general relationship between different childhood adversities and delusional themes, and a specific relationship between Somatic Delusions and childhood neglect. Moreover, we found a progressive increase of severity of Delusions of Influence and Other Delusions in patients who did not take drugs, who abused, and who were dependent once from cannabis and stimulants.
Discussion: The inter-relationships among delusional themes that we found are generally consistent with the few previous factor analytic studies. We acknowledge the primacy of Paranoid Delusions and their association with older age could be consistent with a cognitive model of persecutory delusion development. We confirm the association between delusions and childhood adversities as well as substance abuse, and there appears to be some specificity with distinct delusional themes. Delusions are a heterogeneous phenomenon. Our results support the awareness of delusions not as a unitary symptom type, but rather as different experiences with varying prevalence and correlates.

S139. Is a narrow definition of schizophrenia more heritable than when we embrace the full spectrum of the illness? Heritability of schizophrenia and schizophrenia spectrum in the nationwide Danish twin and health registers

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Background: Twin studies have provided strong evidence for the influence of both genetic and environmental factors on the risk of developing schizophrenia. Schizophrenia has been shown to have a higher heritability than most other psychiatric illnesses, and when expanding the outcome to include the spectrum of schizophrenia, we expect to find a lower rate of genetic influence on the phenotype. With population-based ascertainment, strict diagnostic criteria and a considerable follow-up time we optimize the estimates of heritability by applying a novel statistical method accounting for all censored observations.
Methods: Linkage of two nationwide registers, the Danish Twin Register and the Danish Psychiatric Case Register, identifies a sample of twins born 1951-2000 ($N = 31524$ pairs). Liability threshold models adjusting for censoring and including inverse probability weighting is used to estimate heritability of the diagnoses of schizophrenia and schizophrenia spectrum disorder.
Results: We find the variance of liability explained by additive genetic effects of 77% for schizophrenia and 73% in schizophrenia spectrum, respectively.
Discussion: The key strength of this study is that a novel statistical method accounting for censoring in the follow-up period is applied to an unbiased, nationwide twin sample. Results indicate a substantial genetic risk of illness covering both a broad and a narrow phenotypic outcome (with almost similar estimates of heritability when studying schizophrenia and schizophrenia spectrum). This could reflect that the genetic risk for disease is not restricted to a narrow illness definition, but includes a broader phenotype and furthermore also reflect a robustness of the basic concepts of the disorder despite observed heterogeneity in the clinical presentation across the spectrum of schizophrenia.

S140. Empirically based qualitative and quantitative variations on the psychosis continuum in the 'HowNutsAreTheDutch' population sample

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Background: Subclinical psychotic experiences are common in the general population and form a paradox. On the one hand, psychotic experiences have a relatively high prevalence in the general population and the majority of such experiences is transient. Even most individuals considered to be at Ultra High Risk (UHR) do not develop a clinical psychotic disorder. On the other hand, psychotic experiences are associated with a large number of concurrent mental health problems. Even in individuals at UHR who do not develop a clinical psychotic disorder, psychotic experiences are associated with mental health problems and poorer psychosocial functioning. A challenge for both researchers and clinicians is to adequately distinguish those with benign experiences from those with more pathological psychotic experiences. One possible explanation for this is that most research on psychotic experiences has focused exclusively on positive psychotic experiences. However, psychosis is currently conceptualized as a multidimensional construct. Another possible explanation may be that they form a heterogeneous concept as not all experiences may be pathological in nature. The goal of the present study was to perform quantitative and qualitative examinations of the heterogeneity of individuals reporting subclinical psychotic experiences in a unique Dutch internet-based general population sample.
Methods: The HowNutsAreTheDutch study is a large-scale crowdsourcing project, and its aims are twofold: to (i) investigate the continuity of multiple mental health dimensions in the Dutch population and (ii) gain more insight into the interactions between mental strengths and mental vulnerabilities/problems. Positive and negative subclinical psychotic experiences were measured with the Community Assessment of Psychic Experiences (CAPE) in $n = 2870$ individuals. The prevalence of these experiences and their associations with demographics, affect, psychopathology and quality of life were investigated first. Next, Latent Class Analysis (LCA) was used to identify data-driven subgroups with different symptom patterns. These subgroups were also compared on aforementioned factors.
Results: Subclinical psychotic experiences were commonly reported. Prevalence rates differed strongly between items, ranging from 1-89% (mean: 21% for positive and 56% for negative experiences). Both positive and negative psychotic experiences were associated with younger age, more negative affect, anxiety and depression and less positive affect and quality of life. Seven latent classes were identified that were labeled as 'Mentally fit', 'Lethargic', 'Blunted', 'Distressed', 'Spiritual', 'Grandiose', and 'Pathological'. These classes demonstrated both quantitative differences in the number/severity of reported psychotic experiences and qualitative differences in the patterns of reported experiences.
Discussion: Subclinical psychotic experiences show both dimensional severity variations and discrete symptom pattern variations across individuals in the general population, suggesting that, to understand and capture all interindividual variations in subclinical psychotic experiences, their number, nature and context should all be considered at the same time. Only some psychotic experiences may lay on a true psychopathological psychosis continuum. Taking into account the base rate in the population as well as the context of psychotic experiences (i.e. the larger pattern in which they occur) could help to determine whether such experiences should be interpreted as a warning signal or not. This may help us to identify those individuals who are at most risk for developing mental health problems and may guide services of early detection and intervention.

S141. Mortality in first episode psychosis: a 20-year follow-up of the Dublin first episode psychosis cohort

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Background: Evidence has mounted globally that people with psychotic illness have higher mortality rates than the general population. It remains unclear as to whether this mortality gap has widened or narrowed in recent years, as would be expected given improvements in mental health services and the shift towards more integrated community-based services. In real terms, this equates to a shorter life expectancy for some of up to 20 years. There have been several explanations proposed to account for higher mortality rates in those with a psychotic disorder. Explanations range from unhealthy lifestyle (smoking, alcohol use, and obesity) to inadequate access to good-quality physical healthcare. There is also concern regarding the possible adverse side effects of anti-psychotic medication. Finally, those with mental health difficulties are often more vulnerable than their peers, for example are often unemployed, single, and/or isolated. These factors are considered to contribute to the risk of poor health and premature mortality. The risk of suicide and accidents among those with schizophrenia is high; however evidence as to whether excess mortality is predominantly due to unnatural or natural causes of death remains equivocal. The aim of this study was to calculate the mortality of this cohort in comparison to that of the general population and to examine the clinical and social factors that may impact on increased risk of premature death in psychosis.
Methods: This study forms part of a 20 year follow-up study of a cohort of 171 individuals with a first episode psychosis (FEP), originally identified between 1995 and 1999 in a community mental health service in Dublin, Ireland. The current presentation focuses on mortality among the FEP cohort and the factors related to it. Once ethical approval was obtained, individuals were traced by the project administrator. Mortality was established by reviewing information provided by the Central Statistics Office and the General Registry Office in Ireland, using name, sex, and date of birth. We identified all occurrences and causes of death in the cohort by matching death certificates to deceased cohort members. Crude mortality rates were calculated for all causes of death (natural and unnatural). Date of first presentation to service was used as date of entry point and date of death or end of follow up as the end point (whichever came sooner). Relative survival models were conducted to compare the proportion of observed survivors in the FEP cohort to the proportion of expected survivors in the general population.
Results: Age at point of entry to the study was the only variable associated with an increased risk of all-cause mortality. Mean age (at pointy of entry) of FEP cohort members who were still alive at follow up was 28. Mean age (at pointy of entry) of FEP cohort members who were deceased at follow up was 39. There were no other significant relationships. The explanatory variables in the model were assessed when the dataset was reduced to those who died by natural and unnatural causes. The analysis of this data did not yield any statistically significant results after the Bonferroni multiple test adjustment.
Discussion: Findings suggest that the mortality gap in people with schizophrenia and other psychoses remains high and may be wider for unnatural-cause mortality than previously reported. Those with a diagnosis of psychosis still do not appear to be benefiting from improvements in healthcare and services to the same degree as the general population.

S142. Has deinstitutionalization affected inpatient suicide? Psychiatric inpatient suicide rates between 1990 and 2013 in Israel

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Background: Suicide of psychiatric inpatients is a well-recognized but under researched problem. The aim of this study is first to examine factors affecting the rates of inpatient suicide, such as deinstitutionalization, and to analyze the clinical factors associated with suicide among psychiatric inpatients.
Methods: The National Israeli Psychiatric Hospitalization Case Registry was used to study inpatient suicide between 1990 and 2013. Clinical risk factors for inpatient suicide were examined in a nested case control design.
Results: Between 1990-2013 there were 326 inpatient suicides at an average of one inpatient suicide per 1614 admissions. A significant decline in rates of suicide per admission over time ($P < 0.001$) was associated with a reduced number of beds per person in the population ($P < 0.001$) and a decline in overall nationwide suicide rates ($P = 0.001$). Clinical risk factors for inpatient suicide were: affective disorders (OR = 5.95), schizoaffective disorder (OR = 5.27), schizophrenia (OR = 3.82), previous suicide attempts (OR = 2.59), involuntary hospitalization (OR = 1.67), and more previous hospitalizations (OR = 1.16,). A multivariate model had a sensitivity of 27.3% and specificity of 95.3% for inpatient suicide, suggesting a positive predictive value of a high-risk categorization of 0.4%.
Discussion: The absolute number and rates of inpatient suicide per admission have decreased over the years, probably due to the decreased number of beds decreasing total time at risk for inpatient suicide. As expected, patients suffering from affective and psychotic disorders, and patients who had previous suicide attempts have the greatest risk of inpatient suicide. However, clinical characteristics do not enable identification of patients who are at risk for suicide.

S143. Prevalence and persistence of psychotic-like experiences in Hong Kong

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Background: Psychotic-like experiences (PLEs) are poorly-understood phenomena referring to subclinical psychotic experiences that are reported by individuals without psychotic disorder. Individuals who reported PLEs have elevated risk of developing clinical psychosis, while persistent PLEs might increase the risk further. Studying PLEs could potentially provide better understanding to the development of psychiatric disorders. The current study aims to provide a general picture of the prevalence and persistence of PLEs in the general population of Hong Kong.
Methods: Current on-going study is a 2-year follow-up on the participants who reported PLEs in the Hong Kong Mental Morbidity Survey 2010(HKMMS) – a territory wide epidemiological study carried out between 2010 and 2013, targeted at Chinese residents aged 16-75 years old in the general population. The current on-going study conducts follow-up on subjects who reported PLEs in the HKMMS while having no known psychotic disorder. Prevalence of PLEs at baseline (HKMMS) and persistence of PLEs at follow-up (current study) were assessed by Psychotic Screening Questionnaire(PSQ). Subjects who endorsed one or more items in PSQ at both baseline and follow-up were considered as having persistent PLEs.
Results: Out of 5719 subjects in the baseline study, the one year prevalence of PLEs was 3.04% - 174/5719 subjects free of psychotic disorder reported PLEs. In the first 100 subjects followed up, 63 (63%) were female, aged from 18-72 years (mean = 45.27, SD = 14.88). Mean years of education was 13.09 (SD = 5.05). 49/100 (49%) subjects had persistent PLEs (endorsed ≥ 1 PSQ items at baseline and follow-up). At baseline, the most endorsed item was "hallucination" (40, 40%), followed by "paranoia" (33, 33%), "strange experiences" (32, 32%),

"idea of reference" (21, 21%), "thought insertion" (14, 14%) and "hypomania" (1, 1%). The mean number of item endorsed was 1.41 (SD = 0.70). 49/100 (49%) subjects had persistent PLEs at 2-years follow-up (endorsed ≥ 1 PSQ items at baseline and follow-up). Among the subjects with persistent PLEs (PP), at baseline, the most endorsed item was "hallucination" (21, 42.9%) and "strange experiences" (21, 42.9%); followed by "paranoia" (16, 32.7%), "idea of reference" (11, 22.4%) and "thought insertion" (10, 20.4%). No subject reported the "hypomania" item. The mean number of item endorsed was 1.61 (SD = 0.67). Among the subjects with non-persistent PLEs (NP), at baseline, the most endorsed item was "hallucination" (19, 37.3%), followed by "paranoia" (17, 33.3%), "strange experiences" (11, 21.6%), "idea of reference" (10, 19.6%) and "thought insertion" (4, 7.8%) and "hypomania" (1, 2%). The mean number of item endorsed was 1.22 (SD = 0.42) It was found that subjects with persistent PLEs (PP) at follow-up endorsed significantly more PSQ items at baseline than the non-persistent subjects (NP) (U = 950.50. $P < 0.05$). In particular, PP endorsed the "strange experiences" item significantly more than NP ($\chi 2 = 0.23$, $P < 0.05$) at baseline. Also, PP subjects endorsed significantly less item in PSQ at follow-up than baseline (Z = -2.68, $P < 0.05$).
Discussion: The current study showed the one-year prevalence and two-year persistence of PLEs in the general population of Hong Kong, where the persistent rate is much higher when comparing to western studies. Apart from the "strange experiences" item, the endorsement of PLEs was largely similar between the PP and NP subjects. PP subjects endorsed significantly more items than NP subjects at baseline, though a reduction of PSQ item endorsed at follow-up in the PP subjects was also observed. Further investigation on the psychopathology of these PLEs might provide insights on such phenomenon.

S144. Physical activity in people living with psychotic illness: findings from the survey of high impact psychosis

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Background: In light of the high prevalence of physical comorbidities in people with psychotic illness, there is a need to explore modifiable risk factors. Physical activity (PA) has been shown to improve both physical and psychological well-beings. We aim to examine the patterns and correlates of PA in Australian adults with psychotic illness, based on the Survey of High Impact Psychosis (SHIP).
Methods: The SHIP is a population-based cross-sectional study of 1825 adults with psychotic illness living in Australia in 2010. The level of PA was assessed using the International Physical Activity Questionnaire (IPAQ). Participants were dichotomized into low and moderate-high PA groups. Associations between PA and a range of socio-demographic, clinical and physical comorbidity variables were examined, using logistic regression in bivariate and multivariate models.
Results: Data for PA was obtained for 1801 participants (98.7%) in SHIP. Almost half ($n = 856$, 47.5%) the participants were classified in the low PA level with 685 participants (38.0%) in the moderate PA level and only 260 participants (14.4%) in the high PA level. When dichotomised, 47.5% were in the low PA group, and 52.5% were in the moderate-high PA group. When we examined the level of engagement in any type of PA, nearly half of the sample (48.1%) had engaged in some kind of PA every day in the past seven days. At the same time, a substantial minority (12.3%) of the sample had not engaged in any form of PA whatsoever. With respect to the frequency of different types of PA, nearly half (48.2%) of the sample reported walking as PA in at least five out of the past seven days. However, a majority of the sample reported not engaging in any PA of moderate or vigorous intensity type (69.0%, 79.6% respectively). There were significant statistical associations between greater PA and; current education participation (OR 1.50; 95%CI: 1.07, 2.11) and being employed (OR 1.46; 95%CI: 1.14, 1.87). We also found significant association with lower PA and; older age (OR 0.40; 95%CI: 0.25, 0.65), antipsychotic medication use (OR 0.72; 95%CI: 0.52, 0.99), severe social dysfunction (OR 0.68; 95%CI: 0.47, 0.98), self-reported loneliness (OR 0.67; 95%CI: 0.47, 0.97), obesity (OR 0.66; 95%CI: 0.48, 0.90), and abdominal obesity (OR 0.68; 95%CI: 0.48, 0.97). However, there was no statistically significant association between PA and; sex, psychosis type, duration of illness, physical comorbidity, or negative symptoms.
Discussion: Our study reports correlates that may inform future interventions designed to increase PA in people with psychotic illness. The majority of people living with psychotic illness are engaged in at least some PA, however nearly half score low on IPAQ categorization. We found that variables related to age, antipsychotic use, social function, loneliness, obesity, employment and education statuses were significantly associated with PA levels. These findings can provide insights into the complex web of causation underpinning PA in people with psychotic illness and guide the development of future intervention studies. For example, addressing social connectedness and increasing work force/educational participation as well as programmes to increase the intensity of walking may encourage sustainable increases in PA, which in turn will improve the physical health of people living with psychotic illness.

S145. Systematic review and meta-analysis of the prevalence of psychotic experiences in countries outside of North America, Europe, and Australasia

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Background: In recent years, there has been an upsurge of research on psychotic experiences in general populations, all of which suggests such experiences are common (around 5-10%). The findings from this work further suggests that psychotic experiences are associated with risk of later psychotic disorder and that they commonly co-occur with other psychopathologies including common mental disorders and suicidality.
Previous systematic reviews have found that there is a variation in the prevalence of psychotic experiences between countries, and a later review had shown that this variation may be demarcated by the countries' economic status. As the majority of the studies included in previous reviews (now five or more years old) were in higher income countries, particularly in North America, Europe and Australasia, an updated review of research on psychotic experiences in lower income countries is warranted to examine whether similar prevalence and variation would be found.
Methods: Systematic Review: The systematic review was conducted according to the PRISMA guideline to include studies that were conducted in general population samples of countries outside of North America, Europe and Australasia. Studies needed to clearly state the prevalence of psychotic experiences or clearly state the outcome such that the prevalence of psychotic experiences could be derived. The search was limited to studies published between January 1950 and June 2015.
Using the search terms for "psychotic experiences", "prevalence/incidence", and "population" searches were conducted using the following databases:
1. Medline
2. Psychinfo
3. PubMed
4. Web of Sciences
Eligible studies were selected, retrieved, critically appraised, and the data from each study was then extracted using standardised custom-made form.
Meta-analysis: Pooled-prevalence, forest plots, confidence intervals, Cochrane's Q statistics and I2 were generated with the Quality-Effect model using the MetaXL© version 2.2 (EpiGear International) programme.
Results: Systematic review: A total of 29 studies were included for data extraction after the removal of duplicates, title and abstract screening. These studies together reported the prevalence of 39 cohorts from 17 countries. Of the cohorts, 10 were from Africa, 18 from Asia, 1 from Central America and 10 were from South America. As for countries' economic status, 2 were from low-, 12 from middle- and 3 from high-

income economies. The prevalence of psychotic experiences reported from studies using nationally representative samples within low-income countries was 0.4% to 3.2%, 1.2% to 3.8% in middle-income countries and 0.1% to 3.8% among high-income countries.
Meta-analysis: Primarily, the pooled prevalence calculated using representative studies was 3% (95%CI = 1%-6%) in low-income countries, 8% (95%CI = 4%-13%) in middle-income countries, and 3% (95%CI = 1%-6%) in high-income countries.
Discussion: Although not many studies from low-income countries were uncovered, the preliminary findings from this systematic review and meta-analysis suggest that there might be a variation in the prevalence of psychotic experiences across countries with different income levels. This is similar to what previous research has shown, i.e. that the prevalence is highest in upper middle-income countries, followed by high-income countries and low to lower-middle income countries.
This variation tentatively suggests that socio-environmental exposures may be operating in middle-income countries that amplify the prevalence there. Further studies looking at both individual- and area-level characteristics, and their interactions, will unquestionably help to extend our understanding of this potential variation in prevalence.

S146. Pathways to care and patterns of care in first episode psychosis patients treated in community based-mental health services over 5 years. findings from the PICOS-VENETO project

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Background: The most recent international guide-lines suggest that key elements to reduce the burden of disease in psychosis are an early identification of people in the initial stages of the illness and the adoption of specific evidence based treatments. However, a gap often exists between treatment guidelines and "real world" practice and that the routes of access to help in psychosis patients are complex, heterogeneous and likely to influences the chances of early treatment. This study aims to investigate the pathway to care and the typology of interventions provided to first-episode psychosis (FEP) patients from community based-mental health services over 5 years, exploring in which degree guidelines recommendations are met in a "real world" clinical practice.
Methods: This study was conducted in the context of the Psychosis Incident Cohort Outcome Study (PICOS), a large multisite, naturalistic research implemented in the Veneto Region (Italy), aiming to characterize FEP patients and to develop a comprehensive predictive model of outcome, by integrating clinical, social, genetic and MRI data over a 5-year period. FEP patients included in this study were assessed with a set of standardized measures including ad hoc schedules used for collecting detailed information on referrals to psychiatric services and on both pharmacological and psycho-social treatments at each FU (1-, 2- and 5 years). Further, patients who have interrupted contact with services were asked to complete the Verona Interview for Treatment Termination (VITreT) in order to collect details on treatment termination.
Results: A total of 397 FEP patients were assessed at BL. No specific services for FEP were available in the catchment area. More than one half of patients (60%) entered the treatment route through emergency departments and 55% had a consequent admission in the psychiatric ward; 30% of the sample had a first psychiatric contact through outpatients facilities. With regard to interventions received, 98% of patients had been prescribed neuroleptics; haloperidol (44.5%) and olanzapine (39.6%) were the most frequently prescribed drugs. Only half of the sample also received some kind of psychosocial intervention over 5 years, mainly consisting of unstructured individual support sessions; structured psychotherapeutic interventions, such as CBT, were seldom provided, as well as interventions for family members (generally consisting of non-specific supportive sessions). Respectively 89%, 92% and 85% of patients were still in contact with mental health services at 1, 2 and 5 years.
Discussion: Our findings highlight some discrepancies between interventions provided by "real world" mental health services and the best treatment options recommended by most recent international guide-lines. In fact, most interventions provided are only pharmacological, whereas psychological interventions are mainly unstructured and non-specific. Overall, our results suggest the need to implement specific and large scale initiatives aiming to close the gap between research and clinical practice.

S147. Investigating the association of maternal severe mental illness and exposure to obstetric complications with rates of intellectual disability

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Background: Recent evidence points to partially shared genetics of neuropsychiatric disorders. Previous work has identified children of mothers with psychotic illnesses are at significantly increased risk of developing intellectual disability (Morgan, Croft *et al.* 2012). Evidence exists that familial and obstetric factors also contribute independently to the risk. We investigate joint contributions of all these factors.
Methods: Record linkage across Western Australian population-based registers identified live born children born 1980-2001 as case (those of mothers with severe mental illness ($n = 15,351$)), or comparison (those of comparison mothers with no history of mental illness ($n = 449,229$)). Risk of developing intellectual disability was assessed in the context of maternal psychiatric status (comparison, schizophrenia, bipolar disorder, unipolar major depression and other psychoses) and obstetric complications. The McNeil-Sjöström Scale for Obstetric Complications (McNeil and Sjöström 1995) was applied to the State Midwives' Notification System record of birth. Exposure to obstetric complications was defined as experiencing at least one complication of at least severity level 4 – "potentially clearly harmful or relevant" to the developing central nervous system. Paternal psychiatric status, parental intellectual disability status and other relevant familial and socio-demographic covariates were included in analyses to address possible confounding, effect modifying or other influence.
Results: The risk of developing intellectual disability was increased for case children, differentially across maternal diagnoses. Unadjusted OR (95% CI) for children of mothers with schizophrenia, compared to children of comparison mothers was 3.8 (3.0-4.9). This remained significant 1.7 (1.1–2.5) after adjustment for all relevant covariates. Adjusted ORs for other case children were: maternal bipolar disorder (1.4, 1.04-1.9), maternal unipolar major depression (1.9, 1.6-2.2), and maternal other nonorganic psychoses (2.0, 1.4-2.7). The risk of developing intellectual disability was also affected by exposure to complications during pregnancy (1.3, 1.2–1.4), labour or delivery (1.1, 1.04–1.2), and the neonatal periods (1.7, 1.6-1.8). Exposure to complications in pregnancy and subsequently in the neonatal period affected the risk significantly more than expected by the independent effects attributable separately to each period (adjusted OR, 95% CI for exposure in pregnancy and subsequently in neonatal period: 2.3, 2.2-2.5)
Discussion: We observed elevated rates of intellectual disability in children of mothers with severe mental illness compared to comparison children, supporting accumulating evidence that phenotypically different neuropsychiatric disorders cluster within families. Our further observation of elevated rates of intellectual disability in children previously exposed to obstetric complications points to the contribution of both environmental and familial factors to the risk of developing intellectual disability.

S148. Why are children living in urban neighbourhoods at increased risk for childhood psychotic symptoms? Findings from a UK longitudinal cohort study

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Background: Children who are raised in cities are around twice as likely to develop schizophrenia in adulthood compared to children raised in

the countryside. Urbanicity is therefore a key area for psychosis research, considering that over two-thirds of the world's population are predicted to live in cities by 2050. Emerging evidence also suggests that the effect of urbanicity on psychosis risk is not phenotypically dormant: childhood psychotic symptoms occur more frequently among urban children. As early-life psychotic phenomena conform to the neurodevelopmental model of schizophrenia and are believed to occupy a continuum with adult psychotic disorders, childhood psychotic symptoms provide a useful framework to investigate the urbanicity-psychosis association. However, very little is currently known about what specific features of urban neighbourhoods might be increasing children's risk for psychotic symptoms and disorders. In the present study, we tested whether specific neighbourhood-level characteristics mediated the effect of urban residency on childhood psychotic symptoms.
Methods: Analyses were conducted on over 2000 children from the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally-representative cohort of twins born in the UK. Our neighbourhood-level characteristics included urbanicity, deprivation, social cohesion, social control, neighbourhood disorder, and crime victimisation. These were assessed for each family via postal surveys of over 5000 residents living alongside the children, in-home interviews with the children's mothers, and a geodemographic discriminator derived from the 2001 UK census. Neighbourhood scores from this battery were allocated to children at the postcode-level, thus our analyses had very high geographic resolution. Children were interviewed privately about psychotic symptoms at age 12. Using KHB pathway decomposition, we tested whether low levels of social cohesion and social control, and high levels of neighbourhood disorder and crime victimisation mediated the effect of urbanicity on childhood psychotic symptoms. Analyses adjusted for important family-level confounders including family psychiatric history, socioeconomic status and maternal psychosis.
Results: Urban residency was significantly associated with childhood psychotic symptoms (OR = 1.76, 95% CI = 1.15-2.69, $P = 0.009$), but not with other age-12 mental health outcomes. This association was not attributable to family-level confounders. Compared to nonurban neighbourhoods, urban neighbourhoods had lower levels of social cohesion and social control, and higher levels of neighbourhood disorder and crime victimisation (all p's < 0.05). Psychotic symptoms were more common among children living in neighbourhoods with these adverse characteristics (all p's < 0.05). Mediational analyses indicated that low neighbourhood levels of social cohesion explained 15% of the association between urbanicity and childhood psychotic symptoms (15%; OR = 1.06, 95% CI = 1.01-1.12), following adjustment for family-level confounders.
Discussion: Our findings suggest that low neighbourhood social cohesion partly explains why children raised in cities have an elevated risk of developing psychotic symptoms. Assuming some homotypic continuity between childhood and adulthood expressions of psychosis, our findings support the role of early-life exposure to neighbourhood-level social stressors in the aetiology of schizophrenia. A greater understanding of the mechanisms leading from neighbourhood-level exposures to psychotic symptoms could facilitate more targeted interventions to prevent the onset of childhood psychotic symptoms.

S149. Lower global assessment of functioning (GAF-F) scores predict the risk of hospitalization in male patients with a first-time schizophrenia diagnosis

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Background: Little knowledge exists if a psychosocial measure of functioning can predict the early clinical course of schizophrenia. Our objective was to investigate whether scores on the Global Assessment of Functioning scale (GAF-F) predict hospitalization.
Methods: Population-based cohort-study of adults (≥18 years) with a first-time diagnosis of schizophrenia between 2004 and 2011. Patients were categorized according to the GAF-F score recorded at first schizophrenia diagnosis. We evaluated the internal validity of GAF-F by comparing to other measures of illness severity. Risk of schizophrenia hospitalization within two years of follow-up was evaluated stratified by gender using Cox regression (hazard rate ratios (HRR); 95%-confidence intervals (95%-CI)) adjusted for age, year of diagnosis, and inpatient/outpatient status at diagnosis.
Results: We identified 2,837 incident cases of schizophrenia with a GAF-F score at first diagnosis, 2,070 (73.0%) of those being inpatients. GAF-F correlated with several measures of illness severity, such as educational level, occupational ability and a prior substance abuse diagnosis (all $P < 0.0001$). Lower GAF-F scores at first diagnosis were associated with higher hospitalization risk among men (reference GAF-F 61-100): GAF-F 51-60: HRR = 1.24 (95%-CI = 0.89-1.75); GAF-F 41-50: HRR = 1.31 (95%-CI = 0.97-1.77); GAF-F 31-40: HRR = 1.36 (95%-CI = 1.01-1.82); GAF-F 21-30: HRR = 1.50 (95%-CI = 1.09-2.06); GAF-F 1-20: HRR = 2.30 (95%-CI = 1.36-3.90), fitting a dose-response relationship ($P = 0.031$). A similar association was not found in women.
Discussion: Among men, lower GAF-F scores in relation to the first schizophrenia diagnosis were associated with increased risk of hospitalization. The easily applicable GAF-F may represent an important clinical tool for planning early treatment of incident adult male patients with schizophrenia.

S150. Prevalence and incidence of schizophrenia in Taiwan: 10-year population-based approach

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Background: Schizophrenia is the most severe psychiatric disorder in mental illness, and the mean of its prevalence is 5.4 per 1,000 people around the world. A previous study in Taiwan had used 200,432 random subjects sample to estimate the prevalence and incidence of treated schizophrenia from 1996 to 2001. The aims of this study were to update the prevalence and incidence of treated schizophrenia and to investigate how to estimate a more accurate incidence of schizophrenia.
Methods: The study used the Taiwan National Health Insurance Research Database, which is a population-based database, to estimate prevalence and incidence of treated schizophrenia. Schizophrenic patients were identified based on the primary diagnosis of inpatient or outpatient care. We applied different washout periods to the same sample group to define new cases of schizophrenia and estimate the incidence.
Results: This study found the annual prevalence rate increased from 3.43 to 4.13 per 1,000 people from 2000 to 2010; in contrast, the annual incidence rate decreased from 0.84 to 0.33 per 1,000 person-years during the study period. After testing four different washout periods, we found a washout period of five years provides a more stable incidence rate ratio (IRR range: 1.04-1.16) than a washout period of a year (IRR range: 1.19-1.85) or of three years (IRR range: 1.06-1.34).
Discussion: This is the first study using the entire Taiwanese population's data to estimate the prevalence and incidence of treated schizophrenia. Results indicate that the incidence rate has a descending trend in Taiwan and recommend omitting the previous five years to gain much more of a precise incidence rate of treated schizophrenia while investigating this mental illness.

S151. Psychosis symptom profiles and variability over time in a cohort of marginally housed adults in Vancouver, Canada

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Background: Psychotic symptoms are experienced as transient episodes as well as persistent features of psychotic illness. Little is known about the clinical characteristics and health care needs of

individuals with variable psychotic symptom severity compared to those with persistent mild or severe symptomology.
Methods: The Hotel study is a longitudinal observational study of adults living in marginalized housing in Vancouver, Canada. Presented here are baseline factors, monthly scoring of five key psychosis symptoms (delusions, conceptual disorganization, hallucinations, suspiciousness, and unusual thought content) from the Positive and Negative Syndrome Scale (PANSS), and self-reported service utilization from the first year of study. The maximum and minimum key PANSS scores during this year were identified for each individual. Two separate cluster analyses were employed to identify clusters of people that shared similar PANSS profiles at the time of their maximum and minimum symptom severity. Subsequently, change in cluster membership was examined to identify groups of individuals with variable or stable symptom severity. Multiple logistic regression and multinomial logistic regression analyses were used to test associations between group membership and baseline factors and service utilization over one year.
Results: In the first year of study, 335 participants had at least seven of thirteen 5-item PANSS assessments. Cluster analysis of the 5-item PANSS scores identified two distinct groups at their maximum (High-Max, $n = 131$; Low-Max, $n = 204$) and minimum (High-Min, $n = 36$; Low-Min, $n = 299$) points. The High-Max group exhibited supra-threshold scores for most symptoms indicating psychosis. The High-Min group exhibited supra-threshold scores for delusions, indicating unremitting psychosis. Participants were further subgrouped as follows: Low Stable ($n = 201$; Low-Max, Low-Min), High Stable ($n = 33$; High-Max, High-Min), and Variable ($n = 98$; High-Max, Low-Min). At baseline, the Variable and High Stable groups were younger (Variable: Odds Ratio (OR) = 0.97, $P = 0.027$; High Stable: OR = 0.95, $P = 0.007$) and more likely to report using methamphetamine (Variable: OR = 2.59, $P < 0.001$; High Stable: OR = 3.28, $P = 0.003$) and cannabis (Variable: OR = 2.26, $P = 0.001$; High Stable: OR = 2.99, $P = 0.007$), as well as antipsychotic medication (Variable: OR = 2.70, $P = 0.001$; High Stable: OR = 5.22, $P < 0.001$) than the Low Stable group. Compared to the High Stable group, the Variable group had higher Global Assessment of Functioning scores (OR = 1.09, $P = 0.003$) but was less likely to be employed (Variable 4%, High Stable 15%; OR = 0.19, $P = 0.023$) at baseline. In the first year, the Variable group was more likely to report unmet mental health needs (OR = 2.08, $P = 0.004$) than the Low Stable group and equally likely compared to the High Stable group (OR = 1.18, $P = 0.696$). However, there were no group differences in reporting medical, social work, or counseling care, hospitalization, or police contact for mental health or substance use issues during this year, adjusting for age and sex (all $P > 0.050$). Also, reports of consistent antipsychotic use over one year (>80% of assessments) were similar in the High Stable and Variable groups (OR = 1.01, $P = 0.981$).
Discussion: A subset of marginally housed adults experience variability in psychotic symptom severity. At baseline, these individuals had higher psychosocial functioning but were less likely to be employed compared to those with persistently severe symptoms. Over one year, despite receiving similar levels of mental health care, this group was more likely to report unmet needs. Individuals with variable psychosis symptoms may need greater or alternative forms of mental health and employment support.

S152. A new approach to investigating the association between duration of untreated psychosis and outcomes in psychosis using instrumental variables

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Background: There is evidence that a longer duration of untreated psychosis is associated with poor outcomes. However, it has long been unclear whether this association is confounded by variables such as mode of onset or poor pre-morbid functioning. This has been difficult to investigate in existing cohorts of patients with first episode psychosis because these variables are often unmeasured. Another problem with this association is the difficulty of measuring the duration of untreated psychosis since this is always measured in retrospect and relies on the ability of the patient and carer to remember accurately. Instrumental variables analysis offers an alternative way to investigate this association because it reduces the influence of residual confounding and measurement error.
Methods: Data from two UK cohorts of patients with first episode psychosis were used. The first (EDEN study) was a sample of 1027 people recruited from 14 Early Intervention for Psychosis clinical teams. The second (MiData study) was a sample of 1107 collected from 7 Early Intervention for Psychosis teams in the London area. Both cohorts were followed up for 12 months. For the purposes of this analysis the databases were combined and all analyses carried out on the total sample ($n = 2134$). Measures of duration of untreated psychosis were assessed at baseline and outcomes in terms of psychotic symptoms, recovery (EDEN cohort only) and global functioning were assessed at 12 months. Regression models were used to investigate the association between duration of untreated psychosis and psychotic symptoms, likelihood of recovery and functioning at 12 months. An instrumental variables analysis was also used to investigate the same association. The results of both analyses were compared.
Results: The regression analysis showed an association between DUP and worse standardised positive psychotic symptoms at 12 months (β 0.029 95% CI 0.015, 0.042 $p \leq 0.001$), a reduced likelihood of recovery at 12 months (OR 0.78 95% CI 0.70, 0.87 $p \leq 0.001$) and worse global functioning at 12 months (-0.618 95% CI -1.192, -0.042 $P = 0.035$). However the instrumental variable analysis showed no evidence of an association between DUP and either standardised positive symptoms (β 0.027 95% CI -0.075, 0.129 $P = 0.604$), recovery (Risk difference -0.082 95% CI -0.196, 0.031 $P = 0.156$) or global functioning (1.379 95% CI -3.148, 5.907 $P = 0.550$).
Discussion: Although the coefficients produced by the instrumental variables analysis are in the same direction as those produced by the regression analysis they are smaller and now include the null value of no effect. It is therefore possible that the results produced by the standard analysis methods are effected by unmeasured confounding or measurement bias or both. It is also possible that the instruments we are using are underpowered and therefore a Type 2 error is possible. Further investigation of the association between duration of untreated psychosis and outcomes is required.

S153. Unhelpful metacognitive beliefs in early psychosis are associated with affective symptoms and childhood social adjustment

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Background: Metacognitive beliefs are assumptions that individuals hold about their thoughts that outline the perceived importance or consequences of specific thoughts. In the self-regulatory executive function (S-REF) model (Wells and Matthews, 1996), unhelpful metacognitive beliefs about thoughts and self-regulation are assumed to promote ineffective regulatory strategies that could underlie increased sensitivity to stress and vulnerability to develop or maintain psychological disorder. Previous studies have shown that individuals with schizophrenia exhibit higher levels of unhelpful metacognitive beliefs than healthy controls, but no studies have explored metacognitive beliefs in early psychosis.
We examined i) differences in levels of unhelpful metacognitive beliefs between psychosis spectrum disorders, and healthy controls, and ii) to what extent demographic and clinical characteristics predicted levels of metacognitive beliefs in the early treated phases of psychotic disorders.
Methods: Patients were included within two years of first treatment for a psychotic disorder ($N = 92$). They were assessed on premorbid

adjustment, psychotic symptoms, anxiety/depression, and self-reported metacognitive beliefs (MCQ-30). Ninety-seven controls also completed MCQ-30. Predictors of metacognitive beliefs were explored with multiple linear regression analyses.
Results: Patients scored significantly higher than controls on all metacognitive subscales. The regression model explained 14—38% of the variance on each metacognitive subscale. Current affective symptoms explained a significant amount of variance on all subscales, except positive beliefs about worry. Childhood (premorbid) social adjustment predicted a significant amount of the variance on all subscales, except cognitive confidence. Duration of untreated psychosis contributed significantly to more unhelpful beliefs about cognitive confidence. Negative symptoms predicted lower scores on cognitive self-consciousness.
Discussion: Affective symptoms and childhood social adjustment could be important predictors of unhelpful metacognitive beliefs in the early treated phases of psychosis, indicating potential psychopathological relationships that warrant further investigation for clinical relevance. Understanding whether such beliefs are stable or amenable to illness processes could further our understanding of the role such beliefs play in illness formation and maintenance.

S154. Demographic and socio-environmental predictors of premorbid cannabis use among patients with first-episode psychosis

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Background: Cannabis is the most consumed illicit drug worldwide. Despite the finding that the amount and duration of cannabis consumption can influence the onset of psychosis, no solid conclusions have been made about a causal relationship. As a continuation of a previous study that focused on premorbid cannabis use and age at onset of psychosis among first-episode patients, we identified demographic and socio-environmental predictors of three key variables pertaining to premorbid cannabis use: (1) age at initiation of cannabis use, (2) trajectories of cannabis use in the five years prior to onset of psychosis, and (3) the cumulative "dose" of cannabis intake in the premorbid period.
Methods: 247 consecutively admitted inpatients with first-episode psychosis were assessed as part of the overarching study. Along with sociodemographic data, detailed information on cannabis consumption before the onset of symptoms was collected using the Longitudinal Substance Use Recall (LSUR) instrument. The Premorbid Adjustment Scale (PAS), Traumatic Experiences Checklist (TEC), Neighborhood Disorder Scale (NDS), and Cannabis Experiences Questionnaire (CEQ) were also administered. Bivariate tests were used to test associations between variables pertaining to premorbid cannabis use and hypothesized predictors. Variables that were statistically significant associated with the dependent variables of interest ($P < 0.05$) in bivariate tests were used to built regression models.
Results: Earlier age at initiation of cannabis use was associated with poorer PAS childhood (ages 6–11 years) scholastic performance and earlier age at first cigarette use. Cannabis trajectories of escalation were predicted by PAS childhood sociability subscale, CEQ "euphoric effects" and "reality and self-perception distortions" subscales, and age of first cigarette use. The cumulative dose of premorbid cannabis intake was predicted by male gender, PAS childhood sociability subscale, TEC total score, CEQ euphoric effects subscale, and age of first cigarette use.
Discussion: Four interesting findings emerged from this analysis on the effects of initiation of cigarette use, premorbid social and scholastic functioning, subjective experiences after using cannabis, and adverse early life events, on patterns of cannabis use in a relatively large sample of patients with first-episode psychosis. First, age at initiation of cigarette smoking affects all of the three aspects of cannabis use that we considered, leading to an earlier initiation, faster escalation, and higher cumulative dose. Second, during childhood, poor scholastic performance is predictive of earlier age at initial cannabis use, while poor sociability is related to more rapid escalation to daily use and a higher cumulative dose. Third, while we had expected that experiencing euphoric effects would be positively correlated with trajectories and dosage, we also had expected that negative experiences of cannabis use would have affected the pattern of use; in fact, we did not observe the latter association. Fourth, traumatic experiences are correlated with rapid escalation and amount of cannabis utilized but not with age at initiation of cannabis use. Despite the increasing number of studies focusing on the potential casual effects of cannabis use on psychosis, no major findings have been discovered to apply in preventive or clinical practice. Our study, looking at predictors of premorbid cannabis use, may help developing public health strategies to prevent exposure to cannabis, trying to delay as much as possible the onset of psychosis.

S155. Identifying patients with an indication for clozapine in Dutch outpatient settings

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Background: With a success rate of approximately 60%, clozapine is assumed to be superior in the treatment of treatment-resistant Non-Affective Psychotic Disorder (NAPD). Clozapine is also effective in the treatment of moderate to severe tardive dyskinesia (TD), aggression and suicidality. Estimated proportions of treatment-resistant patients range from 10-40%, proportions of other indications are even less known. The exact proportion of patients with NAPD in an outpatient setting who should be treated with clozapine is therefore uncertain. The objectives of this study are to determine, in Dutch outpatient teams, the proportion of patients with NAPD who already use clozapine and to determine the proportion of those for whom clozapine is indicated, by type of indication.
Methods: All patients with NAPD were identified, by checking the DSM-IV-TR codes. In order to assess which patients had an indication for clozapine (treatment-resistance, moderate to severe TD, aggression or suicidality) a decision tree was developed, including a list of adequate dosages of antipsychotic medication. After determining which patients were already using clozapine, the physician and the nurse practitioner of each team used the decision tree to assess which patients had an indication for clozapine. The interrater reliability of this method was satisfactory (kappa = 0.7).
Results: Preliminary results: 19 teams of four different psychiatric institutions were included. In total there were 1792 patients with NAPD: 18.8% was already using clozapine (with high variability among teams, ranging from 7 to 31%), 3.5% had used clozapine and discontinued using this drug (range: 0 to 8%) and 6.7% had an indication for clozapine (range 0 to 15%). Of the latter group, 94.1% was treatment-resistant, of which 10% also had another indication for clozapine. Few patients were not treatment-resistant and, had (maximally) one other type of indication (2.6% TD and 0.9% suicidality). In addition to the patients on clozapine or those with an indication for clozapine, another 10.4% of the patients with NAPD still suffered markedly from positive symptoms. They did not yet meet the criteria for treatment-resistance or another indication (range: 6 to 27%).
Discussion: Assuming all clozapine use was in accordance with the guidelines, 29% of the patients with NAPD had an indication for this drug (18.8% using clozapine+ 3.5% using before+6.7% with an indication). However, another 10.4% still suffered markedly from positive symptoms. Most of them refused to take antipsychotics in an adequate dosage. Some of them may turn out to be treatment-resistant after they have been treated with an adequate dosage.
There were large differences between teams in prevalence of patients on clozapine and with an indication for clozapine. Possible explanations for these differences are: 1) differences in disease severity, 2) different perspectives of physicians on the burden caused by positive symptoms, TD, aggression and suicidality, 3) different attitudes to clozapine and other antipsychotics, which can result in either high clozapine prescription rates or increasing the dosage of less effective drugs (including polypharmacy), 4) differences in efforts between

physicians/teams to motivate patients to accept medication in adequate dosages. Remarkably, there was no inverse association between the proportion of patients already on clozapine and either the proportion of patients with an indication for clozapine or the proportion of patients with markedly positive symptoms.

S156. Prevalence of childhood trauma in recent onset psychosis and arms subjects: a controlled study

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Background: It is well-known that exposure to childhood trauma, such as abuse and neglect, increases the risk of forthcoming schizophrenia. It has been reported that childhood adversity is associated with persistence of psychotic symptoms and poorer clinical outcomes.
Recently, it has been an increasing interest in studying the impact of childhood adversity in subjects at the early stages of the illness, especially in first episode psychoses. However, prevalence and clinical impact in ARMS (At Risk Mental State) subjects has been scarcely studied. As far as we know, any previous study has compared prevalence of childhood adversity between recent psychosis and ARMS subjects including a healthy control group.
Methods: Participants: One-hundred and eighty-four subjects were recruited from the outpatient Early Intervention Psychosis team in Reus, Spain. One-hundred and thirty one (71.2%) presented their first-episode of psychosis in the last two years and 53 (28.8%) fulfilled ARMS criteria assessed by CAARMS. A group of 60 healthy controls were also recruited from near catchment areas.
Assessments: Exposure to childhood trauma was assessed by means of the Spanish version of the 28-item Childhood trauma Questionnaire (CTQ). This questionnaire assesses 5 types of childhood trauma: sexual abuse, physical abuse, emotional abuse, physical neglect, and emotional neglect. A score is obtained for each different domain, and an overall score for childhood maltreatment is also obtained.
Analysis: As CTQ scores were not normally distributed, differences in CTQ subscales between groups were analyzed by non-parametric Kruskal-Wallis test and Mann-Whitney U-tests for post-hoc comparisons. To control for gender differences, analysis of covariance was performed including gender as covariate. Significance was set at $P < .005$.
Results: More than 85% of recent onset psychosis and ARMS subjects (86.3% and 88.7%, respectively) and 30% of healthy controls reported exposure of any form of abuse or neglect. Emotional neglect (66.4% of recent onset psychosis and 66.0% of ARMS) followed by physical neglect (58.0% of recent onset psychosis and 49.1% of ARMS) were the most prevalent types of adversities reported in both clinical groups.
When comparing groups, both clinical groups did not differ in severity of any of the CTQ subscales. Compared with healthy controls, recent psychosis group reported higher scores of emotional abuse and neglect ($z = -4.36$, $P < 000$; $z = -6.39$, $P < 000$), physical abuse and neglect ($z = -4.3$, $P < 000$; $z = -7.3$, $P < 000$) and higher CTQ total score ($z = -7.50$, $P > 000$). ARMS group also reported higher scores of emotional abuse and neglect ($z = -4.05$, $P < 000$; $z = -4.94$, $P < 000$), physical abuse and neglect ($z = -3.78$, $P = < 000$; $z = -5.99$, $P < 000$) and CTQ total score ($z = -6.55$, $P < .000$) than healthy controls. However, prevalence of sexual abuse was similar in the three groups. When controlling for gender, differences between recent onset and healthy control groups remained significant. With regards ARMS subjects, all differences also remained significant with the exception physical abuse subscale
Discussion: In concordance with previous findings we report elevated rates of childhood adversity in recent psychosis onset and ARMS groups compared with healthy control. Importantly, recent onset psychosis and ARMS groups reported similar rates of all types of childhood adversity highlighting the relevance of assessing traumatic events even in pre-psychotic patients. Very few studies in this area indicate that childhood trauma in ARMS subjects predict transition to psychosis, while other studies do not. Given controversial findings further research in this area is warranted

S157. The epidemiology of first episode psychosis in early intervention in psychosis services: findings from the social epidemiology of psychoses in East Anglia [SEPEA] naturalistic cohort study

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Background: Despite the widespread introduction of Early Intervention Psychosis [EIP] services, there is a dearth of robust epidemiological data on the incidence of psychotic disorders seen through such services. More generally, the epidemiology of psychotic disorders in rural areas is poorly understood. To overcome these issues, we delineated the epidemiology of first episode psychoses [FEP] in a diverse, rural population in England.
Methods: We estimated the incidence of FEP incepted through 6 EIP services in the East of England over a 3.5 year period. All people, aged 16-35 years, presenting with an OPCRIT-confirmed first episode of an ICD-10 psychotic disorder (F10-33) were included, except those with an organic basis to their disorder or severe learning difficulty. The denominator was estimated from the 2011 Census of Great Britain. We estimated crude incidence rates and incidence rate ratios following multilevel Poisson regression by age, sex, ethnicity, socioeconomic status [SES] and neighbour-level deprivation and population density.
Results: We identified 675 people with a confirmed FEP during more than 2 m person-years of follow-up, corresponding to a crude incidence of 33.4 per 100,000 person-years (95%CI: 31.0-36.0). Median age-at-referral was similar for men and women, although incidence was rates were 1.9 times greater amongst men (95%CI: 1.6-2.2) after adjustment for confounders. Rates increased amongst ethnic minority groups (IRR: 1.4; 95%CI: 1.1-1.6) and per downward change in SES (IRR: 1.3: 95%CI: 1.2-1.4). Independent of age, sex, ethnicity and SES, incidence rates were elevated in the most urban (IRR: 1.3; 95%CI: 1.0-1.8) and deprived neighbourhoods (IRR: 2.1; 95%CI: 1.4-3.4) in this predominantly rural region.
Discussion: EIP services in rural populations see a substantial incidence of FEP. In our study, rates were more than double the expected incidence upon which EIP services in England were originally commissioned. Rates varied according to the classic tenets of age, sex, ethnicity, SES and followed non-linear associations with deprivation and population density, where excess risk was confined to the most urban and poor communities. These findings will be essential in delineating the epidemiological landscape of FEP in young people seen by EIP services.

S158. Schizotypy and migration in a general population sample in France

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Background: The construct of schizotypy has been developed as a multidimensional model to understand and investigate the etiology, development, expression and associated risk factors of the broader continuum of schizophrenia spectrum disorders (Kwapil & Barrantes-Vidal, 2015). Migration as risk factor for psychosis has been largely observed and minority ethnic groups at higher risk vary in the different countries (Bourque, 2012). However, schizotypy in migrant or ethnic minority groups have been less investigated although many assessments instruments have been validated across cultures. Higher

prevalence of schizotypy was observed in ethnic minorities such as among African Americans in USA (Kwapil *et al*, 2012) and Maori descent in the Pacific Islands (Linscott *et al*, 2006), but to our knowledge, any study investigated migration as a risk factor of schizotypy. In this study we will analyse the prevalence of schizotypal traits in first generation migrants and their descendants among the most representative migrant groups in France (North Africans, sub Saharan Africans and internal migrants from French West Indies) in a non-clinical sample in the suburbs of Paris. We will use the SPQ-B (Raine & Benishay, 1995) which was validated in a French sampling.
Methods: We recruited a representative sample of general population from three geographic areas called "IRIS" defined by the National Institute for Statistics and Economic Studies (INSEE) as homogeneous areas in types of habitations, and having 1 800-5 000 inhabitants. Sociodemographic data including the country of birth of participants and of their parents were collected. Schizotypal traits were assessed with Schizotypal Personality Questionnaire Brief (22 items) with a Likert format (1: completely disagree – 5: completely agree). We ran multiple regression analyses to compare natives' SPQ scores to first and second generation migrants in function of country of origin adjusting for age and sex.
Results: 220 participants were assessed. Ninety three participants were first generation migrants, 42 were second generation. No differences between total SPQ-B were found between natives and migrants. However we observed higher scores in the interpersonal scales for second generation migrants ($P = 0.035$). A second analyses allowed to identify that it was related to second generation migrants with origin from North Africa ($P = 0.049$). A gender effect ($P = 0.015$) was observed in the cognitive-perceptual scores.
Discussion: The interpersonal scale reflects two distinct constructs: social anhedonia and social anxiety. Our findings could be interpreted in two main different ways. Firstly it may be the results of culture expression of affect and social functioning (Cohen *et al*, 2015). Measurement in invariance in diverse cultures showed that norms and cut-off points may vary in the context of a given culture or ethnic minority groups (Chmielewsky *et al*, 1995; Kwapil *et al*, 2012; Fonseca-Pedrero *et al*, 2015; Cicero, 2015) and these differences can be found across positive or negative dimensions of schizotypy (Chen; 1997; Reynolds *et al*, 2000; Schiffman, 2004). Secondly, it could be the indirect measure of social stress. Discrimination, adversity and trauma have been largely related to increased psychological distress and poor mental and physical health. Religious discrimination seems to have the same effects (Jordanova *et al*, 2015). Selection bias and small samples are main limits of this study. Confounding factors such as cannabis use and social-economic level were not studied.

S159. Closing the gap: sensitivity and specificity of neurological signs across the lifespan profiling in schizophrenia spectrum disorders

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Background: Clarifying the sensitivity and specificity of neurological soft signs (NSS) in schizophrenia spectrum disorders may provide tools for early detection of schizophrenia. Furthermore, profiling the developmental trajectories of NSSs in both healthy and affected individuals will facilitate the understanding of neurodevelopmental abnormalities in schizophrenia.
This study aimed to delineate how NSS differentiate individuals with schizophrenia spectrum disorders from healthy individuals after controlling for age, gender, and intellectual level. It also aimed to estimate the age-related variation of NSS in both healthy and schizophrenia individuals.
Methods: A total of 3105 participants were recruited, consisting of healthy participants (n = 1577), individuals with schizotypal personality disorder (SPD) ($n = 256$), schizophrenia patients ($n = 738$), unaffected first-degree relatives of schizophrenia patients ($n = 155$), and other psychiatric patients ($n = 379$). All participants were free from major motor or cognitive impairments. The abridged version of the Cambridge Neurological Inventory (CNI) was administered to all participants.
Results: Individuals along the schizophrenia continuum showed elevated levels of NSS, in sharp contrast to other psychiatric patients who had minimal NSS, as compared to matched healthy controls. Furthermore, the age-and-NSS relationship in schizophrenia patients was represented by a flat but overall elevated curve, in contrast to a U-shaped curve in typical healthy individuals.
Discussion: NSS capture a moderate portion of the proneness to schizophrenia spectrum disorders with reasonable specificity. Lifespan profiling reveals an abnormal developmental trajectory of NSSs in schizophrenia patients. These findings lay the foundation for future studies to associate schizophrenia-related behavioral endophenotypes with neurodevelopmental biomarkers, and thus promote a better understanding of the pathogenesis and neurological prodromes of schizophrenia.

S160. Neurobiological subtyping of schizophrenic and affective psychoses in cross-disorder cohorts

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Background: Classification of psychiatric disorders is mainly based on the phenotype, i.e. on psychopathological symptoms observed in the patients. More recent approaches have focused on neurobiological markers that i) may qualify as endophenotypes, ii) may be more closely related to genetic factors and iii) may facilitate the identification of susceptibility genes of psychiatric disorders.
Methods: In a large cross-disorder neuroimaging sample, a battery of established experimental fMRI paradigms was applied in order to investigate different core pathophysiological processes and neurophysiological endophenotypes of schizophrenic and affective psychoses, e.g. dysfunctions of the dopaminergic reward system and its top-down modulation.
Results: Endophenotypic brain dysfunctions were identified in patients groups as well as in healthy first-degree relatives. These included hyperresponsivity of the nucleus accumbens as part of a saliency/evaluation network and hyperactivation of the right middle frontal gyrus during verbal working memory. Genome-wide association studies for these endophenotypic neuroimaging markers are currently underway. Multivariate clustering approaches revealed pathological clusters of patients sharing pathophysiological abnormalities independent of the diagnostic category.
Discussion: Neuroimaging of endophenotypic brain dysfunctions and imaging genetics are promising research approaches. Endophenotypes may guide the development of functional neuroimaging biomarkers for clinically relevant pathophysiological processes. These biomarkers may permit a more precise differential diagnosis of pathophysiological and pathogenetic subtypes of the heterogeneous diagnostic categories of schizophrenic and affective disorders.

S161. Early parental loss and NRG1 hapice genotypes are differentially associated with cognitive function in schizophrenia

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Background: Cognitive function in schizophrenia has shown clustering with various groupings of comparatively unimpaired and impaired performance. These clusters have provided a framework to parse schizophrenia and more specifically identify the influence of genetic and environmental risk factors. To further elucidate these relationships

we used an unsupervised clustering algorithm, Kohonen's Self Organising Map, to show three cognitive clusters in a sample of people with schizophrenia and examined for associations with a range of clinical, environmental and genetic factors.
Methods: Cognitive, clinical and socio-demographic data and DNA from participants with a diagnosis of DSM-IV SCZ ($n = 449$ overall, $n = 408$ after 'missing data analysis') were accessed from the Australian Schizophrenia Research Bank and 3 clusters were identified based on WTAR, WASI, COWAT, LNS and 5 RBANS domains. Genotyping for 29 SNPs in 5 genes (EGF, EGFR, NRG1, ERBB4, BTC) within the epidermal growth factor (EGF) system was performed using Multiplex and Taqman assays and a multinomial regression model was created using the clusters 1, 2 and 3 as dependent variables.
Results: Three cognitive clusters with a descending order of cognitive performance were identified: cluster 1 – 'near normal' cognitive performance, cluster 2 – 'intermediate' (between cluster 1 and 3) cognitive performance and cluster 3 – 'poorest' cognitive performance of the 3 clusters. Cluster 3 was strongly over-represented by males by a factor of 1.5 ($P = 0.0007$) and by those with a nominal diagnosis of treatment resistant schizophrenia (65.3% of all TRS cases were found to be members of cluster 3). Cluster 3 was significantly more likely to suffer early parental loss ($P = 0.03$). Cluster 1 members were more likely to have longer duration of illness compared to cluster 2 and 3 ($P = 0.04$) and number of years of completed education ($P < 0.01$). Cluster 3 members were the youngest to leave school (prior to completion of year 12 or equivalent) when compared to cluster 1 and 2 ($P < 0.01$).
A manual backward stepwise multinomial regression with the 3 cluster model as dependent variable revealed that the HapICE SNPs rs35753505 (SNP8NRG221533) and rs6994992 (SNP8NRG243177) associated significantly with cluster memberships. Subjects carrying the rs35753505 CC schizophrenia-risk genotype were more likely to belong to cluster 1 compared to cluster 3 relative to TT genotype carriers (OR = 40.22, 95% CI = 3.73–433.11, $P = 0.002$). Whereas, individuals carrying the rs6994992 CC non-risk genotype were more likely to belong to cluster 1 compared to cluster 3 relative to TT genotype carriers (OR = 12.32, 95% CI = 1.029–147.53, $P = 0.047$).
Discussion: We show here a robust three cluster model of cognitive function in schizophrenia with a wide variation in performance between clusters. The most impaired cluster (cluster 3) was more likely to have experienced early parental loss and be treatment resistant. This may provide evidence for a role of early stress in mediating cognitive function and suggests a relationship with poor treatment response.
Current evidence associates rs35753505 C allelic load with altered brain structure and function findings in the CNS in schizophrenia. In contrast we demonstrate that the CC genotype is associated with higher cognitive function. We also show that the cognitively comparatively higher functioning cluster 1 is also associated with the non-risk C allelic load for rs6994992. This indicates a role for NRG1 SNPs differentially moderating cognitive function in schizophrenia and raises the question as to the relationship between NRG1, cognitive function and psychosis potentially through neurodevelopment.

S162. Correlation of BDNF mRNA expression with Val66Met polymorphism in brain

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Background: Brain derived neurotrophic factor (BDNF) encodes a protein involved in neuronal proliferation and survival. A recent meta-analysis of the BDNF Val66Met polymorphism (rs6265) has confirmed association with schizophrenia. In this study we compared BDNF brain tissue expression between schizophrenia and controls subjects, and investigated the effect of the Val66Met polymorphism on BDNF expression.
Methods: Prefrontal cortex brain tissue was obtained from 22 schizophrenia and 23 control subjects. RNA sequence reads were generated and RPKM (reads per kilobase transcript per million mapped read counts) values were determined for each sample and compared between schizophrenia and control subjects. BDNF mRNA profiles and Val66Met genotype data was also generated. BDNF mRNA expression and Val66Met were correlated using linear regression.
Results: There was significant differential BDNF expression between schizophrenia and healthy controls ($P = 0.00257275$). Linear regression analysis between BDNF expression profiles and rs6265 variant revealed that the expression of the gene (adjusted for age, sex and post-mortem interval) was significantly associated with rs6265 genotype ($P = 0.000014$).
Discussion: In this study we found schizophrenia risk was affected by differential BDNF mRNA expression and the Val66Met polymorphism altered transcriptional activity. The Val66Met polymorphism is likely to play a role in the pathogenesis of schizophrenia.

S163. Auditory processing in autism spectrum disorder: mismatch negativity deficits

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Background: Children with autism spectrum disorders (ASD) often have changes in (automatic) auditory processing. Electrophysiology provides a method to study auditory processing, by investigating event-related potentials (ERPs) such as mismatch negativity (MMN) and P3a amplitude. However, findings concerning MMN in autism are highly inconsistent, partly due to heterogeneity in the disorder. In the current study, MMN and P3a amplitude were assessed in children with autism, and compared with that of typically developing (TD) control children.
Methods: A total of 35 children (aged 8-12 years) with ASD (autistic disorder, $N = 11$; Asperger's syndrome, $N = 7$; PDD-NOS, $N = 17$) and 38 age and gender matched TD control children were assessed with a MMN paradigm with three types of deviants, i.e. frequency, duration and a combination of these two.
Results: The results showed that all participants were able to elicit clear MMN and P3a amplitudes regardless of deviant type, with maxima on electrode FCz. MMN elicited by duration and frequency-duration deviants was significantly reduced in the ASD group taken as a whole, but this was largely driven by the children with autistic disorder and PDD-NOS; children with Asperger's syndrome had similar levels of MMN as TD control children. No between-group differences were found in P3a amplitude.
Discussion: In conclusion, deficient MMN was found in children with PDD-NOS and autistic disorder. This suggests that these children may be less responsive to environmentally deviant stimuli. Furthermore, as deficient MMN is frequently reported in schizophrenia, these two forms of ASD may predispose more to schizophrenia than others.

S164. Primary and secondary alterations of white matter connectivity in schizophrenia: a whole-brain tractography-based analysis

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Background: Studies on patients with chronic and first-episode schizophrenia have found widespread white matter abnormalities. However, it is unclear whether the altered connections are inherent in or secondary to the disease. In this study,we sought to identify white matter tracts with altered connections and to distinguish primary or

secondary alterations among 74 fiber tracts across the whole brain using an automatic tractography-based analysis method.
Methods: Thirty-one chronic, 25 first-episode patients with schizophrenia and 31 healthy controls were recruited to receive diffusion spectrum magnetic resonance imaging at 3 T. This study applied an automatic tractography-based analysis (TBAA) (Wu *et al.*, 2015) to assess white matter connectivity in 74 major tract bundles across the entire brain. The whole-brain white matter tracts were reconstructed on a diffusion spectrum imaging (DSI) template using deterministic tractography (Lo *et al.*, 2011). A transformation map was established between the DSI template and the study subject's DSI data. After transforming the tracts' coordinates to the study subject's DSI data, the microstructural properties of each specific tract bundle were sampled along the entire tract.With the TBAA method, the status of white matter connectivity in 74 tracts can be analyzed automatically. To compare the mean GFA values of the 74 white matter tracts among the three groups, we used analyses of covariance (ANCOVAs) with age and gender as covariates. To correct for multiple comparisons, the Benjamini–Hochberg method for false discovery rate (FDR) control was used due to the dependency among white matter tracts. To determine the differences between the groups, post-hoc Scheffé tests were applied. Multiple regression analysis was used to investigate which clinical variables (age, duration of illness, and dose of medication) affected the altered tracts, as determined by the ANCOVAs.
Results: Seven tracts were found to exhibit significant differences among the 3 groups; they included the right arcuate fasciculus, bilateral fornices, left superior longitudinal fasciculus I, and fibers of the corpus callosum to the bilateral dorsolateral prefrontal cortices (DLPFC), bilateral temporal poles, and bilateral hippocampi. Post-hoc between-group analyses revealed that the connection of the callosal fibers to the bilateral DLPFC was significantly decreased in chronic patients but not in first-episode patients. In a stepwise regression analysis, the decline of the tract connection was significantly predicted by the duration of illness. In contrast, the remaining six tracts showed significant alterations in both first-episode and chronic patients and did not associate with clinical variables.
Discussion: Our findings supports the hypothesis that the altered white matter connectivity observed in chronic schizophrenia patients is partly found in first-episode patients. The results are compatible with a previous study reporting that schizophrenia patients at ultra-high risk showed alterations of white matter integrity similar to, but less severe than, first-episode patients (Carletti *et al.*,2012). Our results imply that the 6 tracts showing abnormality in first-episode patients might serve as potential biomarkers for diagnosing schizophrenia early in the course of the disease. The callosal fibers to the bilateral DLPFC appear to be relatively intact at disease onset, but degrades progressively in the chronic stage.

S165. The benefit of macro-anatomical alignment for fMRI-based imaging genetics of common schizophrenia risk variants

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Background: Imaging genetics is crucial for studying the neurogenetic mechanisms of schizophrenia. Functional magnetic resonance imaging (fMRI) is the most widely and successfully applied method. Despite the high penetrance of some schizophrenia related genes at the neural systems level, reliably detecting the impact of genetic polymorphisms remains a challenge. For instance, one would expect, that the considerable degree of interindividual spatial variability of functional activation patterns particularly in the cerebral cortex might obscure valid effects. This issue would not be addressed properly by standard MRI normalization procedures, which align structural and functional data to a volume-based coordinate system. Surface-based alignment methods, which operate in a cortical coordinate system and align individual brains using the curvature information of the cortex, might offer a solution because they reduce the hetereogeneity of cortical topology within a population to a considerable degree. Here we investigate, whether such an approach improves the effect sizes of common genetic risk variants for schizophrenia on the cortical working memory network in a cohort of healthy subjects.
Methods: We employed a change detection task probing spatial working memory. Genetic and fMRI data were acquired for 98 right-handed individuals without a personal and family history of psychiatric disorders. Genotyping was performed using a custom Illumina HumanCoreExome-24 BeadChip. Polygenic risk scores were calculated based on the PGC data. Structural and functional MRI data were acquired using a Siemens TRIO 3 T MRI-Scanner. Functional data were analysed using BrainVoyager QX 2.8.2. The co-registered functional and anatomical data was transformed into Talairach coordinate space. In addition to this standard volume based approach, we applied a high-resolution, multiscale curvature driven cortex based alignment procedure. To this end, anatomical scans were segmented along the white–gray matter boundary. Cortical hemispheres were reconstructed and morphed into spherical representations. Each cortical folding pattern was aligned to a dynamically updated group average through iterative morphing following a coarse-to-fine matching strategy. We used a region of interest analysis (ROI) to compare the effect sizes of polygenic risk scores on key regions of the working memory network before and after macro-anatomical aligment.
Results: Our method reliably aligned cortical landmarks across participants. Our ROI analysis revealed that applying surface-based alignment lead to a small but robust increase of effect size of polygenic risk scores.
Discussion: Our findings indicate that cortex-based alignment reduces macro-anatomical variability, which increased the effect size of polygenic risk scores. This method might be a useful tool to improve the power of imaging genetic studies and to facilitate the investigation of the genetic architecture of schizophrenia and other psychiatric disorders.

S166. Prefrontal-striatal functioning of effort-based reinforcement in schizophrenia

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Background: Dopaminergic projections to the prefrontal-striatal network underlie various aspects of reward and motivation which are core components of negative symptoms. Amotivation can be defined as diminished effort in acquiring reward. Prior studies showing blunted neural response to prediction errors during reinforcement learning in patients in schizophrenia and depression suggest that amotivation in these disorders involves the dopaminergic pathway. We hypothesized that pathophysiology in the dopaminergic reward system in schizophrenia and depression may be differentiated by examining the neural processing of effort-based valuation of positive and negative reinforcement.
Methods: Functional MRI scanning was conducted on 31 healthy controls, 19 outpatients with schizophrenia and 19 outpatient with depression while performing a modified effort-based cost-benefit valuation task. Neural responses to cue for anticipating effort level and reinforcement contingency (i.e. monetary gain versus loss avoidance), effort readiness and feedback after making effort were analyzed.
Results: Healthy controls showed accelerated responses to cues associated with obtaining monetary gains with low effort and avoiding loss with high effort. In contrast, patients with schizophrenia did not show any response acceleration, while patients with depression showed accelerated response only to cues of low effort monetary gains. In healthy controls, the ventral striatum (VS) and anterior cingulate cortex (ACC) activity changed according to effort level whereas the dorsal striatum (DS) and medial orbitofrontal cortex (mOFC) activity changes were associated with interaction between reinforcement type and effort level. In patients with schizophrenia, the VS-ACC and DS-mOFC activity changes were blunted, whereas patients with depression showed only effort level related VS-ACC and DS-mOFC activity changes associated with one type of contingency (i.e. either monetary gain or loss avoidance).
Discussion: These findings suggest that amotivation in patients with schizophrenia may involve an extensive dysfunction in the prefrontal-striatal network involved in integration of cost-benefit valuation.

S167. Brain activation during facial affect perception differentiates high vs. low functioning individuals with schizophrenia

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Background: A longstanding goal for treatment is to improve the community functioning of individuals with schizophrenia. Community functioning is comprised of functional capacity, social competence, and functional attainment. Prior literature indicates that various cognitive domains contribute to different aspects of community functioning, although the exact nature of these associations is unclear. Thus far, treatment research focused on community functioning has emphasized behavioral and neurobiological differences between individuals with schizophrenia and controls. An alternative approach to investigating cognitive targets to enhance functioning is to compare cognition between individuals with schizophrenia characterized as having 'high' and 'low' levels of community functioning (HF-SCZ and LF-SCZ, respectively). We recently demonstrated a cluster analytic method that classified a sample of individuals with schizophrenia as HF-SCZ and LF-SCZ. In the current study, we evaluated 1) if HF-SCZ and LF-SCZ differed from each other and controls (CON) on their performance of a facial affect perception (FAP) task; 2) if HF-SCZ and LF-SCZ differed with respect to their fMRI brain activation during FAP task performance; 3) if HF-SCZ and LF-SCZ differed from CON with respect to their brain activation during the FAP task; and 4) to explore if brain activation correlated with FAP task performance.
Methods: HF-SCZ ($n = 17$), LF-SCZ ($n = 13$), and CON ($n = 24$) completed a FAP task while undergoing fMRI in a 3 T TIM Siemens Trio system and outside of the scanner. Two functional runs were performed (220 volumes each, 40 axial slices, TR = 2.2 s, TE = 20 ms, field of view (FOV) = 220 × 206 mm, fli$P$ = 80°, 1.7 × 1.7 × 3.0 mm voxels). fMRI analyses were conducted using AFNI. Data were slice-timing and motion corrected, volume registered, spatially smoothed (FWHM = 8 mm) and spatially aligned. Group-level analyses compared the neural activity corresponding to accurate trials of displayed facial affect (i.e., anger, sadness, fear, disgust, happy, neutral) between HF-SCZ and LF-SCZ with a t-test corrected for multiple comparisons (individual voxel threshold: $p < .001$, minimum cluster size = 60 voxels). Post-hoc analyses evaluated the neural activity of the CON group in the regions showing differential activation between the two groups with schizophrenia. We evaluated the associations between brain activation and FAP accuracy using Spearman correlations.
Results: HF-SCZ and CON performed similarly on the FAP task, which was significantly higher than LF-SCZ. HF-SCZ demonstrated hyperactivation in the fusiform gyrus, superior occipital gyrus, medial inferior parietal lobule, and precentral gyrus compared to LF-SCZ. Moreover, HF-SCZ had similar activation in these regions compared to CON, who also hyperactivated them compared to LF-SCZ. We also observed that both CON and HF-SCZ demonstrated deactivation in the angular gyrus, while LF-SCZ did not. Additionally, we observed LF-SCZ hyperactivation in the lateral inferior parietal lobule compared to HF-SCZ and CON. Lastly, we observed that FAP task accuracy from outside of the scanner was correlated with fusiform gyrus activation among HF-SCZ ($\rho = .48$, $P < .05$) and CON at a trend level ($\rho = .35$, $P = .09$), but negatively correlated among LF-SCZ ($\rho = -.58$, $P < .04$).
Discussion: These results suggest that individuals with schizophrenia who have elevated community functioning demonstrated similar neural activation patterns compared to controls during successful facial affect perception. Our findings suggest that these brain regions may be possible neuroimaging markers for monitoring interventions aimed at improving community functioning in schizophrenia.

S168. Task-related network analysis in schizophrenia patients with auditory verbal hallucinations

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Background: Auditory verbal hallucinations (AVH) in patients with schizophrenia may find their origin in the misattribution of internal speech to an external source. This theory is supported by the observation that speech production and speech reception areas show deviant activation during the experience of AVH. Moreover, AVH often have an affective character, which emphasizes the need to also investigate AVH in terms of emotion. With this study, we aimed to investigate whether patients with AVH demonstrate deviations within and between neural networks engaged in inner speech and emotional valence evaluation, in comparison with patients without AVH and controls.
Methods: Hallucinating patients with schizophrenia ($N = 29$), non-hallucinating patients with schizophrenia ($N = 16$) and control subjects ($N = 39$) performed a word evaluation task during fMRI scanning, in which bisyllabic word were visually presented. In the inner speech condition, participants had to indicate which syllable carried the metrical stress. In the emotional valence condition, the words had to be judged on their positive or negative emotional valence. With the use of Independent Component Analysis, brain networks that were related to the task were identified. Group differences in task-related network (component) activation, as well as spatial contribution within networks, and connectivity between networks were calculated.
Results: The six most related and relevant components were selected for analysis. Whereas patients with AVH demonstrated impaired deactivation in the default mode network, their auditory-sensorimotor network showed increased activation in comparison with patients without AVH and control subjects in both task conditions. Also, in patients with AVH, the left angular gyrus appeared to be more strongly connected to the bilateral fronto-temporal network than in the other two groups.
Discussion: The impaired deactivation of the default mode network and increased activation of the auditory-sensorimotor network during word evaluation in patients with AVH may imply an elevated focus on internally generated events, which might be a reflection of the trait to hallucinate. Aberrant functional connectivity possibly contributes to anomalous integration of information.

S169. Functional connectivity of the default mode network in first episode psychosis: preliminary findings

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Background: The first-episode of psychosis (FEP) has a peak onset between ages 15-25, and can cause severe derailment of young individuals' social, academic, and vocational development. An abundance of evidence shows that FEP is associated with structural brain abnormalities, however very little is known about the functional connectivity (FC) of brain networks at this illness stage. Therefore, this study aimed to investigate the differences in FC of the default-mode-network (DMN) in a group of FEP participants in comparison with a group of healthy controls. Secondarily, this study aimed to explore what relationship FC abnormalities, if any, have on symptomatology and global social functioning.
Methods: Resting-state functional magnetic resonance imaging was used to evaluate default mode FC in 16 FEP participants (mean age = 20.7(1.5), 14 males) and 13 healthy controls (mean age = 25.4 (7.6), 11 males). The data was bandpass filtered (0.01–0.1 Hz) and signals from white matter and the ventricles were regressed to

account for physiological noise. The posterior cingulate cortex (PCC; a known hub of the DMN) was seeded as a region of interest, and Pearson's correlations between the PCC and all other voxels comprising cortical and subcortical gray matter were investigated. Threshold-free cluster enhancement was used to identify clusters of voxels whose correlation with the PCC significantly differed between the group of controls and FEP participants. A cluster-size voxel threshold of ≥ 100 voxels was used. For the brain regions that showed significant group differences in FC with the PCC, Pearson's correlations were performed to explore the relationship between FC with PCC and symptomatology/global social functioning. Given findings are preliminary and the sample size is small, we chose not to correct for multiple comparisons.
Results: Compared with healthy controls, FEP participants showed reduced FC between the PCC and the bilateral parietal lobes (right; $P = 0.017$, left; $P = 0.019$), the right frontal pole ($P = 0.029$) and the right middle frontal gyrus ($P = 0.022$). Compared with controls, FEP participants also showed increased FC between the PCC and the bilateral hippocampus (right; $P = 0.004$, left; $P = 0.001$), bilateral temporal pole (right; $P = 0.004$, left; $P = 0.009$) and the left superior temporal gyrus ($P = 0.004$). All reported *P*-values are uncorrected for multiple comparisons. Across the entire sample (FEP and control participants combined), FC between the PCC and regions showing reduced connectivity in the FEP group (i.e. right parietal lobe; $r = 0.550$, $P = 0.002$, right middle frontal gyrus; $r = 0.577$, $P = 0.001$) positively correlated with Social and Occupational Functioning Assessment Scale (SOFAS) scores, that is, the greater the connectivity the better the social functioning. Additionally, FC between the PCC and regions showing increased connectivity in the FEP group (i.e. right temporal pole; $r = -0.562$, $P = 0.001$, left temporal pole; $r = -0.461$, $P = 0.012$) negatively correlated with SOFAS scores, that is, the greater the connectivity, the poorer the social functioning. No FC associations were found with overall symptoms.
Discussion: These preliminary results suggest that the DMN in FEP shows both increases as well as reductions in FC compared with controls. With that said, this study is ongoing and only a subset of the cohort has been analysed. Further analyses of the full data set are currently being undertaken. Furthering our understanding of neurobiological impairments during early psychosis can help elucidate brain regions and networks that may become more dysfunctional in later illness stages, and which may be important targets for early intervention strategies in the future.
*Zalesky and Bartholomeusz share joint last authorship.

S170. Neural mechanisms of how mood modulates reality-monitoring in schizophrenia

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Background: The study of mood-cognition interactions is an emerging area of neuroscience research, and may help inform the development of successful interventions in individuals with mental illnesses. This study investigates the neural mechanisms of how a positive mood can modulate cognition in schizophrenia, specifically, in reality monitoring abilities. Reality monitoring is the ability to accurately distinguish the source of self-generated items from the source of externally-derived information. In a prior fMRI study, we found that healthy individuals showed increased activation in the mPFC during the accurate identification of self-generated items vs. externally-presented items, which correlated with identification of self-generated information. The medial prefrontal cortex (mPFC) is a key region that has been shown to support self-referential processing. Additionally, we have also shown that healthy participants in a positive mood show increased activation in the mPFC and posterior cingulate cortex (PCC). In light of these findings, we predicted that when participants were in a positive mood, they would activate mPFC and PCC, and that mPFC signal would predict better accuracy of self-generated word items.
Methods: Thirty-five healthy comparison participants (HC) and 35 participants diagnosed with schizophrenia (SZ) completed the study. We used fMRI to map brain activation patterns while participants completed a mood-induction reality monitoring (RM) task. In the MRI scanner, we induced positive, neutral and negative mood states through autobiographical recall. Participants then completed the recognition phase of the RM task. The RM task consisted of an encoding phase prior to scanning and a recognition phase in the scanner. In the encoding phase, subjects were presented with "noun-verb-noun" sentences. The final noun was either presented by the experimenter, or left blank for subjects to generate themselves. During the recognition phase, subjects viewed the noun pairs from the sentence list and had to indicate whether the second word was previously self-generated or externally-presented.
Results: HC showed better performance than SZ at identification of self-generated information which contributed to better overall source-memory performance. In HC, we found a strong influence of mood on overall source-memory accuracy ($P < .05$). This accuracy difference was driven by participants performing better in the positive versus neutral mood ($P < .05$) but not in the negative mood condition ($P = .22$). Specifically, HC recalled more self-generated information ($P < .05$) and marginally more externally-presented information ($P = .07$) in the positive vs. neutral mood condition, showing greater activation within mPFC and PCC regions which predicted better self-generated word recognition. No performance changes were seen for negative mood states for either self-generated or externally-presented item identification. In SZ, however, we found that both positive and negative mood states enhanced recognition of externally-presented information only ($P < .05$). When compared to HC, SZ showed reduced activation within mPFC and PCC regions during positive vs. neutral mood states and demonstrated poorer recall of self-generated information during positive and negative mood states ($P < .05$).
Discussion: These data have several interesting implications: 1) People with schizophrenia do not show the normal relationship between positive mood and better reality monitoring, suggesting impairments in how hedonic experiences influence neurocognitive systems that support self-referential processing; 2) They may also show more sensitivity to the effects of a negative mood, in terms of enhancing word recognition.

S171. Frontal hyper-activation during causal word generation in social contexts in schizophrenia

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Background: Background: Schizophrenia spectrum disorders (SZ) are associated with speech production deficits, including continuous single word production (verbal fluency, VF) tasks. Neuroimaging studies frequently find altered response patterns in SZ during VF in frontal and prefrontal regions crucial to executive function, reasoning and language, and particularly in the left inferior frontal gyrus (Broca's area), a core region for semantic aspects of speech production. Whether distinct word contexts (social/physical) and semantic task-requirements (free or causal association) have an influence on patients' response patterns during VF, is yet unknown.
Methods: Methods: In the present study we used functional magnetic resonance imaging (fMRI) to investigate neural correlates of overt VF in a group of SZ patients ($n = 17$) and matched healthy control subjects ($n = 17$) under different task requirements (free semantic association, FA, causal association, CVF, phonological association, PVF). During scanning, subjects performed the three alternating VF tasks in response to identical cue words of social vs. physical contexts (examples: laughter, cheer, sadness vs. heat, light, cold).
Results: Behavioural results: Patients produced significantly less correct words than controls in all three conditions: per 10- second trial of FA, 1.87/3.14 words (SE = 0.17/0.21), in CVF, 1.71/2.85 words (SE = 0.21 /0.21) and in PVF, 1.55/2.38 words were generated on average in the patient/control group (SE = 0.17/0.19).
fMRI-results: Across groups all VF conditions compared to rest (baseline) evoked neural activation in a bilateral fronto-temporo-cerebellar language production network. Both semantic (FA, CVF) compared to phonological (PVF) verbal fluency conditions engaged brain regions associated with semantic processing; i.e. the left inferior and middle frontal gyrus, left angular gyrus and supplementary motor area. Controls here showed greater activity than patients in the cerebellum and precentral gyrus (area 6/44) bilaterally. SZ patients showed however increased activations in the left frontal cortex as

compared to controls; specifically, during CVF in response to social cues in the left superior frontal gyrus (MNI: -22/6/42; Interaction of group*context, t = 4.53). For CVF compared to FA on similar (social) words, a greater BOLD-response in patients compared to controls was found in the left inferior frontal gyrus (MNI: -42/24/6; Interaction of group*task, t = 3.91), indicating both task-related and content-specific frontal hyper-activation during overt VF in SZ. Interestingly, in the patient group left IFG response during causal over semantic fluency was negatively correlated with the SANS sub-scores for anhedonia (correlation coefficient r = -.37 $P = .045$) and apathy (r = -.37 $P = .045$) and positively correlated with SAPS sub-items for (acoustic) hallucinations (r = .49 $P = .023$) and for inattentiveness during testing (r = .50, $P = .017$).
Discussion: This might suggest that the over-engagement of the left IFG reflects aberrant or compensatory executive mechanisms of the semantic network in SZ, specifically for causal association of more complex (social) verbal information. Further analyses will thus aim at assessing the (potentially context-selective) functional connectivity of l.IFG with the contralateral hemisphere and with posterior parts of the language network in patients and controls.

S172. Functional connectivity and delusional cognitive bias: a resting state functional magnetic resonance imaging study on schizophrenia

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Background: Humans form a variety of beliefs in response to the stimuli in everyday life, however such belief formation is influenced by cognitive biases. One example is the conservative bias, which means people need more evidence for decision than rational probabilistic thinking expects. Abnormality of such bias may lead to abnormal belief, i.e. delusion. Indeed, it is well documented that people with schizophrenia show the jumping to conclusions (JTC) bias, which means patients need less evidence for judgment than healthy people. On the other hand, as delusion cannot be attributed to single brain region, connectivity should be taken into account in the research of neural correlates of JTC. In this study, we employed the beads task, which measures conservative bias and JTC, and resting state functional magnetic resonance imaging (rsfMRI) to reveal the neural correlates of these cognitive biases in healthy people and patients with schizophrenia.
Methods: Fourty-two patients of schizophrenia (Sc) and 34 healthy controls (Hc) were recruited. All participants performed the beads task in the following procedure: subjects were presented with two jars containing 80 blue / 20 yellow and 20 blue / 80 yellow beads, respectively. Beads were drawn from one of the jars repeatedly, and subjects were told to decide from which of the two jars the beads were drawn. The number of draws needed to decision (DTD) was used as the index of conservative bias / JTC. The rsfMRI data were acquired from all the subjects, on a 3 T scanner, and analyzed by independent component analysis. Six independent components were identified as the networks of interest: The default mode network (DMN), left and right central executive networks (CENs), and salience network (SN) were selected because their contribution to the pathogenesis of psychosis has been of interest (Menon, 2011; Palaniyappan *et al*, 2013; Wotruba *et al*, 2014). In addition, the medial temporal lobe network (MTLN) (Lois *et al*, 2014) and basal ganglia network (BGN) (Robinson S *et al*, 2009) were selected based on influential circuit model of psychosis (Lodge and Grace, 2011), which postulate that hyper-dopaminergic state of striatum is driven by hippocampal over activation. Group differences, effects of DTD in Hc and Sc, and their interaction were tested for intra-network connectivity within each network, corrected for multiple comparisons (TFCE $P < 0.05$, extent threshold = 5 voxels).
Results: DTD did not show significant group difference between Hc and Sc. For intra-network connectivity analysis, posterior DMN showed significantly reduced connectivity in Sc compared with Hc. In right CEN, DTD was positively correlated with functional connectivity in Hc. On the other hand, BGN and MTLN showed negative correlation between DTD and functional connectivity in Sc. Finally, anterior DMN showed significant interaction between diagnosis and DTD, revealing positive correlation between DTD and connectivity in Hc and negative in Sc. No other significant group difference, correlation, or interaction was found.
Discussion: The behavioral result was largely in line with latest meta-analysis; though DTD was smaller in Sc than Hc overall, 15 out of 33 studies did not show significant difference (Dudley *et al*, 2015). Also, the group difference of intra-network connectivity in posterior DMN is consistent with previous studies. On the other hand, this study revealed neural correlates of conservative bias of Hc in right CEN, and those of JTC of Sc in BGN and MTLN. This study also showed that functional connectivity of anterior DMN differentially contribute to conservative bias and JTC in each population. These findings would be a future target of neurocognitive intervention for delusion.

S173. Functional neuroimaging of working memory encoding in a orientation change detection task in schizophrenia and first-degree relatives

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Background: Working memory (WM) impairments in schizophrenia (SZ) may be attributed to deficits in the encoding of stimuli that are associated with aberrant neuronal activation patterns. As deficits in WM can also be observed in first-degree relatives of SZ patients, WM dysfunctions are considered as a possible endophenotype of the disorder. In this fMRI study we investigated WM encoding and its neuronal underpinnings in a sample of SZ patients, first-degree relatives of SZ patients and healthy control subjects to determine the possible role of impaired WM encoding as an endophenotypic trait marker.
Methods: We examined $n = 30$ patients with paranoid SZ, $n = 25$ first-degree relatives of patients with SZ (REL) and $n = 30$ healthy control (HC) subjects. All subjects underwent whole brain functional and anatomical MRI scans in a 3-Tesla MR system. During the fMRI scan participants performed a change-detection task which required the memorization of three red lines of different orientation. The interval between sample array and a subsequently shown pattern mask was varied between 100 ms and 800 ms (SOA = stimulus onset asynchrony) in order to allow inferences to potentially different encoding times. Furthermore, cognitive performance was assessed using the MATRICS consensus cognitive battery. Psychopathology of SZ patients was examined with the PANSS.
Results: Overall response accuracy in the change detection task was significantly lower in SZ patients compared to HC and REL. In respect of the different SOA intervals, HC showed significant masking effects in the 100 ms condition and SZ patients showed masking effects in all conditions. In REL a significant linear effect of SOA was observed, with masking effects at 100 ms and 200 ms intervals. During the encoding phase SZ patients showed neuronal hypoactivities in WM related areas including the precuneus and the DLPFC. SZ patients' performance in the cognitive test battery was impaired in seven cognitive domains, including WM.
Discussion: Our results suggest that the process of WM encoding is ineffective in SZ, accompanied by abnormal neuronal activation patterns. In REL WM encoding seems to be prolonged, which may be interpreted as a subclinical sign of WM decline independent of disease state. This reinforces the notion of WM encoding as an endophenotipic trait marker of SZ.

S174. Neural, cognitive, and clinical correlates of cerebellar-dependent associative learning in individuals with schizophrenia

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Background: Cerebellar abnormalities in schizophrenia are hypothesized to contribute to disturbances in the fluidity and coordination of motor, cognitive, and affective processes. Most evidence of cerebellar dysfunction in schizophrenia is behavioral, or consists of structural or incidental fMRI findings. However, the relationship between behavioral deficits on putatively cerebellar-dependent tasks and corresponding cerebellar neural activity has been largely unexplored, and abnormalities in cerebellar structure and neural activity during non-cerebellar tasks are of limited utility in elucidating what process the cerebellum is performing aberrantly. Therefore, we examined cerebellar neural function using fMRI during a cerebellar-dependent task in schizophrenia. We used delay eyeblink conditioning (EBC), wherein a neutral stimulus (i.e., tone, called the conditioned stimulus (CS)) is repeatedly presented and co-terminates with an unconditioned stimulus (US) (i.e., airpuff to the corner of the eye) that naturally elicits a response (i.e., eyeblink, called the unconditioned response (UR)). With repeated paired presentations, the CS ultimately elicits an eyeblink prior to US presentation, which is termed the conditioned response (CR). Decades of non-human animal research has shown the cerebellum to be essential circuitry for the associative learning instantiated by EBC.
Methods: Ten individuals with schizophrenia (SZ) and 20 non-psychiatric controls (NC) underwent three 11.5 minute runs of simultaneous fMRI and EBC. Twenty-six airpuffs and 26 tones were presented during run 1 (pseudoconditioning). Fifty-two paired trials (tone and airpuff) were presented during runs 2 (acquisition) and 3 (maintenance). First-level analyses modeled the BOLD response to unpaired and paired trials separately. Second-level analyses consisted of one-sample t-tests (investigating activation in each group independently) and two-sample t-tests (investigating group differences in activation). Behavioral data were segmented by dividing the 104 paired trials (from 2 runs containing 52 paired trials each) into 8 blocks of 13 trials each, and were analyzed using a 2 (group) x 8 (block) repeated-measures ANOVA.
Results: Behavioral results revealed a significant block x group interaction ($P = 0.037$), with NC producing higher rates of conditioning over the course of the experiment. Imaging results for the acquisition run (minus the pseudoconditioning run) revealed significant activation in left Crus I in NC but no significant activation in SZ ($P < 0.001$, extent threshold = 18 voxels) when groups were analyzed separately. Group comparisons revealed significantly increased activation in the right dentate nucleus in NC compared to SZ. NC also demonstrated significant activation in left Crus I, bilateral lobule VIIIa, and vermis lobule VI during the maintenance run. Activation in vermis lobule VIIIa and right Crus II was positively correlated with IQ scores in SZ but not NC. Negative symptom severity was negatively correlated with cerebellar activation in SZ in right Crus I, right Crus II, and right dentate nucleus.
Discussion: Results suggest that cerebellar neural activity is diminished in SZ while the cerebellum is being directly recruited by EBC, and that EBC impairments in SZ may be driven by abnormal neural activity in the cerebellum during learning. The core processes involved in EBC such as timing, associative learning, and coincidence detection provide additional insight into how cerebellar abnormalities in schizophrenia may manifest as pathological processes. Cognitive and clinical correlates of cerebellar activation suggest that cerebellar function may be related to the cardinal cognitive and affective symptoms of schizophrenia.

S175. Functional connectivity between midline structures of the default mode network is increased in first-episode psychosis during a movie stimulus (Alice in wonderland)

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Background: Patients with psychotic disorders have aberrant functional connectivity patterns when compared with healthy control subjects, frequently observed between precuneus and the medial prefrontal cortex hubs of the default-mode network (DMN). Differences are present during rest and while performing simple tasks, but are inconsistent across studies, with patients exhibiting both increased and decreased connectivity. Reasons for these discrepancies remain unknown, but mental state and experience during imaging have been discussed in earlier literature as possible causes. We set out to study direction and consistency of functional connectivity alterations during an audiovisual movie stimulus. Such stimuli, mimicking the complexity of everyday information processing, have proved valuable in basic neuroscience, but have not yet been utilized in the study of psychosis.
Methods: We analysed two samples of first episode psychosis patients from Helsinki Early Psychosis Study (total of 46 patients and 32 controls. Fourteen patients and 12 control subjects were scanned with GE Signa 3 T and 32 patients and 20 control subjects with Siemens Skyra 3 T at Aalto University, while watching scenes from the Tim Burton movie Alice in Wonderland. For the functional connectivity analysis we computed individual contrast images that reflect connectivity of the seed region to other brain regions over all time points. Seed region was defined according to the precuneus voxels that best identified patients in our previous study. We performed one-sample t-tests to identify group-level functional connectivity patterns and two-sample t-tests to identify between-group differences.
Results: In both patients and controls, the precuneus seed was functionally connected with regions in the medial prefrontal cortex and near the temporoparietal junction ($P < 0.05$, FWE-corrected for multiple comparisons), areas suggested to be part of the default-mode network. Patients had increased functional connectivity between the precuneus seed and the anterior cingulate and medial frontal gyrus ($P < 0.05$, FWE-corrected). These findings were consistent across scanners.
Discussion: Our replicated findings show that during naturalistic complex information processing, functional connectivity between the posterior and the anterior midline hub of the default-mode network is consistently increased. These findings open possibilities for use of such stimuli in further studies and to disentangle the movie-bound features of the information processing that contribute to alteration in connectivity.

S176. Widespread reductions in resting-state functional connectivity in a treatment-resistant schizophrenia group

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Background: Despite advances in antipsychotic medications, approximately 5-10% of schizophrenia patients do not experience a clinically significant reduction in psychotic symptoms with pharmacological therapy, and have thus been labeled as having 'treatment resistant' schizophrenia (TRS). The "default mode network" (DMN) has frequently been found to show aberrant activity/connectivity in early and established schizophrenia groups compared with controls. However, little research has investigated the functional connectivity (FC) of the DMN in a TRS cohort. Therefore, this study aimed to investigate resting-state FC of the DMN in a group of TRS patients in comparison with a group of matched controls. Secondarily, this study aimed to explore what relationship FC abnormalities, if any, have on symptomatology and functioning.
Methods: Resting-state fMRI was used to evaluate DMN FC in 42 TRS participants prescribed clozapine (mean age = 41.3(10.2), 28 males) and 33 controls (mean age = 41.1(10.6), 18 males). Head motion was controlled for, data was bandpass filtered (0.001–0.1 Hz) and signals

from white matter and the ventricles were regressed. To investigate group differences in FC across the whole-brain, registered fMRI volumes were parcellated using the automated anatomical labeling (AAL) atlas, and the temporal correlation coefficients between each nodal pair was measured. The bilateral temporal lobes were seeded as regions of interest and Pearson's correlation between the temporal lobes and all other voxels comprising cortical and subcortical gray matter were investigated. Permutation testing and a cluster-based statistic was used to identify group differences in FC with the temporal lobes. Pearson's correlation was used to explore the relationship between FC and symptomatology/functioning. The Global Assessment of Functioning (GAF) and the Social and Occupational Functioning Assessment Scale (SOFAS) were used to assess functioning sample wide, and the Positive and Negative Syndrome Scale (PANSS) (total positive and negative symptoms) was used to measure symptom severity in the TRS group.
Results: We found reduced mean global brain FC in TRS patients ($P = 0.002$), as well as reduced FC between multiple nodal pairs (153) in TRS patients compared with controls. TRS patients showed significantly reduced FC between the bilateral temporal lobes and the bilateral frontal pole (right; $P = 0.008$, left; $P = 0.008$), the bilateral superior temporal gyrus (right; $P < 0.001$, left; $P < 0.001$) and the occipital lobe ($P < 0.001$). All *P*-values reported are family wise error corrected. In the TRS group, FC between the right frontal pole and temporal lobes was negatively correlated with PANSS negative symptoms ($P = 0.016$) and positively correlated with GAF ($P = 0.016$) and SOFAS (0.036) scores. Sample wide, mean global brain FC, and FC between the temporal lobes and regions showing reduced FC in the TRS group positively correlated with SOFAS and GAF scores.
Discussion: These results suggest that FC of the DMN is widely reduced in TRS patients in comparison with healthy controls. This network dysfunction may suggest inefficient system processing that could in turn impact a number of neural processes (i.e. cognition, internal mentation, self reflection) that are found to be especially impaired in TRS patients. In particular, findings indicate that the reduced FC between the right frontal pole and temporal regions may be suggestive of a possible downstream effect that may be influencing symptoms and global functioning. Furthering our understanding of neurobiological impairments in this chronic group can help elucidate brain regions and networks that may be important targets for alternative treatment strategies in the future.

S177. Hypofunction of basal ganglia indirect pathway in schizophrenia

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Background: This study represents our preliminary effort to establish an in vivo human brain circuit and information processing based model of psychosis in schizophrenia, which would significantly facilitate the discovery of neural mechanisms responsible for this condition. This model is centered on the basal ganglia (BG), whose essential functions is to filter and select the appropriate cortically generated signals supporting cognition and action for further processing and execution by downstream networks. According to the classic model of the BG, the functional architecture of its intrinsic circuits, the direct and indirect pathways, promulgates this gating function. The direct and indirect pathways exert opposing effects, with the former lowering and the latter increasing the gating threshold. An examination of DA effects on BG intrinsic circuit function suggests that excess BG DA in schizophrenia may lead to hypofunction of the indirect pathway, resulting in impaired gating such that aberrant cortical signals underlying psychotic symptoms, which normally would be gated out, are instead gated into downstream systems. The subthalamic nucleus (STN) is a key regulator of the indirect pathway, and as such, demonstration of STN hypofunction would support this model of psychosis. However, this structure's function is very challenging to image. We have developed novel high-resolution fMRI methods to accurately measure task-evoked STN activity to test the hypothesis of STN hypofunction in schizophrenia.
Methods: We conducted this case-control study across two separate sets of samples. In one, there were 6 adults with schizophrenia (SZ) and 17 demographically matched healthy control subjects (HC) and in the other there were 9 in the SZ and 9 in the HC samples. Subjects completed two cognitive tasks while undergoing high-resolution (2x2x2 mm voxels) fMRI scans at 3 T. The first task was the Stop Signal Task (SST), a putative driver of STN activity as it entails the cancellation of a planned motor response. The second task was a N-back working memory (WM) task of fractal images. We identified the STN, as well as the SN, and created ROI masks of these regions for each subject directly on their task fMRI volumes in "native space". We then extracted estimates of task-evoked STN BOLD signal for between group comparisons.
Results: In both samples, SZ showed hypofunction of the STN in the Stop Signal and WM task. In contrast, SZ showed hyperactivity of the SN in the WM task. The magnitude of STN hypofunction inversely correlated with magnitude of psychosis.
Discussion: We utilized novel high-resolution fMRI methods to accurately localize the activity of the STN and observed task-evoked hypofunction of this structure and, by extension, the indirect pathway of the BG. This demonstration provides empirical support for a novel BG information processing model of psychosis in schizophrenia: hypofunction of the indirect pathway that may result in impaired gating of aberrant information underlying psychotic experiences. This BG model may be a useful framework upon which new hypotheses can be generated and tested directly in humans, or which can be reverse translated into animal models. Moreover, our results suggest that the STN could be a novel treatment target in schizophrenia and should be a focus of further investigations.

S178. The predictive value of different neurochemical profiles for treatment outcome in antipsychotic-naïve schizophrenia patients

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Background: Insufficient response to antipsychotic medication constitutes a challenge in the treatment of psychotic patients.
The aim of the study is to stratify antipsychotic-naïve first-episode psychotic patients based on striatal dopamine synthesis capacity (DSC) - and evaluate the prognostic value of stratification in terms of treatment response. The study is the first to combine examination of DSC measured by positron emission tomography (PET) with examinations of glutamate levels (MR-spectroscopy) and brain structure (structural MRI). We hypothesize that responders are characterized by DSC-disturbances measurable prior to treatment, while non-responders are characterized by no or minor DSC-disturbances but increased glutamate availability.
Methods: Forty patients and forty matched healthy controls (HC) will be PET-scanned in an integrated PET-CT scanner using 18 FDOPA. Premedication is given to minimize peripheral metabolism of 18FDOPA. Blood samples are collected sequentially to measure peripheral radioactivity over time and the fractions of 18FDOPA and the primary metabolite 3-O-methyl-FDOPA (OMFD).
Patients are examined at baseline and after 6 weeks of treatment with flexible doses of aripiprazole. HC are not medicated, and scanned at baseline only. The baseline DSC of HC, responders and non-responders will be compared and related to psychopathology. At follow-up the DSC of responders and non-responders will be compared.
Pilot data: An initial objective was to validate the PET-method and test if input-functions based on venous blood-measures were comparable with input-functions obtained with arterial samples. Eight HC have been scanned while arterial and venous blood samples were collected simultaneously.
Results: Pilot data: There is a remarkable difference in input-functions from arterial and venous blood. Venous samples failed to detect the initial peak visualized in the curve derived from arterial samples. Arterial samples are most reliable when correcting for peripheral radioactivity originating from 18F-DOPA and OMFD. Based on the

pilot-data, future PET-examinations in the study will be performed with arterial samples.
Status: Three patients have been scanned at baseline, and one patient at six weeks follow-up. We do not yet have preliminary results on patients.
Discussion: Pilot data: The finding of a difference between arterial and venous input-functions is of potential significance for the interpretation of neurochemical PET data where input-functions are based on venous blood-measures.
Perspectives: Previous studies included only few antipsychotic-naïve first-episode patients, and no studies examined antipsychotic-naïve patients before and after first antipsychotic treatment. Data will provide insights to the interaction between dopaminergic- and glutamatergic disturbances, clinical symptoms and level of functioning. Subgrouping patients based on distinct pathophysiological disturbances is crucial, since DSC and glutamate levels may serve as markers for best choice of treatment.

S179. Thalamic and hippocampus driven alterations in large-scale neural oscillations differ across the different illness stages of schizophrenia: an MEG resting-state study

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Background: Schizophrenia has been conceptualized as a disorder of large-scale discoordination of distributed neural activity which may be related to abnormalities in the balance between excitation and inhibition (E/I-balance). There is also a growing recognition that these large-scale neural system disturbances are not only present during the onset of the disorder, but may already be present during the prodromal phase. Specifically, it has been argued that changes in functional connectivity between the neocortex and subcortical structures, especially structures such as the thalamus and the hippocampus, play a major role in the onset of schizophrenia and its progression due to their fundamental role in large-scale networks. Accordingly, identifying the mechanisms underlying these systemic disturbances as well as their trajectory across the disorder is crucial for insights into the pathophysiology of schizophrenia as well as for the development of biomarkers for early intervention.
In the current study, we aimed to address this question through focussing on neural oscillations in large-scale subcortical-cortical circuits in schizophrenia across the different stages of the disorder. Rhythmic activity at low- and high-frequencies has been prominently implicated in the disorder but the contribution of neural oscillations to thalamic and hippocampal-cortical interactions and their presence in the prodromal state is unclear.
Methods: We obtained resting-state MEG-data from four groups of participants: 1) individuals at ultra-high risk for psychosis (UHR), 2) unmedicated first-episode-psychosis (FEP) patients, 3) chronic schizophrenia patients (ScZ), 4) and healthy controls (HC). MEG data were analysed first for spectral power (1-90 Hz), followed by beamformer spatial filters to elucidate the specific contributions of the hippocampus (anterior regions) and the thalamus to these spectral power differences. Finally, thalamus and hippocampus were used as seed regions to study 40 Hz subcortical-cortical functional connectivity.
Results: ScZ group showed increased delta and theta power, originating from (pre)frontal and subcortical regions. The thalamus contributed mostly to the theta power increases, whereas delta power was influenced more strongly by the hippocampus. Secondly, FEP and ScZ patients deviated from controls and UHR-participants in alpha and gamma-band power. Alpha-power differences were indicative of (pre) frontal hypo-activity and sensory-motor and posterior cortex hyperactivity. Gamma power was increased in frontal-temporal areas. Contribution from thalamus and hippocampus to gamma power increases were seen for both FEP and chronic ScZ patients. Functional connectivity measures showed that thalamo-cortical connectivity was increased in frontal-temporal regions in UHR participants, whereas stronger functional connectivity was found for posterior parietal and occipital areas in the FEP and ScZ patients. Importantly, the FEP group differed strikingly from the UHR and chronic ScZ groups in showing hippocampus-driven increased functional connectivity with the visual and sensory-motor areas, while the UHR and ScZ groups showed only increased connectivity with frontal-temporal regions.
Discussion: Our data provide evidence for both thalamic and hippocampus driven alterations in neural oscillations in large-scale networks which differ across different illness stages. Thus, our data may have implications for the understanding of underlying mechanisms for both the transition into psychosis and the changes that occur during the progression of the disorder.

S180. Prolactin levels in patients with a first psychotic episode with no previous antipsychotic treatment. Relationship with sexual side effects.preliminary results

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Background: Hyperprolactinemia (HPRL) is often found in patients with chronic schizophrenia. However, recent studies have suggested that HPRL may not only be due to antipsychotic medication, but a pre – existing condition.
The objectives of our study were: To determine prolactin levels in patients with a first psychotic episode without previous antipsychotic treatment and to compare the results with healthy controls; To determine sexual functioning in patients with a first psychotic episode who have not previously received antipsychotic treatment and to compare the results with healthy controls; To relate prolactin levels with sexual functioning in both patients and healthy controls.
Methods: Cross-sectional study: Inclusion criteria are: Patients with a diagnosis of first psychotic episode (non- affective psychosis) between 16-55 years old without previous antipsychotic treatment and who belong to the sector care of Mental Health of Parc Sanitari Sant Joan de Déu / Child and Maternal Hospital of Sant Joan de Déu (Esplugues). Healthy controls (matched for sex and age) were recruited.
Results: 32 patients and 23 healthy controls were included in the study. (71% men and 29% women). The average age was 27.59 years (SD 9.08). The Duration of Untreated Psychosis (DUP) was 13.44 months (SD 15.91). 22.6% of the patients had a family history of psychosis in first-degree relatives. Higher levels of prolactin were found in patients with a first episode compared to healthy controls ($P = 0.028$).
No differences were found regarding sexual functioning between patients and controls. A negative correlation was found between prolactin and sexual functioning in both groups (patients and controls) but this correlation was not significant
Discussion: In our study detected higher prolactin levels in patients than in controls which is consistent with previous studies. On the other hand, sexual functioning did not differ in patients compared to controls. The negative correlation between prolactin and sexual functioning was not significative, but it is expected that this association will become significant increasing the sample.

S181. Oral health in first episode psychosis: quantitative and qualitative study on prevalence of oral health problems, risk factors and need for intervention

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Background: Poor oral health is related to various somatic diseases. It is well-known that people with severe mental illness (SMI) have a worse dental condition compared to their general peers. Furthermore, they are susceptible to poor mental health for various reasons concerning various illness related factors such as amotivation, fear and side-effects

of psychiatric drugs such as dry mouth. Additionally, people with SMI choose a more unhealthy lifestyle, such as smoking, poor oral hygiene and carbonated drink consumptions, which act as risk factors for oral health. Finally, SMI patients have difficulties in accessing health care facilities. Little is known about first episode psychosis (FEP) patients' dental condition, as well as the prevalence of risk factors they encounter and the subjective need for intervention.
Methods: In order to investigate the overall oral health, patients with a first episode of psychosis of the Early Intervention team ($N = 100$) and healthy controls ($N = 30$) are requested to fill out a Dutch version of the Oral Health Impact Profile (OHIP-NL) to investigate the overall oral health. Additionally, the prevalence of risk factors are examined, such as smoking, poor oral hygiene, carbonated drinks consumption and dry mouth as a side effect of medication. Qualitative data is collected by interviewing patients ($N = 12$) about their reasons for poor oral hygiene, and their need for intervention.
Results: Data collection is still on-going. A preliminary finding is that people with FEP have a poor to moderate dental condition. However, FEP patients report more oral health problems than healthy controls and also report a higher prevalence of risk factors. Qualitative data reveal that people FEP rate their oral health as important and sufficient. Poor oral hygiene are related to dental costs, amotivation, tiredness and lack of experienced need. Participants report a wish for oral health intervention.
Discussion: Preliminary results show that there is a clear need for oral health intervention in FEP patients considering their poor dental condition and high exposure to various risk factors. Patients endorse this need and wish for more attention and intervention on oral health. Final outcomes are expected in the beginning of 2016 and will be presented.

S182. Connectomic correlates of response to treatment in first-episode psychosis

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Background: Connectomic approaches using diffusion tensor imaging (DTI) have contributed to our understanding of brain changes in psychosis, and could provide further insights into the neural mechanisms underlying response to antipsychotic treatment. We here studied the brain network organization in patients at their first episode of psychosis, evaluating whether connectome-based brain networks predict response to treatment, and whether they change after 12 weeks of antipsychotic treatment.
Methods: 76 patients with a first-episode of psychosis and 74 healthy controls were included. 33 patients were classified as responders after 12 weeks of antipsychotic treatment. Baseline brain structural networks were built using whole-brain DTI tractography, and analyzed using graph analysis and network-based statistics to explore baseline characteristics of patients who subsequently responded to treatment. A subgroup of 43 patients was re-scanned at the 12-week follow-up, to study connectomic changes over time in relation to treatment response.
Results: At baseline, those subjects who subsequently responded to treatment, compared to those that did not, showed higher global efficiency in their structural connectomes, a network configuration that theoretically facilitates the flow of information. They also had a less connected left precuneus at baseline (lower degree and strength). We did not find specific connectomic changes related to treatment response after 12 weeks of treatment.
Discussion: Our data suggest that patients who have an efficiently-wired connectome and a less central precuneus at first onset of psychosis show a better subsequent response to antipsychotics. However, response is not accompanied by specific structural changes over time detectable with this method.

S183. Structural brain abnormalities in medication naive offspring of schizophrenia and bipolar patients

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Background: Prospectively studying children of a parent with schizophrenia (SZ) or bipolar disorder (BD) is an important approach to obtain a better understanding of the developmental trajectories of these disorders. The objective of the current Dutch Bipolar and Schizophrenia Offspring Study (DBSOS) is to identify clinical and neuro-imaging characteristics in SZ- and BD-offspring compared to community controls.
Methods: A DBSOS subsample of 29 SZ-offspring, 68 BD-offspring and 44 controls, all medication naïve and aged between 8 and 18 years (mean 13.8 years), underwent magnetic resonance imaging on a 3 T scanner and were assessed for psychopathology (K-SADS-PL, CBCL/6-18) and cognitive functioning (WISC/WAIS). T1-weighted images of the whole brain were obtained and FreeSurfer 5.3.0 was used to estimate global and subcortical brain volumes. In addition, the cortex was parcellated in 34 ROIs per hemisphere. Cortical volume, cortical thickness and cortical surface area was estimated per ROI (left+right). The three offspring groups were compared taken familiar dependency into account using linear mixed effects modeling (SPSS 23). In addition, the three groups were divided based on the presence of any lifetime axis I disorder according to DSM IV and brain measures were compared. FDR correction was applied.
Results: Total brain volume is significantly smaller in SZ and BP offspring as compared with controls, which is explained by smaller volumes of both cortical white and gray matter. In particular, volumes of the pallidum, hippocampus, and amygdala were reduced in both high-risk offspring groups relative to controls. In addition, smaller cortical volume in the lateral occipital cortex, supra-marginal and pre-cuneus cortex, posterior cingulate cortex, para- and postcentral sulci, pars-orbitalis, superior temporal cortex, and insula were found in SZ-offspring and BP-offspring as compared with controls. In addition, cortical surface area of the postcentral gyrus was significantly smaller in both offspring groups relative to controls. No significant differences were found between the groups in cortical thickness for any of the ROIs after FDR correction.
The comparison between those with and without any lifetime axis I disorder showed that most pronounced and extensive cortical volume loss was found in those children and adolescents with a lifetime axis I diagnosis.
Discussion: Here we show that adolescent offspring of schizophrenia and bipolar patients have a smaller volume of the brain, which was most pronounced in the hippocampus, amygdala, and frontal and parietal cortices. The cortical volume loss appears particularly pronounced in children and adolescents with a DSM-IV lifetime axis I diagnosis. In addition, we provide suggestive evidence that neurodevelopmental processes may play a role as the cortical surface area of the postcentral gyrus is smaller in the SZ and BP offspring when compared to age and gender matched controls. The presence and severity of psychopathology, IQ and other relevant factors will be discussed.

S184. Alterations of structural connectivity in patients with schizophrenia: a systematic review

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Background: Many voxel-based morphometry (VBM) studies have reported white matter alternations in schizophrenia. However, a meta-analysis of VBM findings shows inconsistent results due to misalignment and smoothing problems. In order to solve the limitation in VBM approach, Tract-Based Spatial Statistics (TBSS) is widely used in diffusion tensor imaging studies. The aim of this study is to review TBSS results regarding white matter tracts in schizophrenia.
Methods: We manually carried out electronic search of PubMed, Embase and CINAHL to explore impaired white matter tracts with TBSS approach in schizophrenia. All articles are written in the English

language containing the keywords: (1) "DTI" "TBSS" "white matter skeleton", (2) "schizophrenia" "psychosis".
Results: Whole-brain TBSS studies of schizophrenia that we found consistently reported areas with significantly lower FA in patients than controls including superior longitudinal fasciculus, external capsule and corpus callosum.
Discussion: Studies with TBSS approach presented less broad areas for white matter impairments in patients compared to those of VBM analysis. The results tentatively suggest that local and global deficits in structural connections may be critically associated with alternations of brain network in schizophrenia.

S185. Heritability of volumetric brain changes in adolescence

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Background: Volumetric brain abnormalities are consistently found in schizophrenia patients (1). These deficits are likely to be of genetic origin because family members of patients also have smaller brain volumes than healthy controls. Indeed, volumetric brain changes over time have been found to be genetically associated to the liability for schizophrenia (2). In addition, individuals at high risk for schizophrenia already show decreases in brain volumes before the onset of the disease (3). We may therefore assume that brain differences found in patients are at least in part the result of early abberant brain development that is genetically driven. Here we aim to study the influence of genes on volumetric brain development in a longitudinal cohort of healthy adolescent twins.
Methods: From the BrainSCALE cohort (4), structural MRI scans were acquired of 112 twin pairs in three waves, at the ages of 9 years ($N = 190$; mean age 9.1 years, sd 0.1), 12 years ($N = 125$, mean age 12.1, sd 0.3) and 17 years ($N = 176$, mean age 16.9, sd 0.4). Brain volumes (total brain volume, gray and white matter) for each wave were extracted and entered in a multivariate twin model. Heritability (h2) and influences of common (c2) and unique environment (e2) on volumetric brain change was estimated from the variances and covariances of the volumes.
Results: Heritabilty estimates of volumetric change were larger in the second time interval (age 12 to 17) than in the first interval (age 9 to 12) (Table 1). Not only heritability increased over time, but also absolute genetic variance per year, indicating that this increase is not driven by the larger interval, or higher measurement quality.

Table 1: Heritability of volumetric brain changes. Significant estimates are displayed in bold.

	Volume change age 9-12	*Volume change age 12 -17*
	h2 / c2 / e2	*h2 / c2 / e2*
Total brain volume	0.20 / 0.10 / 0.69	0.42 / 0.26 / 0.32
Gray matter volume	0.11 / 0.10 / 0.79	0.45 / 0.02 / 0.52
White matter volume	0.01 / 0.18 / 0.81	0.49 / 0.02 / 0.49

Discussion: Not only brain volumes, but also the extent to which the brain changes over time are driven by genes during the teenage years. As the developmental trajectory of the brain is considered to be an important indicator of developing mental disease5, identifying genes involved in brain plasticity may increase our understanding of the biological pathways involved in healthy development and brain abnormalities in schizophrenia.
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S186. Brain metabolites in ultra high risk patients for psychosis

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Background: Ultra High Risk (UHR) patients have approximately 30% risk to develop psychosis. The causal pathway of this risk is yet unclear, but may in part be related to UHR specific characteristics in cerebral neurochemistry. Previous proton magnetic resonance spectroscopy (1H-MRS) studies have shown some abnormalities in UHR patients, but results have been inconclusive. We aimed to explore differences in brain metabolites between UHR patients and an age, IQ and gender matched control group.
Methods: We recruited 16 UHR patients and 21 healthy controls. UHR patients were recruited through the Early Psychosis Department of the Academic Medical Center (Amsterdam) using the Comprehensive Assessment of At Risk Mental State (CAARMS). Controls were recruited through local advertisement. Participants were antipsychotic naïve. Brain metabolites were measured using 3 Tesla 1H-MRS using two 8 ml voxels in the dorsolateral prefrontal cortex (DLPFC) and hippocampus. We compared creatine, glutamine, glutamate, glycerophosphocholine (GPC), myo-inositol, N-acetylaspartate (NAA), choline, NAA+N-acetylaspartylglutamate, GLX (glutamine+glutamate).
Results: Compared to controls, UHR patients had significantly higher myo-inositol in the DLPFC (0,78 vs. 0,68 $P = 0{,}011$). UHR patients had borderline significant higher GPC (0,28 vs. 0,25 $P = 0{,}052$) and choline (0,29 vs. 0,26 $P = 0{,}053$) in the DLPFC. UHR patients had significantly lower hippocampal GLX (1,81 vs. 2,19 $P = 0{,}046$).
Discussion: UHR have specific differences in brain metabolites compared to controls. The differences found in this study can be linked to previously reported neurochemical differences in UHR patients but also in 22q11 deletion syndrome, another risk group for psychosis.

S187. Arcuate fasciculus size is associated with auditory hallucinations

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Background: The arcuate fasciculus (AF) has been implicated in the pathology behind schizophrenia (SZ) and auditory verbal hallucinations (AVHs), most commonly by findings of disruptions in the white matter integrity. The AF is suggested to be important for language processing, connecting temporal auditory areas with inferior frontal/precentral and inferior parietal regions. Although there have been a number of studies on this topic, there is still a need for replications that include SZ with and without AVHs, and also studies investigating the different segments of the arcuate fasciculus as previously outlined by Catani *et al.*
Methods: Thirty-two SZ patients with frequent AVHs (SZ AVH; PANSS P3 score ≥ 4), 37 SZ patients with less frequent AVHs (SZ nAVH; PANSS P3 score ≤ 3), and 40 healthy controls (HC) were subjected to diffusion tensor imaging (DTI) at 3 T. Tensor estimation and AF tractography was performed using ExploreDTI v4.8.4, and for each individual the anterior, long, and posterior segments of the AF were tracked in native

space. Mean tract volume and tract length were extracted as macrostructural measures and fractional anisotropy (FA) and mean diffusivity (MD) as microstructural measures. A multifactorial general linear model (GLM) with repeated measures was set up, with hemisphere (left/right) and tract (anterior/long/posterior) as within-subject factors, group (SZ AVH/SZ nAVH/HC) as between-subjects factor, and with age and sex as covariates.
Results: There were no significant main or interaction effects including group. However, post-hoc explorations of the tract*group effects for tract volume ($P = .06$) and length ($P = .12$) using Fisher's LSD, showed that SZ AVH had higher volume of the long segments compared to HC ($P < .02$), with SZ nAVH intermediate ($P < .04$ SZ nAVH > HC). The long segments were also longer in the SZ AVH group compared to HC ($P = .009$), with SZ nAVH again intermediate (n.s.).
Discussion: The present results show that SZ patients with frequent AVHs have larger and longer long segments of the AF than HC. This could suggest that this group have increased connections between auditory areas in the temporal lobe and frontal and parietal areas associated with language. Previous studies have indeed found an increase in white matter volume in the regions connected by the AF, and that greater overall white matter volume predicted higher positive symptom score five years later.
From the present findings it is not possible to disentangle whether it is the larger AF that allows for AVHs to be experienced, or if these segments increase in size due to the presence of AVH. However, it could indicate that in these individuals, the information flow between language areas could have multiple destinations and origins not found in HC, so that e.g. more tracts reach frontal and parietal areas from the auditory areas, thus leading to a perception of a voice that is not there.

S188. Influence of environmental risk factors on white matter microstructure: a diffusion tensor imaging study

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Background: Environmental factors such as urban upbringing and early life stress are often replicated risk factors for schizophrenia (van Os *et al.*, 2010). However, the effect of these environmental factors on white matter microstructure – as an intermediate phenotype – is still vague. Therefore, we investigate the influence of environmental risk factors for schizophrenia, such as urban upbringing and early life stress on white matter microstructure in healthy controls, subjects with environmental risk, and patients with schizophrenia.
Methods: To date, $n = 274$ healthy controls (HC), $n = 80$ healthy subjects with environmental risk (early life stress; HCer), and $n = 110$ patients within the schizophrenia spectrum (SZ) participated in our study and were deeply phenotyped. All subjects underwent diffusion tensor imaging (3 T Tim Trio, Siemens) as well as neurocognitive testing. We used tract-based spatial statistics (TBSS) to examine fractional anisotropy (FA) and mean diffusivity (MD) in major fiber tracts in all subjects.
Results: We would expect that environmental risk factors such as early life stress and urban upbringing moderate white matter alterations in the whole sample. Furthermore, we would anticipate the same directions of regression slopes (early life stress or urban upbringing and FA/MD) in all groups (HC > HCer > SZ), indicating an effect of environment on the white matter microstructure.
Discussion: The hypothesized association between brain structural alterations and environmental risk in patients with schizophrenia and healthy subjects experienced early life stress or urban upbringing could further highlight the influence of environmental risk factors on brain structure. Thus, we try to identify mechanisms how environmental risk can lead to psychiatric disorders such as schizophrenia.

S189. Relationships between corpus callosum volume and functional asymmetry in the language network in schizophrenia and bipolar disorder

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Background: The distinction between bipolar disorder (BD) and schizophrenia (SZ) can be a challenge. Therefore, the identification of specific biomarkers of these disorders can be helpful. Some abnormalities of the corpus callosum (CC) as well as a reduced lateralization for language have been described in both these disorders. However, the relationship between the CC volume and the functional lateralization for language has not been established. We first hypothesized that BD patients will present a reduction of callosal volume more marked than SZ patients and HC, impacting on the functional lateralization for language. Secondly, we hypothesized that SZ presented a reduced functional lateralization for language independently of the CC volume.
Methods: Twenty BD patients, 20 SZ and 40 healthy controls (HC) were included in the study. The experimental paradigm consisted in a block-design language comprehension task of listening to a factual French story alternated with the same story in Tamil, an unknown language for all participants. A functional lateralization index (FLI) was extracted in each participant within the language comprehension network. Volumes were extracted individually in total CC and its three sub-regions. The anatomo-functional relationships between these variables were tested between the three groups.
Results: A decreased leftward functional lateralization for language was found in SZ patients but not in BD patients compared to HC. Decreased callosal volumes were observed in BD compared to SZ and HC. A negative correlation was highlighted only in BD patients between the anterior callosal volume and FLI suggesting that a smaller CC predicted a decrease of a leftward functional lateralization for language.
Discussion: The main results of this study revealed a dichotomy between BD and SZ patients. Indeed, SZ patients presented a reduced leftward functional lateralization for language compared to BD patients and HC. Otherwise, BD patients presented a reduction of callosal volumetric compared to SZ patients and HC. Moreover, we observed that this callosal decrease could induce a decrease of leftward functional lateralization for language in BD patients.

S190. Resting state deficits in theta band connectivity in schizophrenia using magnetoencephalography

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Background: Schizophrenia research has covered a broad range of deficits and attempted to address a large range of cognitive, positive and negative symptoms while relating them to brain activity or functional and structural changes. Resting state networks have been examined using EEG and MEG in a number of studies across a large range of frequencies and has found an assortment of results. Theta band activity has been theorised to be involved in the memory encoding process and also in Long term potentiation (Stanton & Sejnowski, 1989). In a review of 12 studies looking at the results of theta band activity in resting state, 11 were found to show increases to Theta (4-8 Hz) band activity during resting state in schizophrenia patients specifically in left temporal regions which positively correlated with positive reported symptoms (Siekmeier & Stufflebeam, 2010). These results have been repeated in the EEG literature and have yet to be as consistently determined in MEG methodologies.
Methods: There were a total of 8 participants in this data set; four healthy controls and four who were diagnosed with either schizophrenia or schizoaffective disorder. Each of the participants underwent a clinical interview including the following measures; Positive and Negative Syndrome Scale, Structured Clinical Interview for DSM-V, the M.I.N.I International Neuropsychiatric Interview, Weschler Test of Adult Reading and the Edinburgh Handedness Inventory. Diagnoses for the patients were confirmed and healthy controls were screened for an absence of diagnoses.

A whole head 306-channel Elekta magnotometer system was used and head position was digitally scanned in the MEG recording position with localisation coils and was registered with the Polhemus FASTRAK head digitising system. Participants were asked to sit still and close their eyes for 5 minutes while we recorded passive activity.
Results: The connectivity between each set of gradiometer sensors was calculated using the Weighted Phase Lag Index (WPLI;squared debiased version). The results showed that patients had a significant decrease in theta band connectivity as compared to healthy controls in frontal, posterior, left, right and centre regions as well as in a whole brain analysis. There is a difference shown between patients and controls in the alpha band as well, however due to power limitations, the difference shown could be an effect of outliers. Beta, low-gamma and high-gamma all showed no difference between the two groups.
Discussion: The above results do not reflect the body of EEG and fMRI literature and present an alternative to the mantra that slow wave activity shows increases in schizophrenia. As mentioned above, Theta band activity has been proposed to play a role in memory encoding and memory processing. However, the cognitive profile of people with schizophrenia is quite varied and rarely shows consistency from one patient to the next. Difficulties with memory and encoding processes are quite mixed in schizophrenia and this shows that there may be differences in cognitive profiles depending on symptomotolgy. This difference in cognition may be what we are seeing in this Theta band connectivity decrease and future research with this data set should look at the cognitive outcomes of these participants and correlations between memory tasks and this difference in activity.

S191. Structural brain network disturbances in the psychosis spectrum

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Background: Individuals with subclinical psychotic symptoms provide a unique window on the pathophysiology of psychotic experiences as these individuals are free of confounders such as hospitalization, negative and cognitive symptoms and medication use. Brain network disturbances of white matter connections are thought to play a central role in the pathophysiology of psychosis. Based on the disconnection hypothesis in schizophrenia, we expected less and weaker connections, and altered brain network organization in individuals with clinical and those with subclinical psychotic symptoms.
Methods: We used diffusion tensor imaging to study 35 patients with a psychotic disorder, 35 subjects with subclinical psychotic symptoms, and 36 healthy controls. The structural brain network was analyzed on three levels: connection density, white matter microstructure (fractional anisotropy, mean diffusivity, and magnetic transfer ratio), and network organization. Network organization was studied with minimum spanning tree analysis, a method to reconstruct a backbone of structural highways in the brain.
Results: Decreased fractional anisotropy and increased mean diffusivity was found in both groups with psychotic symptoms, while their network topology showed decreased overlap with a healthy reference network. Decreased centrality was found in several brain regions, including parietal hubs and language areas, in both groups with psychotic symptoms. Deviation of network characteristics was more apparent in clinical subjects than in subclinical subjects.
Discussion: Weaker connections and decreased centrality of parietal hubs characterize the structural brain network in subjects with psychotic symptoms. These differences are more notable in clinical than in subclinical subjects with psychotic experiences. Our findings are in line with the hypothesis of a psychosis continuum, ranging from healthy subjects to patients with a psychotic disorder.

S192. Insight and white matter changes in first-episode schizophrenia

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Background: Dysconnectivity between brain regions may account for failures of self-monitoring, which may underlie impaired insight in schizophrenia. No known FES studies have examined white matter (WM) and insight, and limited evidence from chronic studies suggest that poor symptom awareness is associated with reduced FA in various frontal, parietal and temporal lobe regions. Meta-analyses of fMRI data implicate Cortical Midline Structures in impaired self-reflective processing. Our aim is to describe WM tract differences in FES patients and controls, and to identify WM tracts associated with impaired insight (using a priori selected tracts associated with insight deficits in fMRI and sMRI studies - cingulate, cingulate hippocampus, uncinate, sFOF, and corpus callosum genu, body and splenium). Our hypotheses are that (a)FES patients would demonstrate widespread WM dysconnectivity vs. controls including for the a priori selected tracts; (b) Alterations in WM microstructure represented by FA values of the chosen tracts would predict insight in patients.
Methods: We compared FA in a priori selected tracts of 89 FES patients and 98 controls, and assessed for an association between FA and insight deficits as measured by the Birchwood Insight Scale. Socio-demographic differences between FES and HC were compared. A linear regression model, controlling for age, education and gender, was used to calculate residual FA differences between patients and controls. We corrections for multiple comparisons and residuals FA values were used for further analyses. For hypothesis (b), we used the Least Angle Regression (LARS) algorithm to build a prediction model.
Results: Patients had widespread decreases in age and gender adjusted mean FA values compared to controls. Our data highlight four white matter tracts as predictors of insight; namely the splenium of the corpus callosum and left hemisphere hippocampus portion of cingulate (positive predictors of insight), and the left hemisphere cingulum portion of cingulate and left hemisphere uncinate fasciculus (negative predictors of insight).
Discussion: Our main finding is that at the time of first episode schizophrenia, FA decreases are widespread and these decreases are also associated with insight deficits. FA decreases associated with insight deficits include but are not limited to Cortical Midline Structures. These results support the hypothesis that insight impairment ins schizophrenia involves a complex brain network.

S193. Brain morphometry correlates of social cognition in schizophrenia: a systematic review

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Background: Schizophrenia has been conceptualized as a disorder of the social brain, with deficits observed in social cognition, social skills, social behavior and social functional outcomes. Several neuroimaging experiments have been performed to identify critical brain networks relevant to processing of social information. We aim to review structural magnetic resonance imaging (MRI) experiments that have examined brain correlates of social cognition in patients with schizophrenia.
Methods: Online databases (PubMed and Google Scholar) were searched using key words [(social cognition, theory of mind, empathy, mentalizing, mental state attribution, emotion recognition, emotion processing, emotion perception, affect perception, affect recognition, affect processing, social perception, social knowledge, attributional style, attributional bias) AND (structural magnetic resonance imaging, cortical thickness, morphometry) AND (schizophrenia, psychosis)] in titles and abstracts. Selection criteria were (a) subjects with a diagnosis of schizophrenia (DSM or ICD), (b) structural MRI scan and (c) quantification of social cognition performance. Two investigators performed the search and selected studies independently. Among the 21 articles retrieved, 14 met the selection criteria and were included in

the review. Data on patient characteristics, image analysis, social cognition tools used, and correlation coefficients of relationship between social cognition performance and structural MRI data were collated and critically analyzed.
Results: The mean sample size in the 14 studies reviewed was 25 (range 18-51), majority of the subjects were stable chronic schizophrenia outpatients on antipsychotic medications. While eight studies examined mentalizing, six studies assessed social cue identification. Voxel based morphometry was the commonest image analysis method used. Most studies (12) reported statistically significant relationships between social cognition performance and gray matter volumes, even after controlling for confounding variables like age, illness duration, IQ and total intracranial volume. Reduced superior temporal sulcus volumes were most commonly associated with impairments in social cue identification (other regions having such a relationship were anterior and posterior cingulate, ventral premotor cortex, medial temporal structures like amygdala and parahippocampal gyrus). Medial prefrontal cortex volumes were most commonly associated with mentalizing tasks (lateral prefrontal cortex, and superior temporal sulcus were other regions with similar correlations).
Discussion: The prefrontal cortex and superior/medial temporal lobe structures seem to play an important role in diverse social cognition abilities. While superior temporal sulcus aberrations are associated with social cue detection deficits, medial prefrontal volume reductions are related to mentalizing impairments.

S194. Functional dysconnectivity in medication-naïve schizophrenia patients with auditory verbal hallucinations

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Background: Schizophrenia has been conceptualized as a brain disorder characterised by aberrant neural integration among distinct regions. How functional dysconnectivity may give rise to the symptoms experienced by schizophrenia patients remains to be elucidated. Auditory verbal hallucinations are hypothesized to arise from abnormal interaction between speech processing areas and other brain regions.
Methods: Resting-state fMRI imaging was acquired in 36 first-episode medication-naïve schizophrenia patients and 18 healthy controls. The patient group consisted of 18 patients with auditory verbal hallucinations and 18 patients without hallucinations. Regions of interest (ROIs) were selected based on meta-analyses on hallucination-related brain activations. Functional connectivity among ROIs were extracted and compared between groups (FDR corrected, $q < 0.05$), followed by correlation analysis with symptom scores.
Results: Patients with and without hallucinations were found to exhibit distinct dysconnectivity patterns as compared to controls. Hallucinating patients demonstrated higher functional connectivity between the right caudal anterior cingulate cortex and other cortical regions, including superior temporal gyrus (left: $P = 0.01$, right: $P = 0.01$), inferior parietal lobule (left: $P = 0.001$, right: $P = 0.002$) and right insula ($P = 0.02$). Functional interaction between the left caudal anterior cingulate cortex and right inferior parietal lobule was also stronger in patients with hallucinations ($P = 0.01$). Further, connectivity between the right caudal anterior cingulate cortex and speech processing areas (left superior temporal gyrus, inferior parietal lobule) co-varied with PANSS positive scores ($P = 0.004$, $P = 0.005$ respectively).
Discussion: Our findings suggest that enhanced functional synchronization between anterior cingulate cortex and language areas may be an integral part of the neuropathology of auditory hallucinations in schizophrenia, in the early stage of the illness and in the absence of potential confounding effects of psychotropic medication.

S195. Musical deficits and cortical thickness in patients with schizophrenia

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Background: We recently reported that deficits in music ability were correlated with clinical manifestations such as cognitive functions and negative symptoms. However, the neural substrate underlying the musical disability remains still unclear. We therefore sought to investigate the relationship between musical deficits and volumetric changes in patients with schizophrenia using structural MRI.
Methods: We recruited 30 patients with schizophrenia (15 males; age mean = 43.5 ± 11.1), 21 controls (13 males, age mean = 46.9 ± 13.5) and measured musical ability, cognitive functions and clinical manifestations. Images were acquired with a 1.5 T MRI scanner, and processed using the automated pipeline of FreeSurfer v5.3.0. A priori knowledge of areas known to be important in music disability was utilized.
Results: As shown in previous paper, patients with schizophrenia demonstrated lower music ability and cognitive functions compared to controls. A hypothesis-driven regional analysis was completed and focused on the cortical thickness and white matter volume in temporal lobe and inferior frontal lobes. In patients with schizophrenia, thicker cortex in the right transverse temporal gyrus and supramarginal gyrus was associated with better musical ability, while in controls the association was in the opposite direction.
Discussion: We reconfirmed that musical disability correlated with cognitive functions and negative symptoms in patients with schizophrenia. Findings from the volumetric imaging study showed that musical disability in schizophrenia positively correlated with ability in some cortical regions. These results shed light on the pathophysiological mechanisms underlying the associations of musical ability, cognitive functions and negative symptoms in patients with schizophrenia.

S196. Phenotypic characterization of schizophrenia patients with linkage to chromosome 13q, 1p and 13q+1p

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Background: Linkage analysis is a standard approach for identifying the location of genes that cause genetic disease. The primary advantage of this approach lies in detecting genes of moderate to major effect. We have performed linkage studies of schizophrenia in the genetically isolated population of the Afrikaners from South Africa. A 10- cM genomewide scan performed on 143 small families identified evidence for linkage to chromosome 13q ($n = 51$), 1p ($n = 23$) and combined 13q+1p ($n = 18$) following both non parametric and parametric linkage analysis. Phenotypic clinical characteristics and functional outcome measures of these groups of patients were investigated.
Methods: Data capturing tool was completed with recruitment and follow up clinical data available.
In the statistical analysis of the data one-way analysis or variance was performed to compare the means of quantitative variables for the 3 groups (linkage to 13q, to 1p, or to both loci). Post-hoc comparisons were performed where differences were significant. Chi-square or Fisher's exact tests were used to determine whether associations between the groups and other categorical variables were statistically significant. Logistic regression models were also fitted to further investigate relationships between the 3 groups and other variables, for example suicidality.
Results: The association between chromosome linkage and diagnosis (Schizoaffective Disorder (SAD) or schizophrenia) is moderately significant (P-value = 0.0755). More patients with linkage to 13q were diagnosed with SAD (39.2%) compared to patients with linkage to 1p (13.0%), whereas when linkage to both 13q +1p was present 33.3% of the patients were diagnosed with SAD. Patients with linkage to only 13q are 4.3 times more likely to be diagnosed with SAD compared to

patients with linkage only to 1p. This is interesting in light of reported linkage for bipolar illness to the same locus on 13q.
Suicidality and diagnosis of SAD are statistically significantly related (*P*-value = 0.0080). Among patients diagnosed with SAD, 51.7% had a history of suicide attempts compared to 23.8% of patients diagnosed with schizophrenia. The odds ratio of 3.4 indicates that patients with a diagnosis of SAD are 3.4 times more likely to have a history of suicide attempts. The odds ratio of completed suicide of patients with linkage to 13q compared to those with linkage to 1p is 1.87. Although not statistically significant the odds of completed suicide was observed to be higher for patients with linkage to 13q than those with linkage to 1p.
Discussion: Patients with linkage to chromosome 13q are more likely to carry a diagnosis of SAD and to have had history of suicide attempts as well as higher rate of completed suicide.

S197. Results from a genome-wide association study with clinical response to duloxetine and placebo

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Background: Major depressive disorder (MDD) is a prevalent psychiatric disorder and frequently a comorbid condition to schizophrenia. Antidepressant medications are frequently prescribed to treate depressed symptoms, including patients with major psychosis. Duloxetine is an antidepressant which is particularly prescribed with co-morbid pain symptoms. Genetic factors are known to influence outcome to antidepressant drugs and possibly to placebo. Identifying a 'genetic signature' for duloxetine response will help to implement personalized treatment care. Notably, a substantial alleviation of mood and pain symptoms is commonly also observed with placebo medication. Placebo response is poorly understood and identifying biological causes will help identifying new drug targets and optimizing clinical drug trials.
In addition, our study allows to investigate if treatment effects for medication and placebo rely on similar genetic factors.
Methods: We performed the first genome-wide association study in patients treated with either duloxetine ($n = 215$) or placebo ($n = 235$) for up to 8 weeks. Genotyping was performed using the PsychChip, which is endorsed by the Psychiatric Genomics Consortium. (The samples and clinical data were provided by H. Lundbeck A/S under Lu activity number 15761.) Treatment response was operationalized as MADRS score changes (%) from baseline and was used as the main outcome variable in an ANCOVA model, including baseline depression severity, length of treatment and cohort as covariates. High standard quality controls were applied on generated SNPs and on study subjects, controlling for factors such as ethnicity, heterozigosity rates, and degree of relatedness. In addition, we conducted imputation analyses allowing us to analyze up to two million gene variants per individual.
Results: As for response to duloxetine, top hits were observed in regions on chromosome 1, 7 and 19 implicating a previously unnoted intergenic variant, resulting in a missense signal in a gene involved in cell cycle progression, and an intronic variant in a gene involved in endocytosis. However, none of the findings reached significance after correction for genome-wide analyses and thus would represent suggestive findings ($P < 10\text{-}6$). In contrast, as for response to placebo, a significant, genome-wide corrected hit was found in a region on chromosome 3 ($P = 1.87\text{E-}09$). This particular locus is located at a relatively short distance (150 kb) from the SH3 and cysteine rich domain (STAC) gene, implicated in neuron-specific signal transduction, and expressed in nociceptive (pain processing) neurons. Carriers of the CC genotype improved on average by 49.6% of MADRS score while non-carriers only improved by 23.9%; a clinically relevant and meaningful difference. A second, suggestive finding ($P < 10\text{-}6$), was found with a marker located in a gene involved in thyroid functioning.
Discussion: Our data provide new insights into genetic pathways implicated in response to antidepressant and in particular to placebo medication. Interestingly, our results do not appear to support the notion that similar pathways were involved in each of the two treatment groups. The genome-wide corrected significant finding for placebo response is particularly interesting given the proximity to a gene involved in pain signalling mechanisms. The region associated with placebo response in our study may harbour gene variants that act as remote promoters to regulate Expression of the STAC gene. In summary and to the best of our knowledge, this is the first study detecting a genome-wide significant association with response to placebo in depressed patients. We are currently evaluating our findings in independent patient samples also treated with placebo for major Depression.

S198. Investigation of the genetic basis of specific psychotic experiences in adolescence

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Background: Psychotic experiences (PEs) include positive, cognitive, and negative dimensions and are assessed as quantitative traits in the general population. PEs during adolescence are associated with a later risk of schizophrenia in adulthood (e.g., J. Welham, J. Scott, G. Williams, J. Najman, W. Bor, M. O'Callaghan and J. McGrath, 2009, Psychol. Med. 39, 625-34). As such, knowledge of the genetic aetiology of PEs could provide insight into the developmental pathways of schizophrenia and other major psychiatric disorders. Twin studies report moderate heritability estimates for adolescent PEs (33-50%) (e.g., H. M. S. Zavos, D. Freeman, C. M. A. Haworth, P. McGuire, R. Plomin, A. G. Cardno and A. Ronald, 2014, JAMA Psychiatry. 71, 1049-57). The aim of the present study is to identify common genetic variation associated with specific PEs in adolescence.
Methods: Adolescents assessed both genotypically and for specific PEs were derived from three general population studies: TEDS (Twins Early Development Study), ALSPAC (Avon Longitudinal Study of Adults and Children) and CATSS-18 (Child and Adolescent Twin Study in Sweden). The three samples have been harmonised phenotypically using a combination of expert clinician advice, principal components analysis and item response theory. Genotypic data from the CATSS sample is still being prepared. Genotypic harmonisation of TEDS and ALSPAC samples using 1000 Genome Phase 3 imputation resulted in over 6 million shared common variants. This approach enables us to perform a mega-genome-wide association study (mega-GWAS), where all three sample are assessed simultaneously. Phenotypic harmonisation resulted in four common scales assessing specific PEs, positive symptoms (n≈8,000), cognitive disorganisation (n≈6,000), anhedonia (n≈6,000), and parent-rated negative symptoms (n≈8,000). Univariate-genetic association analysis will be carried out for each of the specific PEs using PLINK 1.9.
Preliminary univariate-GWAS of related and unrelated TEDS individuals (2,179 unrelated, 837 related) assessed at 16 using the Specific Psychotic Experiences Questionnaire has been carried out.
Results: Principal components analysis of PE items from each sample highlighted the presence of similar specific PE dimensions across samples. The mega-GWAS of all three samples is currently being carried out and will be completed by January 2016.
Preliminary univariate analysis of the six specific psychotic experiences assessed in TEDS has yielded two genome-wide significant variants. One variant, significantly associated with cognitive disorganisation, is within a gene previously associated with schizophrenia, bipolar disorder and adult cognitive disorganisation. With the substantially larger sample size in our current mega-GWAS, we expect to identify a number of variants achieving genome-wide significance.
Discussion: The well-powered genetic association analysis of adolescent psychotic experiences will provide insight into the genetic aetiology of adolescent PEs, as well as associated major psychiatric disorders in adulthood, such as schizophrenia. With our large sample we will be able to address several other key aspects adolescent PEs such as the genetic overlap between specific PEs and major

psychiatric disorders, as well as the interaction of genetic and environmental factors in adolescence associated with specific PEs.

S199. Association of polygenic risk score of dopaminergic pathway with schizophrenia and its grey matter volume alteration of putamen

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Background: Schizophrenia is a complex, highly heritable brain disorder characterised by disturbance in behaviour, emotion and thought. The efficacy of chloropromazine and amphetamine animal model led to the belief that schizophrenia, especially positive symptoms of schizophrenia was caused by overabundance of dopamine in mesolimbic area in the brain. However, evidence about dopaminergic hypothesis from genetic and genomic study has remained insistent. The current study examines the correlation between a direct measure of genetic risk of dopaminergic pathway, using the polygenic risk score, and diagnosis of schizophrenia and putamen grey matter volume in patient and healthy control group.
Methods: First episode schizophrenia patients and healthy controls were recruited from Mental Health Center, West China Hospital, China. All participants were scanned on a 3 Tesla GE system (General Electric, Milwaukee, WI). Genotyped data were imputed referenced by 1000 Genome database and underwent standard quality control and linkage disequilibrium pruning. Further, population analysis was carried out to detection of potential population structure and extraction of principal components of structure. After searching in Mouse Genome Informatics database(MGI) based on the term"dopamine dopminergic", genes were extracted; SNPs located in dopaminergic genes were extracted from SNP138common using UCSC genome browser. After genotypic quality control and cryptic relatedness check, 71 first-episode schizophrenia patients and 85 healthy controls remained in our study. Polygenic risk scores(PRS) for SNPs located within the dopaminergic pathway were calculated using target alleles at these SNPs identified as risk associated based on the PGC GWAS(2013). Image analysis was conducted with the FMRIB software Library (FSL, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL), using the FIRST tool to find the affine transformation to standard space, and then to segment left and right putamen by Morphometric Analysis standard labels after boundary correction, measuring volume by fslstats, respectively. Logistic regression model was used for association study of schizophrenia with first 2 principal components(PCs) being controlled as covariates. Moreover, linear regression model was employed for association study of grey matter volume of putamen in patients and controls with age, sex and population PCs as covariables.
Results: There were no significant difference of grey matter volume in putamen between patients and controls($P>0.05$). The association study of schizophrenia showed that association significance reached its peak at significance threshold of 0.13(105 SNPs, $P=0.002$), explaining 4% of its prevalence and the association of PRS with putamen grey matter volume showed that dopaminergic PRS was significantly associated with left and right putamen grey matter volume in patients group at significant threshold of 0.22 and 0.34, respectively(left putamen: 812 SNPs, $P=0.046$; right putamen: 1024 SNPs, $P=0.045$). Moreover, no significance was found in association with grey matter volume of putamen in health control group.
Discussion: In current study, we observed dopaminergic genes play an important role in prevalence of schizophrenia from perspectives of common variants. Specifically, we show that PRS of dopaminergic pathway with schizophrenia is related globally to alteration of putamen grey matter. It is crucial to understand the genetic imaging correlates. Control brain areas deficient in dopaminergic neurons should be used in the future to validate the prediction efficacy of dopaminergic PRS. Moreover, further analysis should also be focused on the detection of "driver SNPs" in dopaminergic pathways.

S200. Further evidence for vulnerability-stress model of schizophrenia: possible role of FKBP5 gene haplotypes in a Serbian population

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Background: Hypothalamic–pituitary–adrenal (HPA) axis dysregulation is a potential neurobiological mechanism related to the vulnerability-stress model of schizophrenia. Functional single nucleotide polymorphisms (SNPs) in FK506-binding protein 51 (FKBP5) gene, which modulate glucocorticoid receptor sensitivity to cortisol and thus regulate the activity of HPA axis, are reported to interact with trauma and influence stress-related psychiatric disorders. Particularly, minor alleles of the functional SNPs are considered as "risk" alleles. Recent studies highlighted a possible role of the functional genetic variants of FKBP5 gene in psychosis and supported the hypothesis of increased stress sensitivity in schizophrenia. The purpose of this pilot study was to investigate genotype distribution, allele frequencies and frequencies of FKBP5 haplotypes Serbian case-sibling-control sample.
Methods: Genetically homogeneous sample of 52 schizophrenia spectrum patients s, 55 healthy siblings and 51 controls, were genotyped for nine FKBP5 SNPs (rs9296158, rs3800373, rs9470080, rs737054, rs6926133, rs9380529, rs9394314, rs2766533 and rs12200498). Hardy–Weinberg equilibrium (HWE), pairwise linkage disequilibrium (LD) and haplotype frequencies of studied SNPs were computed using the Haploview software. Differences between the genotype distribution and allele frequencies were analyzed by contingency tables using the chi-square test. The data collection was performed in collaboration with EUGEI research network.
Results: The distribution of genotypes for each SNP had no significant deviation from HWE (HWE, $P>0.05$). Results revealed significant difference in functional SNP rs3800373 genotype distribution between patients and controls ($P=.041$). Risk allele (G) of rs3800373 was more frequent in patients compared to controls ($P=.020$) and there was a borderline significance for risk allele (A) frequency of rs9296158 ($P=.053$). There was neither difference in genotype distribution and allele frequencies between patients and sibling, nor in siblings vs. controls. Haplotype analysis showed different frequencies of the haplotypes among the groups in the first block consisted of the functional FKBP5 SNPs (rs9296158, rs3800373, rs9470080) and rs737054. AGTC haplotype combination (with A, G, T "risk"alleles) was more frequent in patients compared to controls ($P=.024$), and GTCC (with no-risk alleles) was more frequent in controls ($P=.0531$). We observed that GTCT (with no-risk alleles) haplotype was more frequent in siblings compared to controls ($P=.0543$). Second haplotype block, with other five SNPs, showed tendency that GTCTC and GTTCC were more frequent in siblings compared to controls ($P=.0765$, $P=.0745$, respectively).
Discussion: To the best of our knowledge this is the first study that analyzed FKBP5 haplotype in schizophrenia patients and their unaffected siblings compared to controls. Our preliminary results revealed that AGTC haplotype combination with risk alleles was more frequent in patients than in controls, while siblings were in intermediate position. Interestingly, we found differences in haplotypes between siblings and controls that warrant further investigation in a much bigger EUGEI sample for the possible resilient biological mechanism. We confirmed that FKBP5 may be playing an important role in schizophrenia, as a part of transdiagnostic neurobiological pathway for stress sensitivity endophenotype.

S201. The role of a cathechol-o-methyltransferase (COMT) Val158/Met genetic polymorphism in schizophrenia: a systematic review and updated meta-analysis of 32 816 subjects

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Background: An association between a cathechol-O-methyltransferase (COMT)Val156Met (rs4680) polymorphism and schizophrenia has been

reported in the literature, although no conclusive outcomes have been attained. The aim of this study was to evaluate the association of the COMT Val108/158Met polymorphism with schizophrenia in a systematic review and meta-analysis.
Methods: We performed a keyword search of the PubMed and EBSCO databases. All English language case-control studies published up to April 2015 were selected. A total of 67 studies that investigated the association of the COMT Val108/158Metpolymorphism were selected for inclusion. The genotype distribution of subjects with schizophrenia was compared with healthy control subjects, using allelic, additive, dominant and recessive models.
Results: The pooled results from the meta-analysis (15,565 cases and 17,251 healthy subjects), after the elimination of the heterogeneity, showed an association between COMT Val108/158Met and schizophrenia (recessive model: OR 1.08 CI95% (1.01-1.15)). We conducted subgroup analyses according to ethnicity. An association was observed in our Caucasian population in an additive model (OR 1.21 CI 95% (1.06-1.37)) and in a recessive model (OR 1.21 CI 95% (1.11-1.32), but not in an allelic or a dominant model. However, when we analysed our Asian population after the elimination of the heterogeneity, no evidence of a significant association was found in any of our genetic models.
Discussion: Our analyses indicate an association between COMT Val108/158Met and schizophrenia in the general population. However, in a Caucasian population, this risk could be increased.

S202. Methylomic changes in individuals exposed in utero to diethylstilbestrol

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Background: In the Western world, more than 2 million people were exposed in utero to diethylstilbestrol. In exposed individuals and in their descendants, several adverse outcomes have been linked to such exposure, like cancers, genital malformations and, less consistently, psychiatric disorders. Disruption of epigenetic homeostasis was proposed as the molecular substratum of this environmental factor but was not fully proven.
Methods: We selected 69 siblings from 30 families. In each family, at least one sibling was exposed in utero to diethylstilbestrol. We analyzed DNA methylation using HumanMethylation450 DNA Analysis BeadChip®. We performed a methylome-wide association analysis searching for specific methylation changes in exposed versus unexposed individuals. Secondary, we compared exposed individuals with and without genital malformation, and with and without psychosis.
Results: No differentially methylated regions were identified between exposed and unexposed individuals. Yet, our analyses showed that exposed individuals with genital or psychotic abnormalities have several specific differentially methylated regions compared with exposed individuals without complication. These CpGs were located in genes relevant for cancer (ADAMTS9), genital abnormalities (HOOK2) and psychiatric diseases (ZFP57).
Discussion: In utero exposure to diethylstilbestrol is not associated with changes in methylation profiles. In exposed individuals though, specific traits are associated with methylomic modifications encompassing genomic regions, mostly involved in cancer and neurodevelopment, leading to heterogeneous consequences.

S203. Genetic overlap between amyotrophic lateral sclerosis and schizophrenia

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Background: Schizophrenia (SZ)-associated symptoms have been noted in patients suffering from amyotrophic lateral sclerosis (ALS), a progressive neurodegenerative disease affecting the upper- and lower motor neurons. Cognitive impairment is found in around 40% of ALS cases without co-morbid dementia, whereas cognitive symptoms are observed in almost all SZ patients. Furthermore, a higher rate of psychotic illness is observed in pedigrees of ALS patients, especially in those carrying repeat expansions in the C9orf72 gene. Conversely, an increasing body of evidence points to neurodegenerative mechanisms of illness in SZ. Given the partial clinical overlap between ALS and SZ, we have investigated the possible genetic overlap (pleiotropy) between these diseases. Access to a unique and to date largest genetic dataset on ALS, combined with publicly available data on the largest genome-wide association study (GWAS) in SZ renders this endeavour highly timely.
Methods: We applied three different methods to assess and cross-validate pleiotropy. First, linkage disequilibrium score regression (LDSC) was used to estimate genetic correlation between ALS and SZ, and secondary traits as negative controls. Second, polygenic risk scores (PRS) were calculated for cases and healthy controls in the ALS dataset, based on the effect sizes of SZ-associated alleles in their genomes. Scores were based on multiple SZ *P*-value cut-offs. A generalized linear model (GLM) was applied to compare variances explained by a full model (including polygenic risk scores) with a baseline model including only covariates (sex and principal components). Finally, conditional false discovery rate (cFDR) *P*-values were calculated for ALS given SZ, and vice versa. Conditional and conjunction Manhattan plots were generated from the cFDR *P*-values values of common genetic variants in both diseases.
Results: Using LDSC we estimated the genetic correlation between ALS and SZ, captured by common genetic variants, to be 14% (SE = 3.7%, $P = 1E\text{-}4$). We corroborate the specificity of this finding by demonstrating the absence of genetic correlation between ALS and all secondary traits tested. Using PRS with stringent correction for covariates, the maximum variance explained (Nagelkerke R2) in ALS by polygenic risk scores based on SZ-associated alleles with *P*-value cut-off 0.1 was 0.08%, which was significantly different from the variance explained in a baseline model with only covariates ($P = 6.3E\text{-}5$). Furthermore, conditional FDR *P*-values < 0.05 for ALS and SZ genetic variants reveal C9orf72 as a shared risk locus for ALS and SZ as well as a number of novel ALS-associated loci.
Discussion: Using all presently accepted methods to examine pleiotropy, we provide converging evidence for the presence of genetic overlap between ALS and SZ. This is reflected by a relatively high genetic correlation between both diseases, higher occurrence of SZ risk alleles in ALS patients and a shared risk locus, C9orf72. Our results support previously detected clinical overlap between these devastating diseases and suggest the possibility of shared underlying disease mechanisms.

S204. Maternal immune activation reduces translocator protein (TSPO) expression in the offspring prefrontal cortex

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Background: Imaging of translocator protein (TSPO) density using radiolabeled ligands is increasingly used to assess signs of neuroinflammation in patients with schizophrenia and related disorders. In view of its co-localization with microglia, elevated TSPO signals are often interpreted as increased microglia activation. Here, we evaluated whether TSPO levels are changed in a well-established neurodevelopmental mouse model with relevance to schizophrenia and related disorders.
Methods: The model used here is based on maternal treatment with the viral mimetic poly(I:C) (5 mg/kg i.v.) on gestation day 9 in C57BL6/N mice. This maternal immune activation model has been shown to capture a wide spectrum of schizophrenia-related brain and behavioral abnormalities in the offspring. Adult offspring were first tested in the paradigm of prepulse inhibition (PPI) of the acoustic startle reflex to ascertain sensorimotor gating impairments as previously described in this model. TSPO levels were then quantified in post-mortem tissue using immunohistochemical techniques and were further correlated with other glial and neuronal markers,

including the microglia marker CD68, the astrocyte marker GFAP, and the neuronal marker NeuN.
Results: Adult offspring of immune-challenged mothers displayed reduced PPI compared to controls. Post-mortem analyses revealed a small but significant (16%, $P < 0.05$) decrease in total TSPO density in the medial prefrontal cortex of poly(I:C)-exposed offspring. The reduction in prefrontal TSPO density was not associated with changes in CD68 and GFAP expression, suggesting that decreased TSPO levels in immune-challenged offspring do not mirror altered microglia and astrocyte activation.
Discussion: Prenatal immune activation leads to decreased levels of TSPO in the offspring medial prefrontal cortex in the absence of overt microglia or astrocyte anomalies. These findings are in contrast to the recently reported imaging studies showing increased TSPO-specific ligand binding in grey matter of people at ultra high risk of psychosis and in patients with schizophrenia. Hence, prenatal viral-like immune activation does not seem to be an environmental factor contributing to schizophrenia-related TSPO alterations. Additional studies are ongoing to further examine the cellular origins of reduced TSPO density following prenatal immune activation.

S205. The acute and chronic effects of antipsychotic treatment on synaptic dopamine levels: preliminary results from a meta-analysis of microdialysis studies

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Background: Evidence from multiple lines of research point to a central role of alterations in dopaminergic neurotransmission in patients with schizophrenia. Consequently it is hypothesized that the clinical efficacy of antipsychotic drugs (APDs) results from blocking the disrupted dopamine signaling particularly in dopamine D2 receptors-expressing neurons. However a substantial amount of patients do not respond sufficiently to the treatment with APDs. It has been suggested that blocking dopamine receptors with APDs might induce adaptive processes ultimately leading to dopaminergic hypersensitivity and treatment failure. Numerous early studies have investigated changes in dopaminergic neurotransmission following APDs in rodents using microdialysis. However there is substantial heterogeneity in the methodological characteristics of the studies that render it difficult to derive conclusions. Thus in the present work, we have conducted a quantitative review of all available microdialysis studies.
Methods: We conducted a comprehensive literature research to identify all studies that applied microdialysis in rodents to measure the acute and chronic effects of APDs on the synaptic levels of dopamine in two regions (nucleus accumbens, striatum). Temporal trajectories of effect size measures from all studies were derived from each study and entered in a random-effects meta-analytical model. The effect of moderating variables (e.g. typical antipsychotic haloperidol vs. atypical antipsychotic clozapine, antipsychotic dosage) was investigated using meta-regression.
Results: For the analysis of the studies investigating acute haloperidol administration we identified $n = 15$ investigating changes in the Nucleus Accumbens and $n = 24$ studies in the Striatum. In the analysis of chronic antipsychotic administration we identified $n = 7$ studies in the Nucleus Accumbens and $n = 15$ studies in the Striatum. For the Nucleus Accumbens there was a significant decrease in dopamine levels in the chronic compared to the acute condition in the time periods 0-60 min, 61-120 min, 121-180 min, 181-240 min, 240-280 min. Similarly for the Striatum there was a significant decrease in dopamine levels in the chronic compared to the acute condition in the time periods 0-60 min, 61-120 min, 121-180 min, 181-240 min, 240-280 min.
Discussion: We present preliminary results of a meta-analysis of microdialysis studies in rodents of changes in dopamine levels following acute APDs administration. Our results demonstrate that chronic APDs treatment strongly decreases the acute stimulation of synaptic dopamine release driven by the same drugs. These results may be of relevance to dissect the neurobiological mechanisms underlying APDs treatment efficacy and failure. Our ongoing analysis will investigate the moderating factors of different APDs, the dosage of administered drugs and the effect of chronic treatment on dopamine metabolites.

S206. Assessing factors of treatment resistance to antipsychotics: nicotine and caffeine affect haloperidol-induced effects on behaviors and on molecules of the post-synaptic density

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Background: Physicians are challenged by factors that may affect response to pharmacological treatments, as in the case of Treatment Resistant Schizophrenia (TRS). Detailed anamnestic and physical examinations are carried out to individuate putative causes of pseudo-resistance. However, often the devil is in the details. Smoking and coffee use may represent two relevant confounders for antipsychotic treatment response. In this work, we asked whether nicotine and caffeine might affect the action of the prototype antipsychotic haloperidol on molecules of the glutamatergic post-synaptic density (PSD), an ultraspecification of excitatory synapses implicated in the molecular basis of schizophrenia.
Methods: Sprague-Dawley rats were randomly assigned to one of the following treatment groups ($n = 8$ each): 1) vehicle (NaCl 0.9%) (VEH); 2) haloperidol 0.8 mg/kg (HAL); 3) GBR-12909 30 mg/kg (GBR); 4) caffeine 40 mg/kg (CAF); 5) nicotine 1.5 mg/kg (NIC); 6) caffeine40 mg/kg+haloperidol 0.8 mg/kg (CAF+HAL); 7) nicotine 1.5 mg/kg+haloperidol 0.8 mg/kg (NIC+HAL). Expression of Homer1a, Homer1b/c, and Arc genes was investigated by In Situ Hybridrization Histochemistry; protein levels were assessed by Western Blot; locomotor activity was evaluated by the open field test. ANOVA and Student-Newann-Keuls post-hoc tests were used to assess treatment effects. In all tests, significance was set at $P < .05$ (two-tailed).
Results: CAF significantly decreased locomotor activity compared to GBR and increased it compared to HAL. Protein levels of all molecules assessed were not significantly modified by CAF. Homer1a expression was not affected compared to VEH, however CAF significantly reduced expression compared to GBR and HAL. Homer1b/c expression was significantly reduced by CAF compared to GBR, but not compared to VEH or HAL. Arc expression was reduced by CAF compared to VEH, GBR, and HAL.
CAF+HAL significantly decreased locomotor activity compared to VEH and GBR, but not to HAL. However CAF+HAL significantly increased Homer1a and Arc protein levels compared to VEH, GBR, HAL, and even CAF. Both Homer1a and Arc genes' expression was consistently and significantly decreased by CAF+HAL compared to VEH, GBR, and HAL. Molecular effects of CAF+HAL on Homer1b/c were virtually absent.
NIC significantly decreased locomotor activity compared to VEH and GBR, but not to HAL. Homer1a protein levels were significantly increased by NIC compared to VEH, GBR, and HAL. Homer1a gene expression was significantly reduced by NIC compared to HAL, but not to VEH and GBR. Arc protein levels were significantly increased by NIC compared to VEH only, while gene expression was significantly reduced compared to VEH, GBR, and HAL. Homer1b/c expression was significantly increased compared to VEH and, to a lesser extent, to HAL.
NIC+HAL significantly decreased locomotor activity compared to VEH and GBR, but not to HAL. Homer1a protein levels were significantly increased by NIC+HAL compared to VEH, GBR, and HAL. Homer1a expression was significantly increased compared to VEH and decreased compared to HAL in the striatum.
Discussion: These results suggest that both caffeine and nicotine have distinct effects on molecules of the PSD. More importantly, both compounds significantly affect the molecular effects of haloperidol. Homer1a and Arc protein and gene expression levels were often uncoupled and in some cases contrasting, as they were controlled by a feedback mechanism.

S207. Influence of Val158Met polymorphism in COMT gene on executive function and grey matter in early onset-first episode patients

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Background: Catechol-o-methyltranferase (COMT) gene is considered a promising schizophrenia susceptibility gene due to COMT enzyme's role in dopamine degradation. Val allele variant has higher activity leading to decreased dopamine bioavailability in prefrontal regions1. Val allele has been associated with weakened executive function (EF) measures in schizophrenic patients2. A relationship between this cognitive domain and frontal volume is widely extended in the same population3. Although there is mixed evidence on the association between COMT variant and volume in the frontal area, no previous studies have reported results regarding early onset psychosis (under 18 years old) (EO-FEP).
With this study we aim to investigate the impact of Val158Met polymorphism on prefrontal gray matter (GM) and EF in EO- FEP and healthy controls.
Methods: 37 EO-FEP (diagnosed with schizophrenia, schizophreniform and schizoaffective disorders) and 23 controls were included in the study. The Val158Met single nucleotide polymorphism was genotyped by GoldenGate assay the Veracode system. Allelic variants were grouped as Met/Met and Val carriers. Magnetic resonance images were processed through a semiautomatic method based on the Talairach atlas and SPM for tissue segmentation. The prefrontal area was divided into superior, medial and inferior areas. To minimize the effect of age, site and total brain volume, the standardized residuals of GM data after a regression were used for the analyses. EF was calculated using z scores of neuropsychological tests based on the controls performance. Comparisons were assessed by means of bivariate (t-student) and multivariate analysis (linear regression using gender, race and socioeconomic status as controlling variables).
Results: 37 EO-FEP (10 females [27%]; mean age 15.68, SD = 1.73; 30 Val carriers (69.6%)) and 23 controls (7 females [30%]; mean age 14.83, SD = 2.59; 16 (81.1%)) were included in the study.
Val carriers showed significant decreased volume in GM compared to Met/Met on the right superior $t(35) = 2.17$, $P = 0.037$ and left medial prefrontal $t(35) = 2.92$, $P = 0.006$ and a tendency of worse performance on EF $t(35) = 1.93$, $P = 0.061$ in EO-FEP patients. This difference did not appear in the control group ($t(21) = -1.09$, $P = 0.287$; $t(21) = -0.54$, $P = 0.596$; $t(21) = 0.007$, $P = 0.994$). No significant differences were found in other prefrontal measures. The linear regression showed that the only significant predictor of the left medial prefrontal was the COMT in EO-FEP group (beta: −0.458, 95% CI[−1.564, -0.129], $P = 0.007$) and a tendency of the right prefrontal superior (beta:-0.295, 95% CI[-1.564, 0.129],$P = 0.094$) and EF (beta: -0.300, 95% CI [-1.281,0.082], $P = 0.083$) but not in the control group.
Discussion: In this study, Val carrier variants were associated with a decreased GM right superior and left medial prefrontal in patients with EO-FEP compared to met homozygotes. No other significant differences were obtained regarding COMT allelic variant. It suggests COMT could aggravate cortical prefrontal alterations in EO-FEP.

S208. Phenotype and function of myeloid cells in schizophrenia patients

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Background: Genetic and epidemiologic studies suggest that immune processes are associated with schizophrenia. It remains unknown to which cell type and which immune process this effect can be attributed. In addition to microglia, the resident innate immune cells of the central nervous system, perivascular and infiltrating monocyte-derived macrophages become part of the immune cell population in a diseased brain. These myeloid cell types have an important function for initiating and controlling inflammation, as well as mediating tissue repair. Moreover, it is becoming clear that they have crucial functions in neurodevelopmental processes and neuronal functioning during homeostasis. It is therefore hypothesized that dysfunction of microglia and/or macrophages is involved in schizophrenia pathogenesis. The aim of this experiment is to investigate whether the phenotype and function of monocyte-derived macrophages are altered in schizophrenia patients compared to controls.
Methods: Monocytes were isolated from blood samples of ten schizophrenia patients with a mean age of 32 years (+/-11) and eleven controls with a mean age of 32 years (+/-5). The cells were cultured with human serum for seven days to generate macrophages. They were characterized at baseline by measuring mRNA expression levels of a panel of 22 genes that reflect different key functions of macrophages. The response to pro- and anti-inflammatory cytokines was determined by stimulating the cells with (lipopolysaccharide, resiquimod/toll-like receptor 7,8 agonist, interleukin-4 & dexamethasone) after which cytokine secretion and surfaces markers were measured by qPCR and ELISA. The phagocytic capacity of the cells was analysed by incubating the cells with IgG-coated fluorescent spheres and subsequent measurements of the uptake of the beads by flow cytometry. All statistical analyses were performed with Mann-Whitney and Wilcoxon-matched pairs tests, as the data was not normally distributed.
Results: The functional phenotype of monocyte-derived macrophages at base line, as well as the response to pro- and anti-inflammatory components, was not different between patients and controls. The phagocytic properties were also not affected in the schizophrenia patients.
Discussion: This study suggests that monocyte-derived macrophages from schizophrenia patients do not demonstrate major intrinsic abnormalities in phenotype and functionality. To draw further conclusions, additional studies are necessary since the study is underpowered to find differences in subgroups, the effect might be visible only at the protein level and state alterations could be lost because of culture of the cells for seven days in vitro.

S209. Abnormalities in the unfolded protein response in schizophrenia

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Background: Schizophrenia (SCZ) is a severe chronic psychiatric disorder that has been associated with cellular dysfunction; however, the exact cause of this debilitating neuropsychiatric disorder is still unknown. Recently, abnormalities in posttranslational protein modifications (PTMs) which can regulate protein targeting, trafficking, synthesis, and function have become targets of SCZ research.
As a major contributor to the synthesis, folding, trafficking, and modifications of proteins, the endoplasmic reticulum (ER) is well-positioned to sense cellular stress. The unfolded protein response (UPR) is an evolutionarily conserved adaptive reaction to environmental and pathological perturbations in ER function. The UPR is a highly orchestrated and complex cellular response which is mediated through three known ER transmembrane stress sensors, protein kinase RNA-like ER kinase (PERK), activating transcription factor-6 (ATF6), and inositol requiring enzyme 1α (IRE1α). When activated, ATF6 is cleaved and translocates through the Golgi to the nucleus, while PERK and IRE1α form homodimers and autophosphorylate themselves. Activation of the PERK pathway leads to phosphorylation of eukaryotic translation initiation factor 2α (eIF2α) and increased expression of activating transcription factor 4 (ATF4), while activation of the IRE1α pathway leads to unconventional mRNA splicing of the transcription factor x-box binding protein 1 (XBP1). Regulating all of these pathways is the ER chaperone, GRP78.
Our lab recently investigated gene expression changes for proteins involved in multiple UPR pathways from the dorsolateral prefrontal

cortex (DLPFC) by using Human Unfolded Protein Response PCR Arrays. To elaborate on abnormal transcription changes, we hypothesized that indicators of UPR activity would be abnormally expressed in SCZ, resulting in reduction in UPR pathway.
Methods: We measured the total expression and subcellular localization of proteins involved in the UPR pathway in DLPFC from12 matched pairs of SCZ and comparison subjects. We used a previously established subcellular fractionation protocol to isolate the enriched ER fractions from DLPFC. Protein expression in the enriched ER fraction sample was measured relative to the corresponding protein in the total homogenate lane.
Results: We found a significant decrease in phosphorylated IRE1α in the DLPFC of subjects with SCZ. In an ER enriched fraction we found reduced expression of GRP78 and ATF6, along with a decreased ratio of phosphorylated to total forms of PERK, eIF2α, and IRE1α. Additionally, we observed an increased ratio of spliced to unspliced forms of XBP1 expression in the ER enriched fraction.
Discussion: Increased GRP78 expression has been commonly used as an indicator of ER stress. Therefore, the reduction in GRP78 expression we observed in this study may be indicative of reduced ER stress response in SCZ. The decreased expression of ATF6 in the ER enriched fraction, along with the decreased ratio of phosphorylated to total forms of PERK and IRE1α support the idea that the UPR is decreased at basal levels in SCZ. When looking downstream of the PERK and IRE1α pathways, however, we observed conflicting results. The ratio of phosphorylated to total eIF2α, a transcription factor phosphorylated by PERK, supports a reduction in this pathway, while the increased ratio of spliced to unspliced XBP1 suggests an upregulation of the IRE1α pathway. Taken together, these findings suggest an abnormal pattern of UPR activity in SCZ. We believe this likely reflects a mechanism to maintain cellular homeostasis in the face of chronic stressors in SCZ, and that the dysregulation of this system may contribute to protein processing abnormalities previously observed in SCZ.

S210. The role of ATP signaling in cannabis-induced psychotic experiences

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Background: Cannabis use is associate with psychosis risk but how cannabis interacts with genetic vulnerability in the etiology of psychosis is not fully understood. In a genome wide environment-interaction study (GWEIS) we identified genetic loci that confer psychosis vulnerability associated with cannabis use. To further understand how these loci interact with cannabis to induce psychosis, in vitro cellular assays were conducted.
Methods: 1262 individuals were selected from the general population. Psychosis vulnerability was measured by a questionnaire assessing subclinical psychotic experiences; the Community Assessment of Psychic Experiences (CAPE). Whole genome genotype data was generated using Illumina arrays and subsequent imputation resulting in 2,504,766 SNP's for analysis. We analyzed the interaction between genotypes and cannabis use (High\Low) and the risk to belong to the top 50 percent for psychotic experiences. Using in vitro experiments we analyzed how the SNP that was identified in the GWEIS affects the function of the respective gene and how this function is altered in the presence of different concentrations of cannabinoids such as cannabidiol and THC.
Results: In the group of heavy cannabis users a SNP in one of the purinergic receptors was strongly associated with an increased risk (OR: 1.746, p: 1.10E-07) for a high CAPE score. In vitro, cannabidiol and to a lesser extent THC decreased the response to ATP of this purinergic receptor. This reduction was significantly enhanced in the cells carrying the risk SNP.
Discussion: Our results indicate that cannabinoids affect ATP signaling and that the interaction between specific genetic variants in purinergic receptors and cannabis use is involved in cannabis-induced psychotic symptoms. Purinergic signaling is crucial to various important functions in the central nervous system and has therefore been hypothesized to be involved in neurologic as well as psychiatric disorders. The present study supports this hypothesis and prompts further studies to unravel the role of purinergic signaling in the pathogenesis of psychotic disorders.

S211. Proteasome abundance and activity in the superior temporal gyrus of patients with schizophrenia

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Background: The ubiquitin-proteasome system (UPS) is a major regulator of protein processing, trafficking, and degradation. Multiple studies have indicated transcript abnormalities of the UPS in both blood and brain in schizophrenia. Additionally, our lab has previously reported decreases in ubiquitin associated enzymes, total and free ubiquitin levels, and K48-linked polyubquitination of 40 and 70 kDA proteins in the superior temporal gyrus in schizophrenia. K48-linked polyubiquitination is primarily utilized to target proteins to the proteasome for degradation, suggesting our findings indicate not only abnormalities in the ubiquitin system, but also abnormal utilization of the proteasome.
Methods: In this study, protein abundance and proteolytic activity were measured in postmortem brain tissue from the superior temporal gyrus of pair-matched comparison and schizophrenia subjects. Western immunoblotting was utilized to determine protein abundance of proteasome catalytic subunits as well as essential subunits from proteasome regulatory complexes, and fluorogenic substrates specific to chymotrypsin-, trypsin-, and caspase-like activity were used to assay proteasome activity. Significant findings were then assayed in rats chronically treated with haloperidol to address the effects of antipsychotic treatment on protein expression and enzyme activity.
Results: We found decreased expression of Rpt1, Rpt3, and Rpt6, subunits of the 19 S regulatory particle, which are essential for ubiquitin-dependent degradation by the proteasome. Additionally, the α subunit of the 11 S αβ regulatory particle, a complex that enhances proteasomal degradation of small peptides and unfolded proteins, was also decreased. Haloperidol-treated rats did not have altered expression of these subunits, suggesting that the changes we observed in schizophrenia are likely not due to chronic antipsychotic treatment. Additionally, we demonstrate the viability of using 8-32% continuous glycerol gradients and Blue Native gel electrophoresis to examine complex-specific protein abundance and proteasome activity in human post-mortem brain tissue. Experiments utilizing these methods to determine potential abnormalities of proteasome complex abundance and activity in schizophrenia are currently underway.
Discussion: These data provide further evidence of dysfunction of the ubiquitin-proteasome system in schizophrenia, and suggest that altered proteasome activity may be associated with the pathophysiology of this illness.

S212. Maternal immune activation induces early changes in neurodevelopment of male and female rats

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Background: There is accumulating evidence for the role of neuroinflammatory processes in the aetiology of neuropsychiatric disorders. In fact, maternal immune activation (mIA) through administration of the viral-mimetic polyriboinosinic-polyribocytidylic acid (poly-I:C) is a key model for neurodevelopmental disorders such as schizophrenia (see Knuesel *et al.* 2014 for review). However, mIA studies predominantly use mice despite the benefits of rats for robust behavioural and developmental neuroimaging read-outs. Furthermore, gestational and early postnatal day neurodevelopmental changes in the offspring of poly I:C treated mothers have yet to be fully explored. Thus this study aimed to establish an mIA model in rats and investigate early neurobiological markers and behavioural changes in male and female offspring from poly I:C-treated rat dams.

Methods: Acute systemic inflammation was induced in female Wistar, hooded-Lister and Sprague Dawley rats ($n = 8$; 182-281 g; 10-weeks old) intraperitoneally (i.p.) with poly I:C (5, 10 or 15 mg/kg) or saline. Subsequently, mIA was induced in pregnant Wistar rats ($n = 6$; 293-347 g) with 10 mg/kg poly I:C or saline i.p. at gestational day (GD)15. To confirm immune response, changes in core body temperature and body weight were measured prior to treatment and at 3 h and 6 h post-poly I:C. Blood samples were taken at 3 h following poly I:C administration and changes in IL-6 expression measured in the plasma by ELISA. Offspring development was assessed in males and females at GD21 ($n = 15$-25) and postnatal day (PD) 21 ($n = 12$). Brains were harvested for quantitative RT-PCR to measure changes in expression associated with neuronal development (myelin basic protein, MBP; myocyte enhancer factor-2, Mef2; major facilitator superfamily domain 2a, Mfsd2a; semaphorin 3a, Sema3a; shank3), glial cells (glial fibrillary acidic protein, GFAP; olfactomedin-like 3, Olfml3), inflammation (monocyte chemoattractant protein 1, MCP-1; granulocyte-colony stimulating factor, G-CSF), and neurotransmitter signalling (cannabinoid receptor 1, CB1 receptor; 5-hydroxytryptamine 2a receptor, 5HT-2a receptor; tyrosine hydroxylase, TH) implicated in schizophrenia.
Results: Poly I:C at 10 mg/kg elevated circulating IL-6 in all strains of rats tested, with the most robust immune response observed in Wistar rats; thus this dose and strain were selected for future experiments. Poly I:C at 10 mg/kg on GD15 induced mIA without affecting litter numbers or maternal weight. However, at GD21, pups of poly I:C-treated dams displayed reduced weight, length, head circumference and placenta weight and this reduction in body weight was maintained in both genders at PD21. Elevated expression of Mef2 and Sema3a was observed in the frontal cortex of offspring of poly I:C-treated dams at both GD21 and PD21, whereas MBP expression was reduced at GD21 but elevated at PD21 and Mfsd2a expression reduced at GD21 only. Additionally, mIA reduced GFAP and MCP-1 expression at GD21 without affecting G-CSF and induced only minor changes in neurotransmitter signalling. Similar results were observed for both male and female offspring.
Discussion: We have established a robust model of mIA in rats and used this to identify early neurodevelopmental changes. Poly I:C-induced mIA resulted in pup and placenta growth restriction alongside changes in markers suggesting delayed myelination and development of the blood-brain barrier but accelerated synaptic pruning and axonal guidance. This work supports existing data in mice and further provides a model to study behavioural changes in rats alongside neuroimaging read-outs.

S213. Reticular thalamic contribution in the control of thalamocortical pathways: involvement in schizophrenia related behaviors

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Background: Early damage of the thalamus induces functional and/or structural abnormalities in the cerebral cortex. However, differences in behavioral and cognitive changes after this damage are not well characterized. Our study assessed whether early postnatal lesion of the reticular thalamic nucleus (RTN), reciprocally interconnected to mediodorsal thalamus, causes disruption of behavior and cognition in young adult rats.
Methods: Rat pups at postnatal day 4 were randomized in 3 groups: the first group received a bilateral electrolytic lesion of RTN; the second corresponding to RTN-sham-lesion group; and the third as classical control group.
After seven weeks, all rats were tested with the following behavioral and cognitive paradigms: T-maze test, open field test, elevated plus maze test and object recognition test.
Results: RTN Lesion rats presented deficits in shifting capabilities and acquiring new strategies, significant hypoactivity, increasing in anxiety-like behavior and disruption of the recognition memory, compared to RTN-sham-lesion and control rats.
Discussion: The different behavioral alterations reported in our study suggest that early damage of the anterior part of the RTN leads to alterations which could be reminiscent to schizophrenia. These alterations could suggest that the RTN may control the development of the mediodorsal-prefrontal cortex pathway.

S214. Pupillary changes as signs of autonomic dysbalance in a rat model of neuropsychiatric disorders

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Background: The decreased parasympathetic and/or enhanced sympathetic tones are well-known signs of psychiatric diseases including schizophrenia and autism, which may be manifested in the alterations of pupillomotor control. The aim of this study was to characterize the potential dysfunction in pupillary light reflex (PLR) in a new substrain of a complex animal model showing disturbances related to schizophrenia and/or autism.
Methods: Two experimental groups of male Wistar rats were studied at the age of 11 weeks: naive rats without any treatments ($n = 15$) and the 24th generation of selectively bred animals ($n = 39$) after postweaning social isolation and subchronic ketamine treatment between 4-7 weeks of age. 10 minutes before the experiment the rats were slightly sedated with diazepam (2.5 mg/kg ip.) and were allowed to adapt to dark room. The consensual response of PLR was recorded with a modified digital camera (Nikon D700) under infrared illumination. Intensive light stimulus was delivered into the right eye together with an infrared flashlight delivered into the left eye. Video records from each animal were evaluated with a video analyser program (Tracker video analyses and modelling tool, 4.91, comPADRE) by calculation of all parameters in the ratio of the iris' diameter (relative diameters, expressed in %). The following parameters were determined: the initial and minimal diameters of pupil, constriction latency, degree of constriction, duration of contraction, velocity of constriction, re-expanded pupil diameter 5 s after reaching its minimal value and degree of recovery.
Results: The initial and the minimal pupil diameters were significantly larger in the new substrain compared to control animals. As regards the latency of pupil to constrict and the degree of the constriction, no significant differences were observed between the two groups. The duration of the contraction was significantly longer and the speed of the constriction was significantly lower in the new substrain compared to the control group. Regarding the relative recovery related to the iris' diameter and the degree of recovery related to the initial pupil's diameter, there were no significant differences between the groups
Discussion: In conclusion, the new substrain showed several alterations in the consensual response to PLR, suggesting a general shift of autonomic balance towards a sympathetic predominance resulted from enhanced sympathetic and/or blunted parasympathetic activity

S215. Familial aggregation of schizotypal traits and its correlation with the presence of dermatoglyphic anomalies: a study based on healthy relatives of patients with schizophrenia-spectrum disorders

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Background: Schizotypy refers to a set of temporally stable personality traits that are considered a source of both healthy variation and predisposition to psychosis. Then, schizotypy is considered a marker of psychosis latent liability not only because it increases with higher genetic similarity to schizophrenics but it is also elevated in relatives of patients (Barrantes-Vidal *et al.* 2015; Solanki *et al.* 2012). Another SZ vulnerability marker is the presence of dermatoglyphic anomalies such as ridge dissociations (RD), which have been described to be more frequent in patients (Rosa *et al.* 2000) and their first-degree relatives (Fatjó-Vilas *et al.* 2008) compared to healthy subjects. The

present study aimed: i) to examine the aggregation of schizotypy in relatives of patients with schizophrenia-spectrum disorders (SSD), by means of estimating the Intra-family Resemblance Score (IRS), and ii) to test the link between schizotypy and the presence of RD.
Methods: The sample comprised 90 healthy first-degree relatives of patients with SZ (from 42 families: 33 fathers, 24 mothers and 33 siblings). Schizotypy was assessed with the Structured Interview for Schizotypy-Revised (SIS-R) (Vollema *et al.* 2000). A two-level linear mixed model (LMM) with the SIS-R total score as the dependent variable, sex, age and years of education as fixed effect covariates and family as random effects (subjects nested within families) was used in order to obtain the Intrafamilial resemblance score (IRS). Bilateral fingers and hand prints were obtained from all participants using non-inky specific methods (Prints-kit, Printscan Verification Systems Ltd). Ridge dissociations (RD) were identified as clear anomalies of the dermal ridges junction (Cummins and Midlo, 1943). All analyses were implemented with the Stata v. 13 (StataCorp, 2013).
Results: Firstly, IRS were calculated for each family and families were ranked according to it. Families with high resemblance displayed low schizotypy scores, whereas families with low resemblance were those including at least one discordant member who presented a higher score ($\beta = 0.50$ $P < 0.001$). Secondly, individuals with RD showed higher schizotypy scores than those without (6.67(0.85) vs 13.27(3.03), respectively; $t = -2.88$ $P = 0.0065$).
Discussion: Our results suggest that both schizotypy and RD, could be, at least partially, influenced by some shared genetic and environmental factors, which in turn could increase the susceptibility for SSD. These results are in line with previous studies in which dermatoglyphic alterations were associated with schizotypy in healthy individuals (Rosa *et al.* 2000; Chok *et al.* 2005).

S216. A role for BDNF in mediating adolescent GABAergic interneuron expression

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Background: Cognitive deficits are a common, crippling and prodromal symptom of schizophrenia. Despite this, there is currently no pharmacological treatment available. Gamma-aminobutyric acid (GABA)ergic interneurons in the forebrain play a major role in maintaining cognitive functioning and their expression and function have been found to be altered in schizophrenia patients. Brain-derived neurotrophic factor (BDNF) is a vital neurotrophin that is essential for the development and function of GABAergic interneurons, including guiding their development throughout puberty, a critical period of interneuron maturation. This time period, extending into early adulthood, is also the period with highest incidences of schizophrenia onset. Sex hormone surges during adolescence and exerts organisational effects on the developing brain. Females are noted to have fewer cases, later onset and milder symptoms compared to males and the protective effect potentially arises from the female sex hormone estrogen, which has been shown to induce BDNF expression. However, little is known about the developmental changes of GABAergic interneurons during the dynamic adolescent period in either male or female frontal cortex. Contrasting the trajectories between the sexes may encapsulate the difference that underlies male vulnerability.
Methods: Here, we examined the interplay between gender and BDNF on GABAergic interneuron development by looking at the expression of GABAergic interneuron markers parvalbumin and calretinin in the medial prefrontal cortex of male and female mice, both wild-type and BDNF heterozygotes, from juvenile age (3 weeks) through to adulthood (12 weeks) on a weekly basis using Western blotting. In addition, immunohistochemistry was utilised to examine parvalbumin and calretinin cell counts in subregions of the medial prefrontal cortex at ages 4, 6 and 12 weeks.
Results: Compared to wild-types, parvalbumin expression was reduced in male BDNF heterozygous mice but was not altered in female BDNF heterozygotes. Cell count largely matches protein expression but suggest that the parvalbumin-expressing cells in the infralimbic cortex to be particularly sensitive to BDNF deficiency. Calretinin protein significantly reduced in male WT mice but remained unaltered across development in BDNF hetrozygotes. Cell counts however show that calretinin immunoreactive cells increase in number in male WT mice. In females, protein level did not significantly differ between genotypes or across age with cell counts also relatively unaltered.
Discussion: This study show case the dynamic and sex-dimorphic influence BDNF has on the maturation processes of GABAergic interneurons across adolescence and may contribute to explaining the palpable sex difference in onset and symptom severity.

S217. Salience processing and psychopathology following very preterm birth

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Background: Backgrounds: Aberrant salience processing is thought to mediate psychotic symptoms in both clinical populations and in individuals with an at risk mental state. Salience attribution may determine the phenomenology and risk of transition from attenuated symptoms to psychotic disorder. To date, no study has assessed salience attribution in adults who were born very preterm (VPT), despite their increased vulnerability to psychiatric risk. The main objective of this study is to evaluate the role of salience processing as a mediator of psychopathology in adults who were born very preterm.
Methods: The current sample consisted of 66 VPT individuals ($<$ 33 weeks of gestation) and 31 term-born controls. All participants completed the Salience Attribution Test (SAT) which measures aberrant and adaptive salience processing. Psychopathology was examined using the Comprehensive Assessment of At Risk
Results: VPT participants demonstrated increased aberrant salience and positive symptoms compared to controls, but this was not statistically significant. However, a significant correlation between positive symptoms and aberrant salience processing was demonstrated only in the VPT group ($r = .250$, $p = .041$) and not in controls ($r = -.220$, $p = .907$). Specifically, severity of perceptual abnormalities and disorganised speech were significantly associated with aberrant salience processing in VPT individuals ($r = .278$, $p = .024$ and $r = .259$, $p = .040$, respectively). These results indicate that the aberrant attribution of motivational salience may be associated with the severity of positive symptoms in individuals who were born preterm but not in controls.
Discussion: Although our VPT participants did not display increased psychosis-like symptoms compared to controls, they showed a significant association between a known mediator of psychopathology, aberrant salience processing and positive symptoms, which is line with observations from clinical samples and individuals with an at risk mental state. We interpret our results as highlighting a possible mechanism underlying an increased psychiatric risk in VPT individuals. Further research is required to ascertain the specificity of this risk and transition rates in VPT populations.

S218. m-RESIST, an integrative M-health solution for treatment-resistant schizophrenia according to user' needs: focus groups findings

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Background: Despite the proven potential of using M-health solutions in the treatment of patients with schizophrenia, we deal with a lack of technological solutions. The aim of this study was to measure patients', informal carers and clinicians-receptivity towards a European integral intervention model currently being designed: Mobile

Therapeutic Attention for Patients with Treatment Resistant Schizophrenia (m-RESIST).
Methods: Before defining the system requirements, a qualitative study on preferences of outpatients with treatment-resistant schizophrenia was carried out in Spain, Israel and Hungary. We analyzed patients, informal carers and clinicians' perspectives towards the services initially thought to be part of the solution. A total of 9 focus groups and 37 interviews were carried out in the three countries, using the discourse analysis framework.
Results: The webpage and the virtual forum were perceived as suitable to get both reliable information on the disease and support. The data transmission service, online visits and instant messages were valued as a suitable way to increase the contact with clinicians. Alerts were appreciated as reminders of daily tasks and appointments. Avoiding stress situations in outpatients, promoting an active role in the management of the disease and keeping the human contact with clinicians are the main suggestions aimed at improving the effectiveness of the solution, spontaneously mentioned by participants.
Discussion: The good receptivity towards m-RESIST services is related with its usefulness to meet users' needs, its capacity to empower them and the possibility to keep human contact.

S219. Change - a randomized clinical trial to investigate the effect of an individualized lifestyle intervention compared to care coordination compared to treatment as usual

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Background: Schizophrenia is strongly associated with lost life years, predominantly due to cardiovascular diseases, which is the largest single cause of death in schizophrenia. Only few studies have investigated the effect og non-pharmacological lifestyle interventions to decrease the cardiovascular risk factors in people with schizophrenia.
Methods: A randomized clinical trial investigating the effect of a lifestyle coach-intervention (focusing on healthy eating, physical activity, smoking cessation and care coordination) compared to care coordination alone compared to treatment as usual. We recruted 429 patients with schizophrenia or schizoaffective disorder who had an abdominal width beyond the recommendations ($>$ 102 cm for men, $>$88 cm for women). The patients were randomized in three arms and the intervention went on for one year. At baseline and follow-up after 1 and 2 years we assessed several cardiovascular risk factors including weight, abdominal width, blood pressure, blood samples for lipids, HbA1c and high sensitive CRP, fitness test, and by oral interview we assessed psychotic symptoms, quality of life, level of functioning, physical activity and eating habits.
Results: The first year follow up showed no significant change in any outcomes. We only have preliminary results from the 2 years follow up.
Discussion: So far it appears that a our non-pharmacological intervention is not effective or feasible. I will at oral presentation discuss the limitations of our intervention and our research, and discuss the possibilities for future non-pharmacological interventions to prevent cardiovascular risk and death in the severe mentally ill

S220. Effect of brief individual cognitive behavioral therapy for auditory hallucinations on negative symptoms in a sample of Egyptian patients with schizophrenia

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Background: Auditory hallucination is one of the most common symptoms in schizophrenia. The increase on frequency of the auditory hallucinations and ensuing distress may increase negative symptoms.
Aim of the study: The application of brief individual cognitive behavioral therapy for auditory hallucinations can decrease the severity of negative symptoms in schizophrenia and so increase the level of functioning.
Methods: This study was performed at the outpatient clinic of El Hadara University Hospital in Alexandria where 40 patients with schizophrenia were referred by consultants psychiatrists and selected according to inclusion criteria and randomly matching into Group I: 20 patients with schizophrenia who received 8 individual sessions of brief Cognitive Behavioral Therapy for auditory hallucinations plus Treatment as Usual (TAU). Group II: The other 20 patients with schizophrenia who were included as control and received Treatment As Usual (TAU) only. There was a drop out of 4 patients in Group I after the first 2-3 sessions and they were replaced by others. The Positive and Negative Syndrome Scale PANSS, the Arabic version of Beliefs About Voices Questionnaire BAVQ and the General Assessment of Functioning scale GAF were assessed at baseline and at the end of the study.
Results: - Both groups were well matched regarding the demographic data (gender, age, marital status, educational level, current work status, family history); and also matched regarding the illness characteristics (age of onset, number of admissions, duration of illness) except the hearing voices duration which was significantly longer in duration in Group II (control group)compared to Group I.
- At the end of the study, in Group I, there was a significant reduction in positive (16.23%), negative symptoms (17.75%),total symptoms (16.55%) on The PANSS, and a significant increase in functioning level by (8.33%) on GAF scale ($P < 0.001$), ($P < 0.001$), ($P < 0.001$), ($P < 0.001$) respectively. Comparing Group I to Group II, there was a significant reduction in negative symptoms, total symptoms on PANSS, and a significant increase in functioning on GAF scale at the end of the study ($P < 0.001$), ($P = 0.008$) ($P < 0.001$) ($P = 0.012$) respectively. There was a significant negative correlation between negative PANSS scores and GAF scores in group I (- 0.387, $P = 0.014$) that increased in strength after the application of sessions (-0.487, $P = 0.001$).
Discussion: To the best of our knowledge, this is the first trial testing the effect of individual brief CBT for auditory hallucinations on negative symptoms in schizophrenia in Egypt.
Brief individual CBT for auditory hallucinations combined with TAU was significantly effective in reducing negative symptoms' severity in patients with symptoms in the mild to moderate range on the PANSS Negative syndrome scale. This is consistent with the study by Habib *et al* (2015); Staring *et al* (2013); Mortan *et al* (2011); Startup *et al* (2005) showing that Brief individual CBT for auditory hallucinations tackles the psycho-social factors perpetuating voices through helping the patient getting a sense of control, coping strategies and change of his beliefs regarding the voices. Patients' beliefs about the voices and the high level of distress caused by voices lead to secondary negative symptoms. Patients were reluctant to engage in social activities and exchange with other people for fear of being judged or mocked due to their auditory hallucinations. After CBT sessions, the reduction in distress; change in beliefs and getting sense of control had numerous implications in patients' life since they were enabling them to start to take action where it was almost impossible to do so previous to CBT, leading to negative symptoms improvement and quality of life amelioration.

S221. The IBEEP study: exploring the feasibility and effects of exercise in early psychosis

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Background: First-episode psychosis (FEP) is associated with a severe decline in physical health, high rates of relapse and poor functional outcomes. Physical exercise has been shown to improve cardiometabolic health, symptoms and neurocognitive functioning in long-term schizophrenia. However, this has not been examined in the early stages of illness, even though this is when exercise may be most effective. We conducted an exploratory study, iBeep ('Investigating the Benefits of Exercise in Early Psychosis'), to examine the feasibility of using individualised exercise training to improve physical and mental health outcomes in early psychosis.
Methods: Thirty-one patients with FEP (aged 18-35) were recruited from 'Early Intervention for Psychosis' services in Manchester (UK) between January 2014 – June 2014. Comparison data was obtained

from seven patients who received treatment-as-usual (TAU) over the same timeframe. The intervention aimed to achieve ≥90 minutes of moderate-to-vigorous activity each week, using exercise activities tailored to individual preferences and needs. Each participant met with a research assistant to formulate a 10-week exercise plan. They were then provided with a 'training partner' (research assistant) for two 1 hour sessions per week to facilitate their engagement in chosen activities. Changes in psychiatric symptoms, cognitive functioning and physical health were assessed using quantitative methods, and compared to a treatment-as-usual (TAU) comparison group recruited from the same clinical services. Additionally, semi-structured interviews were used to explore service users' qualitative experience of exercise. These assessments and interviews were also repeated 6 months after the intervention had concluded.
Results: Participants exceeded the exercise targets, achieving an average of 107 minutes of moderate-to-vigorous exercise per week for 10 weeks, mostly through supervised gym sessions. PANSS assessments showed a 27% reduction in total symptom scores after 10 weeks of exercise, significantly greater improvement than the treatment-as-usual group ($P = 0.010$). The greatest improvements were observed for negative symptoms, which reduced by 33% ($P = 0.013$). Pre-and post-intervention improvements were also observed for waist circumference (-2cm), verbal memory and socio-occupational functioning. In qualitative interviews, participants explained how physical exertion during exercise can direct attention away from symptoms, and thus improve mental health. Exercise was also experienced as a rewarding, sociable activity which increases energy and overcomes amotivation. However, at the 6-month follow-up, symptomatic benefits only persisted for the subgroup of participants ($n = 11$) who continued to exercise weekly. Participants attributed their discontinuation of exercise to insufficient support and lack of training partner.
Discussion: Individualized exercise interventions, which provide autonomy and social support, enable young adults with first-episode psychosis to achieve sufficient amounts of moderate-to-vigorous exercise each week. This, in turn, may reduce psychiatric symptoms while improving cardio-metabolic health, cognition and social functioning. Randomised controlled trials are now required to determine the efficacy of exercise for early psychosis. Furthermore, sustainable methods for implementing exercise into clinical care must now be explored.

S222. The efficacy of non-pharmacological interventions (NPIs) on brain-derived neurotrophic factor (BDNF) in patients with schizophrenia: a systematic review

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Background: Few articles have investigated the relationship between non-pharmacological interventions (NPIs) and brain-derived neurotrophic factor (BDNF) in the patients with schizophrenia, although many articles regarding the correlation between pharmacological interventions (PIs) and BDNF in schizophrenia have been examined. The aim of the present review was to explore the efficacy of NPIs on BDNF in the patients with schizophrenia.
Methods: A systematic computerized search was conducted to identify the effect of NPIs on the serum or plasma levels of BDNF in schizophrenia (including schizoaffective disorder) using EMBASE, MEDLINE, and PsycINFO. The following search terms were used: (schizophreni* AND (brain derived neurotrophic factor OR bdnf)). The reference lists of the identified original articles and reviews were also searched manually for additional studies. Two reviewers screened and assessed articles independently. Any disagreements were resolved by discussion and consensus, and when in doubt, the final decision was made in consultation with a third reviewer. The risk of bias in the included studies was assessed using the Cochrane risk-of-bias tool. The last search was performed on 5 November 2015.
Results: Of the initial search of 2663 records including 967 duplicates, 1683 were excluded after the titles and abstracts screening and 13 articles were assessed as full text. A total of 11 articles with 563 participants were finally included. Of these included trials, seven studies were randomized controlled trials (RCTs) and the other trials were Non-RCTs or open trials with a pre-post analysis. Only three studies were conducted under active control (AC) conditions and two of them were under a two-arm control design, i.e. AC and passive control (PC). Six studies used diet products, four used exercise or physical training, and one used cognitive therapy. Our findings revealed inconsistent effects of non-pharmacological treatments on the serum or plasma levels of BDNF. Whereas four studies demonstrated that there was a significant difference in the levels of BDNF between the groups with higher levels in the intervention group, or with higher levels after the non-pharmacological intervention, the others showed borderline or no effect of the intervention. The main limitation of this review is that all but two studies were considered high risk of bias according to the Cochrane risk-of-bias tool. Another limitation is the heterogeneity of NPIs.
Discussion: This is the first review to elucidate the efficacy of NPIs on BDNF in the patients with schizophrenia.
Our results suggest that it is unclear whether NPIs mainly related to diet or exercise may have a beneficial effect on BDNF in schizophrenia patients. Future study protocols addressing NPIs implementation targeted on BDNF changes in the patients with schizophrenia should include also psychological treatments; in addition more RCTs and AC interventions are needed; and finally body mass index (BMI) and smoking status should be assessed in each participant.

S223. The role of comprehensive psychosocial outpatient programming in the treatment of first episode psychosis patients

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Background: The University of Minnesota has developed a comprehensive intensive outpatient psychosocial program for patients presenting with First Episode of Psychosis. Patients may have started participating in the program after inpatient hospitalization at the University of Minnesota or from referral from other hospitals within the area. The components of the intensive outpatient psychosocial program at the University of Minnesota's clinic includes Adult Day Treatment with Cognitive Remediation Therapy, Adult Cognitive Behavioral Therapy (CBT) Group, Individualized CBT, Family Psychoeducation Group in addition to appointments for medication management and case management.
These services are intended to provide patients with the resources to improve functional status and prevent re-hospitalization. The University of Minnesota assessed the rate of first episode psychosis patient engagement in the Adult Day Treatment, Adult CBT Group, Individual CBT, and Family Psychoeducation Group. Rates of re-hospitalization and program utilization were also compared.
Methods: The University of Minnesota assessed patients followed in the First Episode Psychosis outpatient clinic from 2012-2015. Gender, age, diagnosis, hospitalization dates and participation in Family Psychoeducation Group, Adult CBT Group, Individual CBT and Adult Day Treatment were assessed to determine program utilization. 1-year re-hospitalization admission rates were also assessed and compared to program utilization. An IRB chart review waiver was obtained. Criteria for inclusion in the analysis also required each patient to have a signed a consent form allowing medical record review and consent for services on an annual basis.
Results: 59 First Episode Psychosis patients were seen for medication management in the outpatient clinic. Patients included 14 females and 43 males, age range 14-45 years. Two patients did not allow their medical records to be used in research and were excluded from analysis.
In total, of the 57 patients assessed, 81% of patients were not hospitalized within 1 year. The program maintained a 70% retention rate overall. 21 of the patients included in the analysis have been in the program for less than 1-year, and of those patients, only 1 has been re-hospitalized thus far. Regarding the number of re-hospitalizations within 1 year, 1 patient had 3 admissions alone, 4 patients had 2 admissions each, and 6 patients had only 1 admission.

1-year re-hospitalization admission rates by number of outpatient services:
No services: 5/13 = 38.5%
1 services: 4/15 = 26.6%
2 services: 6/13 = 46.6%
3 services: 1/8 = 12.5%
4 services: 0/6 = 0%
1-year re-hospitalization admission rates by outpatient service:
Adult Day Treatment: 11/27 = 40.7%
Family Group: 5/18 = 27.8%
Individualized CBT: 3/25 = 12%
Adult CBT Group: 21/23 = 8.7%
Discussion: Previous studies have shown inconclusive results about the impact of family therapy, group therapy and day treatment programs on 1-year re-hospitalization rates and no difference in re-hospitalization rates for patients that participated in individual cognitive behavioral therapy.
The results of this assessment indicate that patients who participated in either day treatment, family therapy, individual therapy, and especially group therapy had lower 1-year re-hospitalization rates. In addition, the results imply that the more outpatient services patients participated in, the lower the chance of 1-year re-hospitalization rates. This preliminary data suggests that patients may benefit from a comprehensive psychosocial outpatient program. Two additional years of data have already been collected and will be analyzed next. The next phase of the project also includes an analysis of program engagement and functional status.

S224. MODen: a therapeutic integrative educational program for people with schizophrenia focusing on negative and cognitive symptoms: preliminary results in 22 patients

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Background: Residual symptoms as negative persistent symptoms and cognitive deficits represent a challenge in the treatment of people with schizophrenia, especially as pharmacological treatments are not actually very effective. An integrative approach including pharmacological and psychosocial treatments, cognitive remediation and educational skills must be proposed in order to improve functional abilities, social rehabilitation, then quality of life and recovery. One of the limitation to access to these integrative rehabilitation programs is negative symptoms and especially lack of motivation and anhedonia. Likewise, 40 to 60% of these patients suffer from an excess of weight or obesity, which can also have an impact in cognitive deficits. In this context, we created a therapeutic educational group program, called MODen, using cognitive and educational strategies, taking account ecological issues and focusing on negative and functional symptoms (ex: hedonic ingredients, nutritional balance, home tasks)
Methods: we recruited 22 patients with schizophrenia, according to DSM-IV-TR criteria and especially people with persistent negative symptoms and deficits in social abilities, from the Clermont de l'Oise Psychiatric Departments (Picardie area, France). We used PANSS for clinical assessment (22 patients) and memory tests (15 patients) before and after 2 cycles. We used Wilcoxon test analysis with a level of significancy $< 0{,}05$
Results: (1) description of the different steps of this program (4 cycles of 4 steps each);(2) we found statistical significative improvement in global and each sub-score of the PANSS ($P <$ 0,005) and in verbal memory ($P <$ 0,03)
Discussion: MODen is a promising tool including ecological, clinical and cognitive axis, in an integrative approach, that can serve as "a springboard" to a more specific and personalized cognitive program. Further studies must be conducted in larger and randomized samples.

S225. A new recovery focused intervention combining peer support and skill training for people with schizophrenia: results of a pilot study

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Background: The majority of people with schizophrenia have a poor social network and experience loneliness. Peer support groups have demonstrated positive effects on social networks and social support (Castelein *et al.* 2008). Moreover, patients often report problems in social and independent living skills. These skills are often trained in the clinical setting, but poorly generalize to everyday life. Therefore, development and research on skills training 'on the spot' has been recommended (Glynn *et al.* 2002). In the Hospitality Project (HY), a new intervention is developed which combines peer contact and skills training 'on the spot' in an eating club.
Methods: The HY intervention has been developed using a focus group consisting of patients and professionals. During the intervention, patients with schizophrenia living in the community organize dinners in their own homes for peers: once in two weeks during five months; maximum three peers per group and one nurse. Skill training 'on the spot' is guided by self-set goals by participants. In hosting a dinner participants will work on several skills like planning, cooking, self-care and social skills. Subsequently, during dinner, nurse guided peer support is carried out by an already established method, characterized by a background role of the nurse (Castelein *et al.* 2008). The intervention will be tested in a pilot study with three 3 groups ($N = 9$) during five months. Primary outcome is personal recovery assessed with the Recovery Assessment Scale (RAS) (Giffort *et al.* 1999). Secondary outcomes are: social network (Social Network Assessment), QoL (12 Item - Short Form Health Survey. V2), life skills (Daily Task List) empowerment (Dutch Empowerment Scale), (psychosocial) functioning (Personal and Social Performance scale, Global Assessment of Functioning) and psychopathology (Community Assessment of Psychic Experiences). Measurements were taken before and after the intervention.
Results: All patients who participated in the study completed the intervention. Patients reported being nervous to invite people over in their home and that the intervention was demanding. However, patients were pleased they joined the HY intervention and they would suggest peers to participate in this intervention. Personal interviews showed that patients report positive effects on social support, loneliness and self-esteem. Support of a nurse during the intervention was perceived as useful. Nurses reported participating in the intervention was intensive. However, progressively patients became more independent during the intervention. Also nurses highlighted the contrast between the routine problem focused care and the recovery based care they offered during the HY intervention. Patients did not improve on personal recovery and most secondary outcomes in five months. However, the HY intervention did show a positive effect on quality of life. Moreover, a significant effect was found on connectedness (Factor 4 of the Dutch Empowerment Scale).
Discussion: A new intervention for personal recovery has been developed using a focus group with patients and professionals. The pilot study demonstrated that the HY-intervention is feasible for patients suffering from schizophrenia. Patients as well as nurses reported positive effects of the intervention. A multicenter randomized controlled trial will start in the near future. As the process of personal recovery in patients is extensive, positive findings are expected by extending the HY-intervention to eight months in the RCT.

S226. Interventions for carers of people with psychosis: is it time to consider a role for massive open online courses (MOOCs)?

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Background: A significant and important component of the care and support for patients with psychosis is provided by close relatives,

namely the parents, partners, siblings and children. Patients with the support of relatives obtain superior recovery outcomes, which can include significantly fewer relapses and improved rates of mortality. However, caregiving can have a deleterious effect on carer health and wellbeing. High levels of burden are frequently recorded in carer populations, many report being at breaking point and social isolation can be as much as ten times the levels observed in the general population. Digital interventions are increasingly playing a role in healthcare provision and can offer novel and innovative treatment approaches in mental health conditions. Data remains scarce on their application to addressing caregiving issues. King's College, London recently delivered the very first massive open online course (MOOC) for people interested in exploring key issues faced by those caring for people with psychosis and schizophrenia. The 2 week, globally accessible course, was free to access. We provide preliminary data on course acceptability, feasibility and learner satisfaction.
Methods: Participants completed the 2 week MOOC, which comprised opportunities for peer-to-peer learning, moderated discussion boards, talking head videos with some of the world's leading experts in schizophrenia, and downloadable resources. The course content, based on 3-4 hours study per week, focused on: understanding psychosis and schizophrenia including key symptoms such as hallucinations and negative symptoms; causal processes including cannabis, and trauma, medication and psychological therapies, physical health, recovery, and carer wellbeing including the needs of siblings. The course was based on individual and flexible styles of learning, which enabled learners to engage with the course in a way that best suited their own timetable and daily demands.
Results: 16, 313 people drawn from more than 100 countries and across six continents enrolled on the course. There were 27, 065 comments posted over the course. Most learners engaged with the course programme in their home (94.2%) and 61% of learners were visiting the course a few times each week. The learners were predominately female (83%) and approximately half fell within the 46-65 years age group. Ninety-six percent of learners reported the course as being of good or excellent quality and a similar proportion felt the course had met or exceeded their expectations of learning about caregiving issues. 96% reported finding the course educators engaging.
Discussion: This the first course of its kind to explore this topic area. MOOCs might offer an acceptable framework to support, on a global platform, the key information and peer support needs of those caring for people with psychosis conditions. However, further investigation is required to assess the relevance and impact on a broader range of carer outcomes.
The course was funded by Otsuka Lundbeck Alliance. Neither Otsuka nor Lundbeck had any influence on or input into the development of the content or materials for this course.

S227. The practice and effectiveness of electroconvulsive therapy

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Background: Electroconvulsive therapy (ECT) has been widely used to treat many psychiatric disorders. However, after the introduction of effective psychotropic drugs such selective serotonin reuptake inhibitor and atypical antipsychotics, the use of ECT was sharply declined. Furthermore, electroconvulsive therapy use was impeded by excessive concern for adverse effects and distorted perspectives to the therapy. Recently, transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) was introduced to replace ECT but it has been indicated that tDCS and rTMS were not effective as ECT. There are few studies about ECT in Korea. The authors examined the practice of ECT between January 2007 and Dec 2013 at the Asan Medical Center and reconsidered the effectiveness and safety of ECT.
Methods: Data on patients who went modified ECT from Jan 2007 to Dec 2013 were collected by retrospective chart review. Patients' sociodemographic and clinical characteristics, prescriptions, the use of ECT were recorded. Improvement was assessed using Clinical global impression (CGI) scale and recurrence after the acute phase ECT was defined as re-hospitalization or recommendation to re-hospitalization.
Results: A total of 191 patients underwent 1,648 sessions of modified ECT from January 2007 to Dec 2013. Major depressive disorder ($n = 76$, 39.8%) was the most common diagnosis and poor response to medication ($n = 189$, 75.3%) was the most common indication. Treatment response rate was 64.5% in acute phase courses and 61.4% in the courses of which indication were poor response to medication. It showed the significant association between initial treatment response and final treatment response. ($\chi 2 = 75.289$, $P < 0.001$) As the number of session of initial treatment response increased, the odds for final treatment response decreased. ($P < 0.001$) The probability of remaining disease remission was estimated to 71.4% at the 6 months after the end of acute phase courses not followed continuation or maintenance ECT. Memory impairment or amnesia ($n = 523$, 33.7%) was the most common adverse effect and life-threatening adverse effect did not occur.
Discussion: Our results indicated that ECT is an effective and safe treatment. ECT proved beneficial not only for psychiatric disorders, but also for neurologic disease such as Parkinson disease. It demonstrated a remarkable improvement following ECT in patients who had poor response to medications. Most of memory impairment or amnesia, the most common adverse effect, persisted temporarily and life-threatening adverse effects did not occur.

S228. Predictive value of the premorbid adjustment scale and the strauss and carpenter prognostic scale for global functioning at 2 years after the first presentation of psychotic symptoms in adolescents with early onset psychosis

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Background: Predicting the course of illness in adolescents with a first episode of psychosis has been a topic of great interest. A number of variables conferring high predictive value for the course of illness have been identified, including premorbid functioning, duration of untreated psychosis, previous psychiatric hospitalizations, and age of illness onset (1,2). The objective of the current study is to explore the predictive value of the Prognostic Adjustment Scale (PAS) in comparison/together with the Strauss and Carpenter Prognostic Scale (SCPS) for global functioning at 2 year follow-up in adolescents with a first episode of psychosis.
Methods: A subsample of 60 patients with EOP schizophrenia completed both baseline and two year follow-up assessments from the original CAFEPS sample (3). A total of 12 additional EOP patients were included from a short-term inpatient psychiatry unit (4). Clinical diagnosis was determined using the Spanish version of the Kidde-Schedule for Affective Disorders and Schizophrenia, Present and Life-time version (K-SADS-PL) at 2 year follow up. Premorbid adjustment was assessed using the PAS. Other outcome predictive variables were determined using the SCPS. Global functioning at 2 year follow up was assessed using the Children's Global Assessment Scale (CGAS). Pearson coefficient correlation analyses were performed to determine the associations between PAS subscales, total and change scores, total SCPS and individual SCPS items and functioning at 2 years. Significant variables were included as predictors in a backwards-stepwise regression analysis in order to explore the predictive value of premorbid and prognostic variables on functioning at 2 years.
Results: Results of a backwards stepwise regression model revealed that negative change from childhood to adolescence in the PAS social dimension ($T = -2{,}417$; $P < 0.05$) and the total SCPS score ($T = 3.963$; $P < 0{,}001$) predicted a significant amount (total 31.5%) of the variance in functioning at 2 year follow up. Specifically, change in the PAS social dimension explained 26.5% of the variance and total SCPS score 43.4%.
Discussion: Both changes in social premorbid adjustment from childhood to adolescence and prognostic variables such as quality of work, social relationships, and time since onset of psychotic symptoms as assessed using the total SCPS score add to the prediction of global functioning outcome in adolescents with a first

episode of psychosis (FEP). In addition to premorbid variables, total SCPS proves valuable as a second-step assessment tool conferring improved precision in prediction of functioning at two years after a FEP.

S229. Could events of wonderland happen in real life—generalization of reality distortion in first episode psychosis

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Background: Loss of contact with reality is the common denominator for schizophrenia and other psychotic disorders, defined as a distinct category in psychiatric classifications. Typically the loss of contact with reality is manifested as delusions, hallucinations, and disorganization. However, whether such reality distortion generalizes beyond these specific symptoms remains poorly understood.
Methods: We included 47 first-episode psychosis patients and 32 healthy control subjects from the Helsinki Early Psychosis Study. The patients were recruited among those admitted to psychiatric care due to first psychosis episode, and inclusion criteria included Brief Psychiatric Rating Scale (BPRS) hallucination or delusion score of at least 4. Patients were evaluated as soon as the most prominent psychosis had been attenuated and they were able to co-operate. We showed the participants scenes from Tim Burton's fantasy movie Alice in Wonderland as a part of a larger imaging study. After the movie, we asked the participants to evaluate on a visual analogue scale (0–100) how likely they consider it to be that the events of the movie could happen in real life. Symptom severity was assessed with the BPRS. The visual analogue ratings were compared between groups with Mann-Whitney U test and correlated with symptoms by using the Spearman's test in the patient group.
Results: At the inclusion, median (range) of the BPRS symptom scores were 4.0 (1–7) for delusion, 2.5 (1–6) for hallucination, and 1 (1–5) for disorganization. The patients considered the probability of the movie events happening in real life higher (median 4, 25% at 2, 75% at 17) than the controls (median 2, 25% at 0, 75% at 5) ($P = 0.02$). The ratings of the probability were positively correlated with delusion scores in patient group (rho = 0.428, $P = 0.004$).
Discussion: In the present sample, we found the generalization of the loss of the sense of reality in patients to be statistically significant, but relatively small. Such tendency was most evident in patients with high delusion scores. This would suggest the generalization to be stronger during the acute phase of psychosis. Our findings give insight into the nature of the loss of the sense of reality in psychosis, and may be helpful in understanding patients with psychotic disorders.

S230. Deficit syndrome in schizophrenia is not related to duration of illness, age of onset, or gender, in a Spanish sample of patients

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Background: The presence of an anhedonic and amotivational syndrome, found in some patients with schizophrenia (SZ), has always been an object of research. These symptoms that include processes related to cognition, affectivity, and volition, have been regarded as "negative" symptoms, and their existence implies a mark of poor outcome. Thereby, the concept of deficit schizophrenia (DS) is proposed to be a clinical subtype centred in the presence of stable and primary negative symptoms, with a distinct neurobiological pathophysiology and etiology. Diagnosis is based on clinical criteria (curbing of interest, diminished sense of purpose, diminished social drive, restricted affect, diminished emotional range, or poverty of speech) and the Schedule for the Deficit Syndrome (SDS) is the most used scale to evaluate those symptoms as primary and stable. It is estimated that the prevalence of DS is about 30%, where increase of a longer duration of illness is more frequent in male patients. However, these differences have not been well-tested in Spain, where there is a paucity of studies that directly address the topic. Our study aimed to observe DS distribution in a sample of Spanish patients with schizophrenia, and to analyse whether there is statistical relationship with gender, duration of illness, and age of onset.
Methods: Forty adult patients with SZ, according to the International Classification of Diseases (ICD-10), were recruited for this observational study, including 20 males and 20 females, under a stratified sample design. DS was evaluated with SDS (Spanish version), and performed by semi-structured interviews, with the observer in a community mental health centre. Chi-squared test, Student's t-test, and Mann–Whitney U test were conducted, as appropriate, in order to detect significant differences between DS and non-deficit groups in gender, duration of illness, and age of onset. Statistical analysis was performed using MedCalc software, and the significance level was set at $P < 0.05$.
Results: Mean values for sociodemographic data were 41.22 (SD 13.76) years for age, 14.62 (SD 10.51) years for the duration of illness, and 26.6 (SD 9.16) years for age of onset. Disease types of SZ were paranoid in 23 (57.5%), undifferentiated in 9 (22.5%), residual in 5 (12.5%) and disorganized in 3 (7.5%) patients. DS was rated to be 42.5% (one sample z-test for proportions: $P = 0.08$). There were no statistical differences between DS and non-deficit groups in their duration of illness ($P = 0.358$), and age of onset ($P = 0.73$). Likewise, statistical significances in DS between gender groups was not found ($P = 0.74$ for prevalence rate, $P = 0.7$ for duration of illness, and $P = 0.56$ for age of onset).
Discussion: Results obtained in this study differ from what was expected, and did not reveal associations between DS and key factors, such early onset of SZ, the duration of illness, and male gender. Also, proportion of DS was higher than the estimated prevalence in the previous researches. Potential explanations for these differences included a modest sample size, the cross-sectional design of the study, and the lack of premorbid functioning data.

S231. A linguistic comparison between auditory verbal hallucinations in patients with a psychotic disorder and in nonpsychotic individuals: not just what the voices say, but how they say it

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Background: Auditory verbal hallucinations (AVH) in psychotic patients are associated with activation of right hemisphere language areas, although this hemisphere is non-dominant in most people. Language generated in the right hemisphere can be observed in aphasia patients with left hemisphere damage. It is called "automatic speech", characterized by low syntactic complexity and negative emotional valence. AVH in nonpsychotic individuals, by contrast, predominantly have a neutral or positive emotional content and may be less dependent on right hemisphere activity. We hypothesize that right hemisphere language characteristics can be observed in the verbatim of AVH, differentiating psychotic from nonpsychotic individuals.
Methods: 17 patients with a psychotic disorder and 19 nonpsychotic individuals were instructed to repeat their AVH verbatim directly upon hearing them. Responses were recorded, transcribed and analyzed for total words, mean length of utterance, proportion of grammatical utterances, proportion of negations, literal and thematic perseverations, abuses, type-token ratio, embeddings, verb complexity, noun-verb ratio, and open-closed class ratio.
Results: Linguistic features of AVH overall differed between groups $F(13,24) = 3.920$, $P = 0.002$; Pillai's Trace 0.680. AVH of psychotic patients compared with AVH of nonpsychotic individuals had a shorter mean length of utterance, lower verb complexity, and more verbal abuses and perseverations (all $P < 0.05$). Other features were similar between groups.
Discussion: AVH of psychotic patients showed lower syntactic complexity and higher levels of repetition and abuses than AVH of nonpsychotic individuals. These differences are in line with a stronger involvement of the right hemisphere in the origination of AVH in patients than in nonpsychotic voice hearers.

S232. Symptom content study of perceptual abnormalities in those at clinical high risk for psychosis

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Background: Much of the research on perceptual abnormalities (PAs) has been conducted in schizophrenia patients. In recent years, there has been a growing interest in studying attenuated psychotic symptoms, including PAs, in those who are at clinical high risk (CHR) for developing psychosis. PAs are frequently endorsed positive symptoms in CHR populations. While the importance of phenomenological studies to understanding PAs has been emphasized, only a few studies have explored their phenomenology in CHR individuals.
Methods: The primary study sample consisted of 442 CHR individuals (254 males, 188 females) who met the criteria for attenuated psychotic symptoms syndrome (APSS). A subsample of $n = 43$ from the Calgary site also endorsed PA at 12 and 24- month follow-ups. CHR status was determined with the Structured Interview for Prodromal Syndromes (SIPS). The Scale of Prodromal Symptoms (SOPS) was used to measure the presence and severity of attenuated psychotic symptoms. The content of PAs were coded as being present or absent using the Content of Attenuated Positive Symptoms codebook. The symptom contents of PAs were then classified into four categories based on the perceptual modalities: auditory, visual, tactile and olfactory.
Results: Among the 442 CHR individuals, 348 (78.7%) had at least a moderate rating on PAs. For those 348 individuals, the most frequently endorsed PAs were auditory (84.2%) and visual (80.7%). Tactile PAs (33.9%) and olfactory PAs (11.2%) were less frequent. Approximately 80% of the individuals who endorsed auditory PAs also had visual PAs and/or tactile or olfactory PAs. Olfactory PAs did not occur without the presence of other PAs. There was no association of any of the modalities PAs with age, gender, education or race. The most frequent content for auditory PAs were indistinct noises (40.5%), distinct noises (32.5%) and voices (31.9%). Among the individuals who reported voices, negative content (57.7%) and neutral content (45.9%) were common while positive contents were rarer (11.7%). Among the individuals who endorsed visual PAs, the most common content were seeing vague figures (69.0%), seeing patterns (40.2%) and seeing formed figures (33.1%). In the sub-sample at follow-up, these rates were very similar.
Discussion: In our CHR sample, similar to schizophrenia samples, the most common modality of PAs was auditory, and co-occurrence of auditory PAs together with other PAs were common. Visual PAs however, were more prevalent in our CHR sample than reported for individuals with schizophrenia. These observations raise the importance of exploring the diverse phenomenology of perceptual abnormalities in CHR populations.

S233. Insight evolution: is their a difference between self and hetero assessment?

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Background: Lack of insight is a well-recognized clinical characteristic of schizophrenia. Over 20 years, comprehension of insight has dramatically changed. Currently, the most common definition of insight describes a multidimensional state, heterogeneous in it's intensity. This multidimensional state makes it challenging to create tools for insight assessment. Amador (1994) distinguishes 2 main dimensions: awareness of the disorder and ability to attribute symptoms to the disease. Awareness comprises 4 sub dimensions: awareness of (1) "having a mental disorder", (2) "effects of medication", (3) "social consequences of the mental disorder" and (4) "a list of 17 symptoms of mental illness". The Scale to assess Unawareness of Mental Disorder (SUMD, Amador *et al*, 1994), based on a clinical interview was built on this model. Birchwood *et al*, 1994 proposed a self report (Birchwood Insight Scale BIS) based on a very closed paradigm. The aim of the present study was to explore prospectively the evolution of clinical insight using two scales, one based on a clinical interview and one self report questionnaire in patients suffering from schizophrenic spectrum disorders.
Methods: The FondaMental Advanced Centers of Expertise in Schizophrenia (FACE-SZ) cohort is issued from an ongoing French national network of 10 schizophrenia expert centers. They propose standardized psychiatric, somatic and neuropsychological assessments, using dedicated electronic medical records. All patients evaluated in an Expert Center and diagnosed with schizophrenia or schizoaffective disorder according to DSM-IV-TR criteria were enrolled in the FACE-SZ cohort.
Insight was measured using the abbreviated version of the SUMD and the BIS. Antipsychotic use was systematically recorded as well as all other psychiatric treatments. At one year, data on psycho-social care such as cognitive remediation, cognitive and behavioural therapy, psycho-education during the past year were recorded.
Correlations between the different insight subscales for both instruments, at inclusion and at the one-year follow-up, were examined. We compared scores between inclusion and the one-year follow-up using the paired t-test, after testing the normality of the distributions of score differences.
Results: 182 patients were included in the analysis. Of the sample, 78.6% were male and the median age was 33.1 years (range 16–62). Correlation coefficients between BIS and SUMD subscales varied widely. The highest correlation coefficients were between BIS Illness dimension and SUMD Awareness of Illness ($r = 0.43$) and symptom attribution ($r = 0.43$), and between BIS treatment dimension and all SUMD subscales, except for SUMD awareness of symptoms (correlation coefficients ranging from 0.43 to 0.48 for SUMD need for treatment).
Correlations at the one-year follow-up followed the same pattern. At one year, we found improvement in the awareness of illness, awareness of need of treatment and awareness of symptoms dimensions for the SUMD, and for the BIStreatment dimension and total score.
Discussion: Our results showed that even though they are based and built on very close concepts, the items composing both scales did not totally overlap. Patients may find difficult to accept or understand some medical terms such as "symptoms" or "unusual things" used in the BIS. This dimension of insight would need more items or more precise descriptions, in a self-report, in order to be explored in its complexity. The differential evolution of insight dimensions in the SUMD and the BIS underline the importance of using several scales to capture the multidimensional nature of insight. The development of therapy aimed to improve insight must take into account these different evolutions.

S234. Tardive dyskinesia and tardive dystonia with second-generation antipsychotics in schizophrenia and bipolar disorder patients unexposed to first-generation antipsychotics

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Background: The anticipated reduction of the risk of tardive movement syndromes in the era of second-generation antipsychotics (SGAs) is not yet well documented and clinical characteristics of SGAs-induced tardive movement syndromes have yet to be fully explored. This study investigates the prevalence, clinical nature, and associated factors of SGA-related tardive dyskinesia and tardive dystonia.

Methods: Subjects were eighty-two non-elderly patients with schizophrenia ($n = 80$) and bipolar disorder ($n = 78$) who received SGAs for more than one year without exposure to first generation antipsychotics or unknown psychotropic medications for more than two weeks since illness onset. All subjects had at least one-year of records including movement symptoms history at a single university-affiliated hospital. Multiple (≥2) direct assessments of movement symptoms and review of hospital records were performed.
Results: The prevalence rates of tardive dyskinesia and tardive dystonia (including oculogyric crisis) were 12.5% and 21.3%, respectively in the schizophrenia group, and 7.7% and 6.4%, respectively in the bipolar disorder group. These patients were being treated with risperidone, paliperidone, amisulpride, olanzapine, aripiprazole, ziprasidone, quetiapine or clozapine at the time of the onset of the movement symptoms. The most frequent form was orolingual dyskinesia as dyskinesia, and oculogyric crisis as dystonia. A significant association was found between the two tardive movement syndromes. A past history of acute dystonia was significantly associated with tardive movement syndromes in both schizophrenia and bipolar disorder groups. Comorbid obsessive-compulsive (OC) syndrome was an independent associated factor for both tardive dyskinesia and dystonai in the schizophrenia group.
Discussion: Tardive dyskinesia or dystonia occurs in a substantial portion of out-patients with schizophrenia and bipolar disorder who had been treated with SGAs. In addition to a well-known risk factor of tardive movement syndromes, i.e., acute extrapyramidal symptom, this study first identified OC syndrome as an associated factor that needs future investigations for the replication.

S235. PAM-2, a positive allosteric modulator of the α7 nAChRs, reverses schizophrenia-like cognitive deficits in rats

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Background: The cognitive impairments experienced by schizophrenia patients still await effective. From among the multiple therapeutic approaches that have recently been proposed, α7 nicotinic acetylcholine receptors (α7 nAChRs) have generated great interest as targets for cognitive enhancement in schizophrenia. α7 nAChRs not only play important roles in the regulation of cognitive functions, but have also been implicated in the pathophysiology of schizophrenia. The activity of α7 nAChRs can be modulated through either orthosteric agonists or positive allosteric modulators (PAMs). The PAM-induced activation of α7 nAChRs occurs exclusively in the presence of an endogenous agonist, thereby preserving the temporal integrity of neurotransmission. Thus, α7 nAChR PAMs might offer several advantages over the direct agonist approach. Recently, a series of PAMs with selectivity for the α7 nAChR have been synthesised and pharmacologically characterized. Among them, 3-furan-2-yl-N-p-tolyl-acrylamide (PAM-2) presents procognitive and antidepressant-like activities in rodents. To complete the preclinical studies on the pro-cognitive activity mediated by PAM-2, the ability of this modulator to reverse schizophrenia-like cognitive deficits was assessed.
Methods: In the current studies, Sprague-Dawley rats were tested in the attentional set-shifting task (ASST), the novel object recognition task (NORT) and in the discrete paired-trial delayed alternation T-maze task. In the ASST, the animal's performance at the extra-dimensional (ED) shift stage, expressed as the number of trials required to achieve the criterion of six consecutive correct responses, was considered an index of cognitive flexibility. Based on the exploration time of the novel and familiar objects in the NORT, a discrimination index was calculated. The percent of correct choices in the discrete paired-trial delayed alternation task, i.e., entering the arm opposite to that visited on the "forced" trial, was considered as a measure of working memory. To evoke schizophrenia-like cognitive deficits, the pharmacological model based on administration of antagonists the N-methyl-D-aspartate receptor (NMDAR), ketamine or MK-801, to rats was applied.
Results: The acute administration of ketamine significantly and specifically impaired the performance of rats at the ED stage of the ASST, indicated as an increased number of trials to criterion during this phase. The administration of PAM-2 (0.5 and 1.0 mg/kg) ameliorated the ketamine-induced cognitive inflexibility (three-way ANOVA interaction: $F[18,180] = 6.61$, $P < 0.001$). Moreover, the administration of ketamine abolished the ability to discriminate novel and familiar objects in the NORT. This impairment was abolished by PAM-2 (0.5 and 1.0 mg/kg; one-way ANOVA effect: $F[3,34] = 35.18$, $P < 0.001$). Finally, MK-801 significantly reduced choice accuracy in a discrete paired-trial delayed alternation T-maze task, and this working memory deficit was attenuated by administration of PAM-2 (1.0 mg/kg, one-way ANOVA effect: $F[3,31] = 12.41$, $P < 0.001$).
Discussion: The results of the present study demonstrated that PAM-2 reversed ketamine-induced set-shifting and object recognition deficits as well as MK-801-induced working memory impairments in rats. Thus, the preclinical efficacy of a strategy based on allosteric modulations of α7 nAChRs against schizophrenia-like cognitive deficits is further supported.
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S236. GABAergic dysfunction following prenatal infection in mice: modulatory activity of chronic lurasidone administration

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Background: Prenatal maternal infection is an environmental risk factor for schizophrenia and related disorders. Accordingly, prenatal immune challenge is capable of inducing long-term deficits in different behavioral and cognitive domains, some of which are highly implicated in schizophrenia and related disorders. This is associated with a number of molecular alterations, largely reproducing changes that have been observed in schizophrenic patients. As an example, we have previously shown that impairments in the GABAergic transcriptome, including GAD65/67, VGAT and selected alpha-subunits of the GABA(A) receptor, can be found in the prefrontal cortex after infection during late gestation (1), thus reproducing decreased GABAergic signaling that is among the more robust change observed in schizophrenia. In the present study, we specifically investigated the modulation of GABAergic markers in dorsal and ventral hippocampus in response to prenatal immune challenge, and explored the possibility that chronic administration of the multireceptor modulator lurasidone (2) during adulthood could normalize some of the alterations produced by the gestational manipulation.
Methods: Pregnant C57BL/6 mice were treated with the synthetic viral mimetic poly(I:C) (5 mg/kg, i.v.) or control (saline, i.v.) solution on gestation day 17. At adulthood, a cohort of control or poly(I:C) mice was treated for 30 days with lurasidone at the dose of 1 mg/kg/day by oral gavage. Animals were sacrificed 24 h after the last drug administration and different brain regions were dissected and frozen on dry ice for later analyses.
Results: We found that the mRNA levels for GAD67, parvalbumin and VGAT were not significantly altered in the dorsal or ventral hippocampus of poly(I:C)-treated mice, although chronic administration of lurasidone produced a significant up-regulation of VGAT and PV gene expression selectively in the dorsal hippocampus. Moreover, we found that prenatal immune challenge was able to reduce PV protein levels in the dorsal hippocampus, an effect that was normalized by chronic lurasidone administration. Furthermore, we found that the levels of neuroligin-2 (NLGN-2), a synaptic cell adhesion molecule involved in the stabilization and maturation of GABAergic synapses, was decreased in the dorsal hippocampus of poly(I:C) mice and that these changes were also ameliorated by lurasidone administration.
Discussion: Our findings demonstrate that poly(I:C)-induced immune challenge late in gestation produces enduring changes in GABAergic markers, primarily affecting the dorsal hippocampus. These changes may sustain behavioral defects produced by the prenatal infection, which may be associated with abnormal function of PV neurons. Interestingly, chronic treatment with lurasidone was able to counteract some of these changes in line with its potential to ameliorate cognitive functions that are deteriorated in psychiatric patients (2, 3).
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S237. A polygenic score reflecting prefrontal dopamine D2 receptor co-expression and administration of bromocriptine interact non-linearly on prefrontal activity during working memory

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Background: Genetic variation of dopamine D2 receptor gene has been associated with Schizophrenia risk and related intermediate phenotypes such as prefrontal activity during Working Memory (WM). Genes do not work in isolation, rather they are co-regulated in co-expressed networks. Furthermore, converging evidence indicates that prefrontal function is modulated by D2 receptor (D2R) agonists and antagonists. An influential hypothesis assumes an inverted U-shaped relationship between dopamine (DA) signalling and cortical activity. According to this model, prefrontal response is optimal within a critical range of DA stimulation, with inefficient responses when receptors are poorly or overly stimulated. We examined, in healthy humans, the interaction between multiple genetic variants associated with a co-expression network including D2R and prefrontal function at different WM loads after pharmacological D2R stimulation with bromocriptine. We hypothesized that this relationship would be non-linear.
Methods: Weighted Gene Co-expression Network Analysis (WGCNA) was used to identify modules of co-expressed genes from the Braincloud post-mortem prefrontal mRNA dataset. The gene set containing the D2R long isoform transcript (D2L) was selected and the first principal component (ME) reflecting expression of the whole network was computed. One-way ANOVA was used to test the association between independent single nucleotide polymorphisms (SNPs) within the gene set and the ME. Results of this analysis were then used to compute a D2L co-expression polygenic score (PGS). Fifty-one healthy volunteers (27 males, age 26.9+4.2) entered a double-blind, randomized, placebo-controlled fMRI trial with administration of a single dose of Bromocriptine 1.25 mg (Br). Individuals performed the NBack WM task. Subjects was genotyped for the whole genome in order to compute the PGS. Peripheral prolactin levels were also evaluated. Flexible factorial models in SPM8 tested the interaction between Br administration, PGS and WM load (3Back 1st level ma$P > 2$Back 1st level map). Monte Carlo simulation at cluster level was used to correct for multiple comparisons.
Results: The gene set containing the D2L transcript was composed by 85 genes. D2L expression was correlated with the ME (r2 = 0.4, $P =$ 1.25x10-23). Eight SNPs were associated with ME after correction for multiple comparison (FDR < 0.25). PGS was correlated with D2L transcript (r2 = 0.14, $P =$ 1.0x10-7). SPM analysis revealed that Br administration interacts with PGS only using a quadratic model. The interaction was found in right BA46 (k = 105; F(1,48) = 20.52; Z = 3.95; MNI = 46 38 2) and in right BA9 (k = 243; F(1,48) = 19.69; Z = 3.88; MNI = 34 8 36). Extracted BOLD measures revealed that Br inverted the relationship between PGS and WM-Load-related activity observed during placebo. Analysis on behavioural data indicated an interaction between squared PGS and Br administration on WM Accuracy (difference between 3Back and 2Back % of correct response; $P =$ 0.039; F(1,49) = 4.53). Here, there was again a U-shaped relationship during placebo that was inverted by Br. Interestingly, the pattern was opposite to what seen in fMRI data, consistently with current models of prefrontal efficiency during WM. PGS also predicted prolactin levels (F = 3.98; $P =$ 0.05).
Discussion: This study suggests that multiple genetic variants associated with D2L receptor expression predict prefrontal function during WM with an inverted-U non-linear relationship that is reversed when individuals are challenged with a D2 agonist. It also suggests that stratifying individuals depending on DA-related genetic background can be useful to characterize the effect of pharmacological manipulation on intermediate phenotypes relevant to schizophrenia.

S238. How well do patients with a first episode of schizophrenia respond to antipsychotics: a meta-analysis

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Background: Response to antipsychotics differs considerably among patients with schizophrenia. It is assumed that first-episode patients generally have higher response rates and require lower dosages compared to chronic patients. But to what extent the former respond better than the latter is less known and a systematic review on this topic is not available. The purpose of the current study was to address the following issues: i) to what extent is the response rate of antipsychotic treatment in first-episode schizophrenia higher than chronic patients; ii) what kind of factors affect the clinical response.
Methods: Previous publications and multiple databases were searched to identify all the randomized controlled trials of antipsychotics for first-episode schizophrenia. The primary outcome was response rate to antipsychotics. All definitions of "response" used by the original authors were acceptable. Based on the equipercentile linking study of BPRS/PANSS to CGI ratings by Leucht *et al*, studies in acutely ill patients with schizophrenia should use at least a 50% reduction from baseline as the definition of response rather than lower thresholds. We therefore excluded the 20% reduction cut-off or lower thresholds in a sensitivity analysis. Study selection and data extraction were done independently by two reviewers. We performed meta-analysis using Comprehensive Meta-Analysis 2.
Results: 23 studies with a total of 3536 participants were included in the analysis. Of the 23 included studies, 17 studies reported the response rate with any definition by the authors. Eleven were short-term studies ($< = 12$ weeks), and six were long-term studies (> 12 weeks). The mean study duration was 22.4 months. The mean baseline severity (PANSS equivalent) was 90.6. The mean duration of illness was 1.71 years. The mean dosage of antipsychotics (olanzapine equivalent) was 11.6. The pooled results of all drug arms with random-effect model showed that the average response rate in first-episode schizophrenia was 57.5%. We made a sensitivity analysis and found that the average response rate (40% or 50% reduction cut-off) in first-episode schizophrenia was 59.3%. We further conducted subgroup analyses and meta-regressions to explore the reasons for heterogeneity (I2 = 80.7%). The test for subgroup differences of response rate between short-term and long-term studies was statistically significant (53.5% vs 62.8%, respectively, $P = 0.0124$), reflecting that the response rate was associated with study duration (slope = 0.009, $P = 0.0008$). The meta-regression with percentage of male as a moderator suggested that female patients might have a better clinical response than males (slope = -0.012, $P = 0.0239$). We found no statistically significant effect for average antipsychotic dosage ($P = 0.9514$), baseline severity ($P = 0.9935$) and duration of illness ($P = 0.8039$).
Discussion: First-episode patients with schizophrenia had a relatively high (more than 50%) response rate of antipsychotic treatment, while the response rate of chronic patients based on the 50% cut-off was approximately 20% as reported previously by Leucht *et al.*. Most of the studies used 40%-50% reduction from baseline as the definition of response, which was demonstrated to be appropriate to estimating the clinical response in first-episode patients. Subgroup analysis showed that the response rate was significantly higher in long-term studies than in short-term studies. Meta-regressions showed that female patients had a better clinical response than males. Unfortunately, no data of drug-naive patients and no placebo-controlled study were available. Given the high clinical response in first-episode patients, the drug registration studies should be more inclined to focus on the first-episode patients.

S239. Trajectories of treatment response in hallucinations

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Background: Hallucinations are common in schizophrenia and related disorders, and may be associated with great suffering and even harm to self and others. Antipsychotics are generally effective in treating hallucinations, but treatment response is highly variable and unpredictable in the individual patients. To untangle the heterogeneity and predictors of anti-hallucinatory treatment response could pave the way to more targeted treatment.
Methods: A latent mixture model was used to analyze heterogeneity in the treatment response of hallucinations (P3 in PANSS) in data from the Bergen Psychosis project (BPP). The BPP included a consecutive sample of 226 acutely admitted adult patients with schizophrenia and related disorders. Patients were randomized to one of the following antipsychotics at admittance: risperidone, olanzapine, quetiapine or ziprasidone and followed for up to 6 months in a pragmatic design
Results: One third of all the patients were female (32.7%). The mean age at baseline was 34.1 (SD 13.5). Nearly half the sample consisted of patients not earlier medicated with antipsychotic drugs (Mednaive) (44.2%).
The mean score of hallucinations at baseline was 3.5 with individual variance 2.7 (SD 1.6), the mean change from T1 (baseline) to T2 (about four weeks) was -0.4 per week ($p = .000$), and the latent change from T2 through T3 (3 months) to T4 (six month) was -0.01 per week ($p = .06$). The individual variance (SD) around mean change for the two slope factors were; S1 = 0.4 ($p = .00$); S2 = 0.03 ($p = .51$). A stronger reduction in scores from baseline to the second period of change were seen in patients with higher baseline scores than in patients with lower baseline scores ($r = -.71$, $p < .001$). A two class model was chosen and it showed a high level group (65%) with PANSS P3 $\geq$ 3 and decreasing mean scores to T2, and the low group (35%) with PANSS P3 $<$ 3 with minimal change. The Mednaive variable and the medication effect variables including the interaction terms and the covariate variables PANSS Positive, PANSS Negative and CDSS were entered as predictors of the level and change in the model for patients scoring PANSS P3 $\geq$ 3. Baseline level was related to the PANSS positive scale ($b = 0.05$, $p = .000$), but was not found to be related to the other variables. Stronger reduction in the hallucination level from T1 to T2 was found in the medication naïve group than in those earlier being medicated for psychosis ($b = -0.26$, $p = .000$). No differences between the riseridon and the other three groups were seen in this acute period. In the later period (T2-T4), olanzapin was found to be associated with stronger reduction per week than risperidon ($b = -0.05$, $p = .013$). In addition, stronger reduction was seen among medication naïve patients receiving quetiapin ($b = -0.08$, $p = .011$). No other medication differences were seen, nor any main effect difference between medication naïve patients and patients earlier medicated for psychosis.
Discussion: The study reveals heterogeneity in treatment response of hallucinations.
This study shows a non-linear change in hallucination over time in a six month period. The symptom level decreases considerable over the first four weeks, then the trajectory plateaus over the rest of the follow-up period. Interestingly, no differences were observed among medications in the acute phase. The effect of antipsychotics differentiates in the second period where there is less improvement. This finding does not depend on whether patients had used antipsychotic drugs earlier or not. That could raise the question if the mechanisms underlying antipsychotic effects differ between the early and late phases.

S240. Prior D2 antagonist antipsychotic drug treatment prevents response to novel target compounds in MAM model of schizophrenia: potential circumvention using aripiprazole

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Background: Novel target compounds for the treatment of schizophrenia have shown promise in preclinical research, but failed to show efficacy in clinical trials, which has led some to conclude that results from preclinical studies do not translate to the human condition. However, preclinical research is typically performed on drug naïve rats, whereas clinical trials are performed on patients that have received only brief withdrawal from years of prior antipsychotic drug treatment despite potential pervasive changes to the DA system, including D2 supersensitivity. We previously found that withdrawal from repeated haloperidol (HAL) treatment produces persistent alterations in the state of the DA system, interfering with the ability of a novel target compound to reverse the hyperresponsive state of the DA system in the methylazoxymethanol acetate (MAM) neurodevelopmental model of schizophrenia. In the current study, we examined the effects of withdrawal from mechanistically distinct first- and second-generation antipsychotic drugs, with a focus on the D2 partial agonist aripiprazole (ARI) to determine whether ARI, in contrast to D2 antagonists, causes DA neuron depolarization block leading to D2 receptor supersensitivity.
Methods: Saline (SAL) and MAM-treated offspring received repeated HAL (0.6 mg/kg), clozapine (CLO; 10 mg/kg), ARI (10 mg/kg), or vehicle (0.23% glacial acetic acid) for 21 d, p.o. followed by 7d withdrawal. The population activity of DA neurons in the VTA was measured by passing an electrode in a preset pattern and counting the number of spontaneously firing DA neurons, their firing rate and pattern in anesthetized rats. Additional electrophysiological recordings were conducted in a separate group of SAL and MAM rats following acute treatment with ARI (10 mg/kg, p.o). After electrophysiological sampling, a subset of rats received a low dose of apomorphine (40 ug/kg, i.v.) followed by resampling the VTA in the opposite hemisphere to test for the presence of antipsychotic drug-induced depolarization block.
Results: Acute ARI treatment reduced spontaneous DA neuron population activity in MAM rats while having no effect in SAL rats, compared to vehicle. SAL rats withdrawn from repeated HAL and CLO treatment demonstrated reduced spontaneous DA neuron activity, compared to drug-naïve animals, likely due to depolarization block. This effect was not observed following ARI withdrawal, in which there was no change in DA neuron activity. In MAM rats, withdrawal from all three compounds caused a reduction in the number of spontaneously active DA neurons compared to vehicle-treated animals. Preliminary data show that the reduction in spontaneously active DA neurons in MAM rats following both acute and repeated ARI treatment is maintained following apomorphine.
Discussion: In contrast to D2 antagonists HAL and CLO, withdrawal from repeated ARI treatment did not reduce spontaneous DA neuron activity in normal rats. In addition, ARI-induced down-regulation of DA neuron activity in MAM rats was maintained following administration of apomorphine, suggesting that it is unlikely a result of depolarization block. Lack of evidence for depolarization block following repeated ARI treatment would suggest that ARI may decrease DA stimulation by direct attenuation of DA neuron activity rather than by overdrive-induced depolarization block. As a consequence, ARI may not produce antipsychotic drug-induced supersensitivity, and may be an effective transitional drug to test novel potential antipsychotic drugs without requiring an extended withdrawal period.

S241. Maintenance antipsychotic dose can be decreased in late-life schizophrenia: a prospective dopamineD2/3 receptor occupancy study with [11C]-raclopride

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Background: Patients with late-life schizophrenia (LLS) are highly susceptible to antipsychotic adverse effects. Treatment guidelines endorse lower antipsychotics dosages. However, optimal dose of antipsychotics and associated dopamine D2/3 receptors (D2/3 R) occupancies remain largely unexplored in patients with LLS. The goal of the study was to characterize the range of striatal D2/3 R occupancy

corresponding to the optimal antipsychotic treatment in patients with LLS.
Methods: This open-label prospective study included outpatients with stable schizophrenia (the Positive and Negative Syndrome Scale (PANSS) scores ≤ 3 for positive symptoms), ≧ 50 years, treated with the same dose of oral olanzapine or risperidone for at least 6 months. Participants were assessed with clinical scales for symptoms and adverse effects at baseline. A [11C]-raclopride positron emission tomography (PET) scan was performed to determine baseline antipsychotic D2/3 R occupancy. Antipsychotic dose was gradually reduced to 60% of the baseline dose with a target dose not lower than the recommended dose (olanzapine = 7.5 mg/day or risperidone = 1.5 mg/day). Clinical assessments and a [11C]-raclopride PET scan were repeated at least 2 weeks after reaching the final target dose. Participants were clinically followed up for at least three months using the Brief Psychiatric Rating Scale (BPRS), Simpson-Angus Scale (SAS), Barnes Akathisia Scale (BAS) and Abnormal Involuntary Movement Scale (AIMS). The subjects that experienced clinical deterioration, defined as 20% or more increase in the total BPRS score at baseline, had the dose titrated up until clinical re-stabilization and had a third PET scan. Venous blood was collected before each PET scan to measure levels of the antipsychotic and prolactin. D2/3 R occupancies were estimated using 10 antipsychotic-free participants with schizophrenia to derive an age-and-sex matched non-displaceable binding potential. Relationships between clinical outcomes and striatal D2/3 R occupancies were assessed.
Results: We included 35 clinically stable patients with LLS (age = 60.1 ± 7.0 years) treated with oral olanzapine (20.8 ± 6.6 mg/day) or risperidone (4.7 ± 2.9 mg/day). The dose of olanzapine was reduced to 13.5 ± 4.4 mg/day ($P < .001$) and the dose of risperidone to 3.0 ± 1.7 mg/day ($P = .002$). During the follow-up phase 29 subjects remained stable after the dose reduction. Two subjects presented clinical deterioration during the dose reduction phase and 3 subjects during the follow-up phase. Following dose reduction, PANSS ($P = .02$), BPRS ($P = .03$), SAS ($P < .001$), BAS ($P = .03$), UKU ($P < .001$), and prolactin ($P < .001$) and blood antipsychotic levels ($P < .001$) all decreased. Those with clinical deterioration were associated with younger age of onset ($P = .03$) and greater number of hospitalization ($P = .04$) and lower follow-up serum prolactin concentrations ($P = .04$). D2/3 R occupancy of the entire sample decreased by 6.2 ± 8.2% following dose reduction (70 ± 12% to 64 ± 12%, $P < .001$). D2/3 R occupancy of those who remained stable during follow-up phase decreased from 72 ± 10% to 66 ± 10% ($P = .001$). The baseline D2/3 R occupancies were lower in patients with clinical deterioration ($N = 5$) than in those who remained stable ($N = 29$) (58 ± 15% vs. 72 ± 10%, $P = .02$). The lowest D2/3 R occupancy associated with clinical stability was 50%. Extrapyramidal symptoms were more likely with D2/3 R occupancies higher than 60%.
Discussion: Antipsychotic dose reduction is feasible in stable patients with LLS, improving side effects such as extrapyramidal symptoms and hyperprolactinemia and illness severity measures. The results suggest a lower therapeutic window of D2/3 R occupancy in patients with LLS (50%–60%) than previously reported in younger patients (65%–80%).

S242. The phosphodiesterase 10A selective inhibitor TAK-063 improves cognitive functions associated with schizophrenia in rodent models

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Background: Cognitive deficits in various domains, including recognition memory, attention, impulsivity, working memory, and executive function, substantially affect functional outcomes in patients with schizophrenia. Phosphodiesterase 10 A (PDE10A) hydrolyzes both cAMP and cGMP and is selectively expressed in both direct and indirect pathways of medium spiny neurons (MSNs) within the striatum. These pathways are considered critical for modulating learning behaviors via corticostriatal circuits. TAK-063 is a potent and selective PDE10A inhibitor. Binding of TAK-063 to PDE10A activates both direct and indirect pathways, leading to potent antipsychotic-like effects and a more favorable side effect profile than do current antipsychotics in rodents. In this study, we evaluated the effects of TAK-063 on multiple cognitive functions associated with schizophrenia using naïve and drug-perturbed rodents.
Methods: Novel object recognition task experiments were performed in male Sprague-Dawley rats to assess the effects of TAK-063 on recognition memory performance. To assess the effects on attention and impulsivity, a five-choice serial reaction time task was performed in male Long-Evans rats. To evaluate the effects of TAK-063 on the spatial working memory deficits produced by NMDA receptor antagonists, a Y-maze test in male ICR mice and a radial arm maze task in male Long-Evans rats were performed. Phencyclidine (2 mg/kg s.c.) and MK-801 (0.08 mg/kg s.c.) were used to induce memory deficits in a Y-maze test and a radial arm maze task, respectively. To assess the effects of TAK-063 on executive function, an attentional set-shifting task was conducted in female hooded-Lister rats treated subchronically with phencyclidine (2 mg/kg i.p. twice daily for 7 days).
Results: TAK-063 at 0.1 and 0.3 mg/kg p.o. improved time-dependent memory decay in object recognition in rats. TAK-063 at 0.1 and 0.3 mg/kg p.o. increased accuracy rates, and TAK-063 at 0.3 mg/kg p.o. reduced impulsivity in a five-choice serial reaction time task. TAK-063 at 0.3 mg/kg p.o. attenuated both phencyclidine-induced working memory deficits in a Y-maze test in mice and MK-801-induced working memory deficits in an eight-arm radial maze task in rats. An attentional set-shifting task using subchronic phencyclidine-treated rats was used to assess executive function. TAK-063 at 0.3 mg/kg p.o. reversed cognitive deficits in extra-dimensional shifts. No significant differences were observed in any other parameters in this task.
Discussion: TAK-063 improved the performance of mice and rats in various cognitive domains that are impaired in schizophrenia, including recognition memory, attention, working memory, and executive function. These preclinical data suggest that TAK-063 has the potential to treat cognitive deficits in schizophrenia. Procognitive effects of TAK-063 in these domains were observed at around 0.3 mg/kg p.o. TAK-063 at this dose also showed a potent antipsychotic-like effect in methamphetamine or MK-801 induced hyperactivity in rodents. Thus, TAK-063 may improve multiple symptomatic domains, i.e., positive symptoms and cognitive impairments, in schizophrenia at a similar dose level.

S243. Long-term antipsychotic use and brain volume changes in schizophrenia: the Northern Finland birth cohort 1966 study

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Background: Antipsychotic medication may have a role in structural brain changes found in schizophrenia. Most imaging studies are from the early phase of the illness when the possible medication effects may not yet be noticeable. Studies focusing on more chronic stages of the illness, are often based on clinical samples, when the patients might not represent the variety of different trajectories of the disease. In addition, the effects of long-term antipsychotic medication use on structural brain changes in schizophrenia are still unknown. Our aim was to analyze whether lifetime antipsychotic use associates with brain structural changes during a 9-year follow-up in a population based sample of schizophrenia cases with illness duration on average 10 years at baseline. Our focus was on cortical gray matter and subcortical structures.
Methods: The Northern Finland Birth Cohort 1966 (NFBC 1966) is an unselected, general population birth cohort identified during mid-pregnancy. Cohort members with history of psychotic episodes were invited to participate in the field study conducted in 1999-2001, when the participants were at age 34 on average. The diagnoses were confirmed using Structured Diagnostic Interview for DSM-III-R (SCID).

The participants had an average illness duration of 10.4 (SD 3.7) years before the baseline MRI scan. All participants who had undergone a baseline MRI scan were invited to a follow-up examination after a nine-year interval at the age of 43 on average (during 2008–2010) including a repeat MRI scan. The same 1.5 T GE Signa scanner was used at both baseline and follow up in Oulu University Hospital. Brain structures were extracted from MRI scans using volBrain automated volumetry system (http://volbrain.upv.es). Life-time antipsychotic medication use was collected using all the available medical records (hospital and out-patient care case notes), and an interview conducted during the field studies. This information was used to calculate the cumulative dose of lifetime antipsychotics expressed as dose-years of a daily dose of 100 mg chlorpromazine.
The final sample includes 32 individuals with schizophrenia with available data of all needed variables. The data were analyzed using linear regression model with intracranial volume as a covariate. In additional analyses, we added the average PANSS total symptom score of 34 and 43 year follow-up studies as a covariate.
Results: Higher scan interval antipsychotic dose associated with increase in both right and left lateral ventricles (standardized beta, b = 0.45, $P = 0.006$; and b = 0.43, $P = 0.010$; respectively) and with decrease in left caudate (b = -0.38, $P = 0.023$), right accumbens (b = -0.38, $P = 0.036$), and total gray matter (b = -0.38, $P = 0.035$). When the PANSS score was added to the model, findings regarding lateral ventricles (b = 0.510, $P = 0.007$; and b = 0.456, $P = 0.017$ respectively) and left caudate (b = -0.406, $P = 0.035$) remained significant.
Discussion: In this unique sample we were able to study schizophrenia cases with approximately 20 years of medication history. We found that even after ten years of illness onset it is possible to detect structural brain changes that antipsychotic medication may contribute to.

S244. The dopamine D2 receptor partial agonist 2-bromoterguride ameliorates PCP-induced deficits in prepulse inhibition and novel object recognition in rats

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Background: Schizophrenia is a disabling mental disorder affecting more than 21 million people worldwide. Available medical therapies are effective in the treatment of psychosis and other positive symptoms, however come with considerable side effects and often fail to ameliorate cognitive deficits and negative symptoms of the disorder. The dopamine D2 receptor partial agonist 2-bromoterguride (2-BT) has recently been shown to exhibit antipsychotic effects in rats without causing adverse side effects common to antipsychotic drugs [1]. To determine its atypical character in vivo, the ability of 2-BT to antagonize the disruptive effects of phencyclidine (PCP) and apomorphine on sensory motor gating was determined in the prepulse inhibition paradigm. The effect of 2-BT on cognitive deficits was assessed in the Novel Object Recognition (NOR) test after object recognition memory deficits were induced by PCP treatment.
Methods: 10 week old male Sprague-Dawley rats were injected with 2-BT (0.1 or 0.3 mg/kg; i.p.) followed by PCP (1.5 mg/kg; s.c.) or apomorphine (0.5 mg/kg; s.c.). Prepulse inhibition was measured in two sound-proof startle chambers. The attenuating effect of 2-BT (0.1 or 0.3 mg/kg; i.p.) on visual learning and memory deficits following subchronic administration of PCP (5.0 mg/kg; i.p.; twice daily for 7 days) was assessed in the NOR task consisting of a 3 min acquisition trial and a 3 min retention trial separated by a 1 h inter-trial interval. Clozapine (5.0 mg/kg; i.p.) or haloperidol (0.1 mg/kg; i.p.) were used as positive controls.
Results: The dopamine D2 receptor partial agonist 2-BT (0.3 mg/kg) and the typical antipsychotic haloperidol successfully antagonized apomorphine-induced PPI-deficits. Interestingly 2-BT also ameliorated the PCP-induced PPI-deficits to the same extent as the atypical antipsychotic clozapine. Preliminary data from the NOR test indicate that 2-BT reduces subchronic PCP-induced cognitive deficits in novel object recognition analogous to clozapine.
Discussion: The disrupting effects of PCP on PPI are mediated by non-competitive antagonism at N-methyl-D-aspartate (NMDA) sites indirectly influencing a series of neurotransmitter systems. Our results indicate that 2-BT acts on multiple neurotransmitter receptors as it successfully ameliorated both the PCP- and apomorphine-induced PPI disruptions in rats, showing an atypical antipsychotic character. Furthermore, our preliminary results support the potential atypical antipsychotic effect of 2-BT as it restored performance in the NOR test, a test with good predictive validity. Due to the previously shown properties and antipsychotic-like effects of 2-bromoterguride [1], this substance may be a promising candidate for treatment of schizophrenic patients. Ongoing experiments investigate the potency of 2-BT to improve social deficits following a subchronic PCP regime in rats.

S245. Prescribing patterns of antidepressants and other drugs in Korean bipolar affective disorder patients

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Background: Depressive episode has a considerable effect on progress and functional impairment in patients with bipolar disorder. It has been known that use of antidepressants in bipolar disorder is at risk of aggravating mood fluctuation, inducing rapid cycling or switch to mania or mixed episodes. But currently there are few evidence implying a causal link between use of antidepressants and mood switching, and benefit and loss of antidepressant treatment in bipolar disorder is still controversial. The purpose of this study was to examine the prescription profile of antidepressant and mood stabilizer, using the Health Insurance Review & Assessment Service-National Patients Sample(HIRA-NPS).
Methods: Using the Health Insurance Review & Assessment Service-National Patients Sample(HIRA-NPS), descriptive statistics for the patterns of the antidepressants, mood stabilizers, and antipsychotics. Frequencies of individual antidepressants were also reviewed.
Results: Of 1978 patients with bipolar disorder, 38.9% of patients were prescribed with antidepressants. In patients with bipolar depressive or mixed episodes, 44.9-70.1% were receiving antidepressants. A combination of a antidepressant and a mood stabilizer was the most common medications. 9.78% of bipolar patients were prescribed with antidepressant monotherapy. Among the antidepressants, escitalopram and venlafaxine were used most common. Valproate and quetiapine were the most frequently used combination agents with antidepressants.
Discussion: This study found that antidepressants are prescribed for a sizable number of patients with bipolar depression, and escitalopram is most highly prescribed as an individual antidepressant.There are some limitations in this study including absence of clinical features of the patients and information about comorbidity, a short follow-up period, less consideration about subtypes of antidepressants and therapeutic dosage. Further studies are needed.

S246. Patterns of use of aripiprazole long-acting injectable in standard clinical practice

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Background: The aripiprazole long-acting injectable (LAI) is the last appeared LAI. The equivalence of 10 to 30 mg of oral aripiprazole is useful to treat a wide range of patients. Initiation of treatment is marked by the need for supplementation with oral aripiprazole over a period of two weeks until aripiprazole LAI plasmátic concentrations reach therapeutic levels. The aim of this study is to analyze the different patterns of oral supplementation.
Methods: 40 clinically stable consecutive outpatients treated with aripiprazole LAI were selected The sample consists of 40 patients, 21 men and 19 women. The diagnoses found are psychotic disorder ($N = 21$), schizoaffective disorder ($N = 8$), Delusional Disorder ($N = 4$) and bipolar disorder ($N = 7$). We measure Oral supplementation time by gender, diagnosis, previous oral dose of aripiprazole, years of illness evolution and number of previous incomes.

Results: The average days of oral supplementation is 59.43 days, being 28 days the more observed supplementation time. The percentage of patients with less than 21 days of oral supplementation is 42.5% ($N = 17$). In the overall sample, 42.5% ($N = 17$) of patients required oral supplementation below 21 days. 27.5% ($N = 11$) need a supplementation between 21 to 42 days. Only 2 patients (5% of the sample) required up to 60 days. 25% ($N = 10$) of the sample maintained oral supplementation beyond 60 days. Patients with previous oral dose of aripiprazole equal or less than 30 mg required shorter times of oral supplementation (86.2% ($N = 25$) < 42 days). In contrast, 54.5% ($N = 6$) patients with oral doses above 30 mg needed overlap periods longer than 60 days ($P = 0.002$).
Discussion: In this sample, less than half of patients observed in this sample show overlap periods of less than 21 days.
Of all the factors studied in relation to oral supplementation period, only previous oral dose of aripiprazole is statistically significant. Patients with of oral aripiprazole doses higher than 30 mg require longer oral supplementation times.

S247. Use of aripiprazole long-acting injectable in two inpatient units

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Background: A naturalistic study on the use of aripiprazole long-acting injectable (LAI) in acute psychotic inpatients of two hospitals is presented.
Methods: In this study, 50 inpatients (26 men, 24 women) are treated with aripiprazole LAI; in 1 patient this treatment was removed before discharge because of lack of efficacy. 30% of patients are diagnosed of schizophrenia ($n = 15$), 10% schizoaffective disorder ($n = 5$), 8% disorder delusions ($n = 4$), 26% psychosis NOS ($n = 13$) and 26% of manic episode with psychotic symptoms ($n = 13$). 50% of patients have a damaging drug consumption (80% of them consume cannabis).
Results: The average hospital stay (HS) was 15.98 days. The HS was smaller when the dose of aripiprazole LAI was administered earlier (linear regression; $p < 0.001$). When the dose of aripiprazole LAI was administered in the first week of admission the HS was 13.2 days, in comparition when administered over a week, 22.9 days (t test; $P < 0.0001$). Further, when aripiprazole LAI was administered in the first week of admission, the rate of antipsychotic monotherapy was increased (t test; $P = 0.045$) and the rate of polytherapy was decreased (t test; $P = 0.01$). At discharge, mean dose of aripiprazole LAI was 385.7 mg.
Discussion: In this sample, inpatients in treatment with aripiprazole LAI had a short average HS. The early use of aripiprazole LAI in the first week of admission, reduced HS and polytherapy, and increased antipsychotic monotherapy.

S248. The modulation of cyclic nucleotide dependent pathways in the rat striatum by CPL-500-036-02 - a phosphodiesterase 10A inhibitor

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Background: Phosphodiesterase 10 (PDE10) is a dual-substrate (cAMP and cGMP) phosphodiesterase that is highly expressed in striatal medium spiny neurons (MSNs). MSNs modulate both corticostriatal and nigrostriatal transmissions. Disruption of these pathways leads to aberrant neuronal activity in the cerebral cortex. Therefore, it is believed that inhibition of PDE10 in these neurons may alleviate both positive and negative symptoms of schizophrenia – the feature of which present antipsychotic drugs are practically deprived of. In the present study, activity, selectivity and ex vivo pharmacodynamics of CPL-500-036-02, a novel PDE10A inhibitor, were assessed.
Methods: IC50 and selectivity against representative members of all other PDE families was determined by PerkinElmer Discovery Services at 100 nM. In a dose-response relationship study, male Sprague-Dawley rats ($n = 4$ per group) were sacrificed by focused microwave irradiation 2 h after single oral administration of 0,3, 1 or 3 mg/kg of CPL-500-036-02 or vehicle (0,5%MC+2%Tween80). In a time-response relationship study, rats ($n = 4$/group) were sacrificed 1 h, 2 h, 4 h or 8 h after single oral application of 3 mg/kg of PDE10A inhibitor or vehicle. Striata from all rats were dissected and frozen at -80 °C. Subsequently, they were homogenized in RIPA buffer or trichloroacetic acid and then sonicated. Lysates were used to western blot analysis of total and phospo protein levels using antibodies against: GluR1, GluR1 pSer845 (both from Merck Millipore), DARPP-32, DARPP-32 pThr34, CREB,CREB pSer133, MSK1, MSK1 pSer376, ERK1/2, ERK½ pThr202/Tyr204, histone H3, histone H3 pSer10 (all from Cell Signaling Technology), all normalized to β-tubulin (Merck Millipore) levels. All antibodies were used according to manufacturer's protocol.
Results: In vitro experiments revealed that the compound inhibits PDE10A in a nanomolar range (IC50 = 1 nM) and is selective against a panel of representative members of all other PDE families (PDE1-11). Pharmacodynamic study performed on striata of rats treated with CPL-500-036-02, showed significant and dose dependent phosphorylation increase of multiple proteins including AMPA receptor subunit GluR1, dopamine- and cAMP-regulated phosphoprotein 32 (DARPP--32), histone H3 or mitogen- and stress-activated protein kinase-1 (MSK-1) at 2 hours after administration, compared to the vehicle. The control analysis for lysates from hippocampus or prefrontal cortex showed no changes in the phosphorylation of mentioned targets' set. For the dose of 3 mg/kg the study was continued and revealed the time dependency in the time range of 0,5–8 h after administration of the compound.
Discussion: Inhibition of the PDE10A activity provides a modulation of pathways in medium spiny neurons. It could offer a novel treatment approach for diseases whose pathology is associated with disturbances of striatum functions (e.g. schizophrenia or Huntington's disease). CPL-500-036-02 is a potent and selective PDE10A inhibitor. A pharmacodynamic study confirmed that a single oral administration of CPL-500-036-02 provides changes in phosphorylation of several targets indicating expected activation of cyclic nucleotide dependent pathways in the rat striatum, in a dose and time dependent manner.

S249. Relative efficacy and safety of individual second-generation antipsychotics in treating first episode psychosis: a systematic review and meta-analysis

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Background: Early treatment choice in first episode psychosis is important. Our previous meta-analysis compared the efficacy and tolerability of individual first-generation antipsychotics (FGAs) with second-generation antipsychotics (SGAs) (Zhang *et al.* 2013). SGAs are the predominant medications in treating psychosis in clinical practice. However, no systematic reviews have examined the relative efficacy and safety of various SGA agents in the treatment of first episode psychosis.
Methods: Meta-analysis was conducted on randomized, head-to-head trials comparing SGA medications in first episode psychosis, published by 10/31/2015. Random effects model was used to pool effect sizes, either Hedges' g for continues variables or risk ratio for dichotomous outcomes. Heterogeneity across studies and potential publication bias were examined. Primary outcomes were total psychopathology change, response rate and all-cause discontinuation. Secondary outcomes included specific-cause discontinuation, changes in positive and negative symptoms, depression and adverse effects.
Results: Literature search yielded 20 studies consisting of 2,995 patients comparing 7 SGAs (olanzapine, risperidone, quetiapine, ziprasidone, aripiprazole, clozapine, and amisulpride). Pair-wise comparisons of individual SGAs were conducted. Clozapine and amisulpride were used in only one study each, therefore excluded from analysis. For total

symptom reduction, olanzapine and risperidone were significantly better than quetiapine, Hedges'g =.20 ($N=4$) and.38 ($N=5$), respectively, p's < .05. No significant difference was found among other SGAs, although aripiprazole might have a small advantage over risperidone and ziprasidone, but these comparisons consisted of only two studies. No significant difference was found in response rate and all-cause discontinuation among included SGAs. Consistently, olanzapine and risperidone outperformed quetiapine in reducing positive symptoms. However, there was no significant difference in reduction of negative symptom and depression among SGAs, except that aripiprazole was better than risperidone in treating negative symptoms in one study. For adverse effects, risperidone induced more extrapyramidal symptoms (EPS) than olanzapine while ziprasidone had worse EPS than quetiapine, Hedges' g =.23 ($N=5$) and.35 ($N=2$), respectively, p's < .05. Olanzapine was the worse in inducing weight gain than other SGAs, all p's < .05. Quetiapine was also worse in weight gain liability than ziprasidone, Hedges' g =.42 ($N=3$), $P<.01$.
Discussion: SGAs have variable efficacy and side effect profiles in treating first episode psychosis. While olanzapine, risperidone, and aripiprazole seemed to be more efficacious than quetiapine and ziprasidone, olanzapine and quetiapine induced more weight gain and risperidone was associated with higher EPS. Clinicians need to individualize treatment decisions, weighing different aspects of efficacy, tolerability, availability and cost.

S250. Electroconvulsive therapy augmentation in clozapine-resistant schizophrenia: a French sample

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Background: Forty percent to 70% of patients with schizophrenia demonstrate only a partial response to clozapine and become ultra-resistant. We examined the use of electroconvulsive therapy (ECT) as an augmentation to clozapine for treatment-refractory schizophrenia.
Methods: From January2009 to November 2015, patients from a French psychiatric hospital (Rouvray Hospital) in whom ECT was used to augment treatment with clozapine were followed. They had shown a partial response to clozapine. The patients received bitemporal brief pulse ECT at threshold two times a week. Clozapine dosages remained constant during the ECT. Patients were assessed by the Brief Psychiatric Rating Scale (BPRS) at baseline and at the end of ECT.
Results: The sample included 12 participants. All patients had a diagnosis of schizophrenia, with paranoid subtype (92%) being the most common. The mean age was 35.5 years (SD = 8.9), with a range of 23–48 years. Patients were mostly males (75%). All of them were unemployed and unmarried. The total duration of illness ranged from 1 year to 28 years (mean 12.4 years [SD = 9.3]). The mean dose of clozapine was 567 mg/day and all patients were demonstrating only a partial response at the time of initiating ECT. The mean number of ECT treatments administered was 18 (SD = 8), with a range of 7–36. The mean charge was of 946 millicoulombs (SD = 217). All the patients showed improvement in their clinical status as assessed by the BPRS. The mean reduction in the BPRS total score was 24.6% from baseline after the course of ECT, with a range of 9-55%. The improvement was superior on the items "hallucinations", "hostility" and "suspiciousness". In 75% of the cases, the symptomatic improvement allowed a hospital discharge. In terms of complications, one patient developed seizures, which were managed with valproate and ECT must be stopped.
Discussion: In this ultra-resistant group of patients for whom there are few clinical alternatives, we demonstrated an average response rate of 25%. Our observations also support the beneficial effect of ECT as an augmentation strategy for patients with treatment-resistant schizophrenia who partially respond to clozapine.

S251. Erroneous interviewing and rating patterns detected during screening predict subsequent quality issues

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Background: We have previously identified seriously flawed interviewing or rating technique in approximately 5% of possible visits in global schizophrenia clinical trial data sets. (Kott and Daniel, 2014). In the current analysis we address whether early detection of rating and interview errors during the screening process is predictive of flawed data after randomization.
Methods: Using logistic regression we have analyzed data from thirteen international double blind schizophrenia trials involving 7,142 subjects (60,795 visits). Quality indicators included logical inconsistencies in scoring among PANSS items, unusually large changes in the PANSS and identical scoring of 30/30 PANSS items across consecutive visits.
Results: The odds of detecting an error after randomization were significantly higher in those cases where an error was detected prior to randomization than in those cases where such an error was not present before randomization. The quality indicator with the greatest face validity implications for interview and ratings quality is identical ratings (30/30 PANSS items rated identically across visits). Across clinical trials the odds ratio of having an identical rating in the post-baseline visit for those subjects who had identical rating at baseline vs. those who had not ranged from 5.1 to 51.3.
Discussion: Our results indicate that the odds of detecting seriously flawed interviewing or rating technique after randomization are significantly higher in those subjects where an error was recorded during the screening phase than in those subjects where such as early error was not detected. If replicated, our findings suggest that raters likely to commit serious rating and interviewing errors potentially attenuating the signal can be identified early and potentially removed or remediated before a study subject is randomized.

S252. Relationship between psychiatric prescription pattern and adherence in patients with schizophrenia

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Background: Antipsychotic adherence is major issue in successful treatment of schizophrenia. Previous research in order to find factors affecting antipsychotic adherence focused on clinical and psychosocial factors, such as severity or symptoms or ethnicity. There has been little attention on psychiatric medication itself as a factor influencing on antipsychotic adherence although antipsychotic medication is definitely clinician modifiable and has a direct effect on patients' severity of symptoms and adverse event related psychiatric treatment. This study aimed to examine the relationship between psychiatric medication and antipsychotic adherence in patients with schizophrenia.
Methods: Health Insurance Review and Assessment Service-National Patients Sample (HIRA-NPS-2011), a whole national population based stratified randomized data of South Korea was utilized for this analysis. Total 2,926 patients met the inclusion and exclusion criteria. Adherence and all psychiatric medications were investigated along with demographic and clinical characteristics. Adherence group with psychiatric medication prescription for more than 80% of observation period was defined and identified and it was compared with non-adherence group.
Results: Use of any antipsychotics was lower in the non-adherence group than adherence group ($P<0.0001$). Use of typical antipsychotics was lower in the non-adherence group than in adherence group ($P=0.001$). Use of atypical antipsychotics failed to show statistically significant difference between two groups ($P=0.978$). Use of mood stabilizers was in non-adherence group than in the adherence group ($P=0.001$). Use of antidepressants, benzodiazepines and sleep pills didn't show statistically significant difference between two groups ($P>0.05$). Use of antipsychotic combination and use of high dose antipsychotics were significantly higher in the adherence group than the non-adherence group. Use of atypical antipsychotics and mood stabilizers were significantly predicted good adherence. Adherent patients were about 30% higher in the atypical antipsychotics users and mood stabilizers users.
Discussion: Use of atypical antipsychotics and mood stabilizers may be beneficial to antipsychotic adherence in patients with schizophrenia. Use of high dose antipsychotics and antipsychotic combination strategy may be useful to improve not only efficacy but also adherence to psychiatric medication. However, augmentation

polypharmacy with non-antipsychotic agents may not increase non-adherence.

S253. 1 year mirror study using paliperidone palmitate for relapse prevention of schizophrenia in 4 university hospitals in Canada

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Background: Schizophrenia and schizoaffective disorder can be treated effectively with medication, psychological and social interventions. Non-adherence is a major issue that plagues their management. 10 studies published since 1980 reported a mean rate of non-adherence to antipsychotic medication of 41%. Attempts were made to determine if long-acting injectable antipsychotics (LAI) are more effective than oral administration. A meta-analysis of 21 randomized controlled trials showed no difference in the effectiveness of LAIs over oral antipsychotics, but a meta-analysis of 25 mirror-image studies showed LAI superiority over oral antipsychotics in preventing admissions. The literature on the superiority of LAIs over oral antipsychotics remains controversial.
Methods: A multicentric retrospective mirror-image study was designed to determine the efficiency of paliperidone palmitate (PP) compared to oral antipsychotic treatment. The first injection of PP was the index event. Mirror periods were 365 days before (period A1) and after (period C1) the index event in model 1, and 365 days before (period A2) the index admission (period B2) and after discharge (period C2) in model 2. Patients prescribed PP were selected using pharmacy software and through injection clinics. Schizophrenic or schizoaffective patients were included if they had received 3 doses of PP, were between 18 and 65 years old, and had valid prescriptions of oral antipsychotics for 1 year to calculate mean possession ratios. They were excluded if they had received clozapine, had switched onto PP from another LAI or if they never received PP as outpatients. Hospitalization day distribution did not follow normality, so a Wilcoxon signed rank test was used. Potential confounders were tested using a generalized regression with a negative binomial model.
Results: 114 patients were recruited in 4 university hospitals in Quebec. 77% were male, mean age 37 years, mean disease duration 10 years, of which 70% had schizophrenia, 30% schizoaffective disorder, and 53% substance use disorder. Court treatment orders were issued for 36% of them. Most patients received only one antipsychotic in period A, mostly (67%) risperidone. Mean possession ratio was 43%. 69% of patients bought fewer than 70% of their drugs, and 20% never filled their prescriptions. Modal dose was 100 mg per 28 days. Mean duration of treatment was 297 days (estimated adherence rate of 81%). For model 1, mean annual hospitalization days were not significantly different in periods A1 (45 days) and C1 (39 days) ($P = 0{,}072$). For model 2, mean annual hospitalization days was significantly lower in period C2 (16 days) than period A2 (26 days) ($P = 0.013$). 97% of patients had at least 1 admission in period A, whereas it fell to 39% in period C (RR 2.5). In period A, 1.9 admissions per patient fell to 0.64 in period C ($P < 0.0001$). In a patient-centred cost analysis, PP was approximately cost-neutral. We found no predictor of outcomes with our generalized model.
Discussion: PP as a first LAI improved mean adherence from 43% to 81% and decreased the frequency of admission from 1.9 to 0.64 with a net effect in spending. Another mirror-image study on PP included 67 patients who had received PP for 12 months. Their results are similar: no difference in total bed days if index hospitalization is included, but a significant difference when it's excluded. Our drawbacks are the retrospective design, lack of comparators, lack of safety data, and a possible selection for patients who received oral risperidone (52%). Strengths is our non-enriched group of patient and measurement of mean possession ratios of oral antipsychotics. We hypothesize from our data that a subset of patients responds well to any LAI and decrease significantly their use of hospital services.

S254. Augmenting NMDA receptor signaling in schizophrenia enhances neural responsivity and working memory without affecting experience-dependent plasticity

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Background: The N-methyl-D-aspartate receptor (NMDAR) is a primary glutamate receptor and is a critical substrate underlying experience-dependent plasticity and working memory. Convergent evidence implicates impaired NMDAR signaling in schizophrenia and NMDAR hypofunction may contribute to deficits in plasticity and working memory in patients with schizophrenia. Ameliorating NMDAR hypofunction using the partial NMDAR agonist d-cycloserine (DCS) may improve such deficits.
Methods: We examined the effects of DCS in patients with schizophrenia on an EEG paradigm that utilizes high frequency visual stimulation (HFvS) to induce long-term potentiation (LTP) in visual cortex neurons, as well as on three cognitive tasks: a weather prediction task (WPT), an information integration task (IIT), and a n-back task. The WPT and IIT are incremental learning tasks that require practice with feedback to reach optimal performance; the n-back assesses spatial working memory. Forty-five patients with schizophrenia were randomized to receive acute DCS (100 mg; $n = 24$) or placebo ($n = 21$).
Results: In contrast to our prior findings in healthy individuals, DCS increased baseline neural responsivity and enhanced working memory in patients with schizophrenia without improving learning or electrophysiological measures of experience-dependent plasticity. Thus, patients receiving DCS showed enhanced baseline amplitude of the C1 visual evoked potential (VEP) relative to patients receiving placebo and enhanced performance during the 2-back condition of the working memory task. Conversely, there were no group differences in VEP potentiation following HFvS or on WPT or IIT learning.
Discussion: The dissociation of effects of DCS in schizophrenia patients on baseline neural responsivity and working memory versus experience-dependent plasticity suggests that DCS increased signaling at the NMDAR, but that increased NMDAR activation was not translated into structural changes at the synapse required for experience-dependent plasticity. This finding is consistent with emerging genetic and post-mortem findings that abnormalities at the NMDAR in schizophrenia involve not only the receptor, but also NMDAR-associated proteins that are critical for the expression of experience-dependent plasticity. Results highlight the importance of considering how different biophysical properties of the NMDAR contribute to cognitive deficits in schizophrenia in distinct ways and have important implications for treatment.

S255. The relation of thought disorders in schizophrenia with remission of symptoms and psychosocial improvement

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Background: Thought and language disorders are one of the fundamental symptom clusters of schizophrenia. Thought disorders that exacerbate in acute episodes might persist during the illness chronically in a vague form. İn severe mental disorders such as schizophrenia, psychosocial functioning is an important dimension as well along with symptoms in phases of diagnosis and assessment. The aim of this study is to investigate the relation between thought and language disorders and the course of symptomatic remission (SR), and psychosocial functioning in schizophrenia.
Methods: The study included 117 patients diagnosed as schizophrenia according to DSM-İV-TR. Severity of schizophrenia symptoms was assessed with the Positive and Negative Syndrome Scale (PANSS). Thought and language disorders were evaluated using the Thought and Language İndex (TLİ) and the Personal and Social Performance Scale (PSP) was used for detecting psychosocial functioning.

Results: There was a statistically significant difference between patients in SR and patients not in SR regarding poverty of speech, weakening of goal, peculiar logic, impoverishment of thought and disorganization of thought. İmpoverishment of thought and disorganization of thought were found to be significantly related to the dimensions of psychosocial functioning.
Discussion: Patients in SR show less impoverishment of thought/speech and disorganization of thought compared to patients not in SR. Thought and language disorders may play an important role in psychosocial functioning in schizophrenia patients. Patients having severe impairment in impoverishment of thought and disorganization of thought may present less social activities, personal/social relations and more aggressive behaviors.

S256. Effect of brexpiprazole on long-term functioning in adults with schizophrenia: results from a randomized, double-blind, placebo-controlled, maintenance study

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Background: Brexpiprazole is a partial agonist at 5-HT1A and dopamine D2 receptors at similar potency, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors [1]. The efficacy and safety of brexpiprazole for the treatment of adults with schizophrenia have been demonstrated in two 6-week phase 3 trials [2,3] and one maintenance trial [NCT01668797]. Brexpiprazole was approved in July 2015 by the FDA for treatment of schizophrenia and as adjunctive treatment of major depressive disorder. Deficits in psychosocial domains are a core feature of schizophrenia and social functioning is an important outcome parameter for evaluating successful long-term treatment. Here we describe the effects of brexpiprazole on long-term social functioning based on data from the maintenance trial.
Methods: Patients experiencing an acute exacerbation (PANSS total score >80) of schizophrenia were cross-titrated from current antipsychotic treatment(s) to brexpiprazole over a period of 1 to 4 weeks if required, before entering a 12 to 36 weeks single-blind stabilization phase on brexpiprazole (1 to 4 mg). Patients with stable symptoms over a period of 12 consecutive weeks and on a stable dose of brexpiprazole for at least the last 4 weeks of the stability period were then randomized (1:1) to either the stabilization dose of brexpiprazole or placebo for up to 52 weeks (maintenance phase). The primary efficacy endpoint was the time from randomization to exacerbation of psychotic symptoms/impending relapse. Social functioning was measured using the clinician rated scales Global Assessment of Functioning (GAF) scale, and Personal and Social Performance (PSP) scale. The GAF assesses the patient's psychological, social, and occupational functioning on a hypothetical continuum of mental health-illness using a scale that ranges from 1 to 100 points. The PSP measures personal and social functioning in 4 domains: socially useful activities, personal and social relationships, self-care, and disturbing and aggressive behaviors (range: 1 to 100).
Results: A total of 202 patients were randomized to either treatment with brexpiprazole ($n=97$) or placebo ($n=105$). The primary endpoint analysis showed a beneficial effect of brexpiprazole relative to placebo on the time to exacerbation of psychotic symptoms / impending relapse (log-rank test: hazard ratio = 0.292, $P<0.0001$). Mean GAF scores at randomization were 63.1 and 64.3 in the placebo and brexpiprazole groups, respectively. Least Squares (LS) mean change from baseline to Week 52 was -6.0 for placebo and 0.6 for brexpiprazole (LOCF, ANCOVA; treatment difference in favor of brexpiprazole: 6.6 [95% CI: 3.3, 9.8]; $P=0.0001$). Mean PSP total scores at randomization were 48.7 and 50.1 in the placebo and brexpiprazole groups, respectively. LS mean change from baseline to Week 52 increased in both groups (placebo: 10.3; brexpiprazole: 15.1), with the treatment difference representing a greater increase in social functioning for subjects in the brexpiprazole group compared with the placebo group (LOCF, ANCOVA: 4.8 [95% CI: 1.3, 8.2]; $P=0.0071$).
Discussion: In addition to being effective in preventing exacerbation of psychotic symptoms/impending relapse in patients with schizophrenia, brexpiprazole significantly improved long-term social functioning on the PSP scale, and maintained good overall function on the GAF scale.
References:
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S257. Psychosis in intra-familial homicide

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Background: The homicide of another person due to psychotic symptoms is an uncommon but severe complication of psychotic illness. Psychotic individuals will most often target acquaintances or individuals with whom they interact. Homicide of strangers by individuals affected by a psychotic illness is rare. (1) Parricide (the killing of one's parent) is a type of intra-familial homicide where psychosis was identified in up to two-thirds (67%) of male parricide offenders in a study sampling 64 consecutive cases of parricides. (2) The offenders were motivated by paranoid delusional beliefs against one or two parents and in certain cases, the presence of Capgras syndrome, a particular form of delusion where the person believes that another has been replaced by an impostor, was noted. This poster presentation will summarize salient findings in relation to psychosis and homicide, particularly within the familial context. It will further address the results of an original study comprising over one-thousand cases of intra-familial homicide coroner cases, collected over a period of 25-years in the province of Quebec, Canada, with respect to incidence and impact of psychosis in intra-familial homicide.
Methods: The authors examined all consecutive cases of coroners' files involving a victim of intra-familial homicide over a period ranging from 1990 to the present. Those records, including medical and psychiatric records when available, were reviewed and analysed by two forensic psychiatrists with training as coroners. The coroners' files typically contained the victim and offender characteristics, the circumstances and manner of death, the spatial location of the homicide, the type of weapon used in each case, the coroner's report for the particular death (including opinion and recommendations), the police report (including statements by the accused and witnesses), the autopsy report, and toxicology report. The authors also reviewed any other available examination, including expert opinions and legal outcomes. The design of this descriptive study raised no ethics related concerns, and the conduct of the study was granted approval by the coroner's office and the institutional review ethics board.
Results: The prevalence of major mental illness, in all categories of intra-familial homicides, was found to be much higher in the study population than in the overall population. The existence of psychosis was revealed in a high number of cases, especially in the fratricide (33%) and parricide (about 60%) cases. In contrast, filicide (killing of one's child by a parent) was more often associated with a depressive illness (62%) although a psychotic illness was also detected in over 7% of cases. Surprisingly, offenders who had committed spousal homicide and the homicide of a lover were also affected with a psychotic illness in a greater ratio than general population but this remained much lower than for other categories.
Discussion: Intra-familial homicide is often considered a crime of passion. This study examined the prevalence of psychosis in intra-familial homicides in a large sample of consecutive cases in the province of Quebec. While it is imperative to bear in mind that the risk of homicidal violence by psychotic individuals is low in general, our findings call for a consideration of risk factors in certain populations. Often times, intra-familial homicide is the first time an offender comes under psychiatric scrutiny. Risk factors, such as specific delusions, behavioural disorganisation, and other clinical characteristics including worsening of pre-existing psychosis, might serve as potential indicators of an increased risk for violence in predisposed individuals.

S258. Researcher know thy audience: getting translation right

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Background: Psychosocial interventions sit alongside medication-based interventions as mainstays of treatment for mental health

issues. Medication-based interventions typically target the symptoms of mental ill health. While psychosocial interventions can also target these symptoms, more often they tend to be targeted at the disability that accrues as a consequence of mental ill health. This can be social isolation, family dysfunction, dropping out of education, being unemployed or not taking good care of oneself. Many psychosocial interventions are supported by extensive research findings that attest to their effectiveness in aiding the recovery of young people with mental ill health. Sadly, most psychosocial interventions have been lost in translation to policy and practice and are not routinely available to young people presenting at mental health services.
We have conducted two randomized controlled trials showing that Individual Placement and Support is an effective method of helping young people with mental ill health return to school or work. As a consequence of our research, we were interested in ensuring that this intervention was made widely available to young people with mental ill health. Employment and education are key goals of young people presenting at mental health services and they are often not assisted with these goals in their mental health treatment.
Methods: Between 2008 and 2011 we pursued a translational strategy of the Science is Right and therefore policy should fall in line. This produced a lot of interest but little change. From 2012 we changed strategy. We conducted a review of the Australian policy landscape as it pertained to employment and young people with mental ill health. Importantly this also included coverage of welfare benefits and the existing employment system. We then engaged in a co-ordinated advocacy strategy, including multiple audiences, and made good use of media to support our agenda.
Results: This multi-pronged strategy has yielded great success in the advancement of the cause of making evidence-based integrated employment and education assistance more widely available to young people presenting to mental health services. In the Federal Budget 2015 $16.8million was allocated to expand IPS employment services to a large national trial. This is the first key step on a long translational journey.
Discussion: The translation of research requires a multi-pronged approach. Researchers need to move away from a stance of believing that results alone will convince policy makers and funders to implement interventions. Instead, a process of situating research findings in a broader context, understanding the economic and political needs of decision makers and involving the public through the media are needed to achieve translational aims.

S259. Prevalence and correlates of self-stigma among a sample of Nigerian patients with schizophrenia

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Background: Generally, literature suggests that self–stigma is highly prevalent among patients with schizophrenia with far reaching adverse consequences on successful treatment and patient outcome. Self stigma has been linked with enormous social, psychological and clinical consequences including, poor social networks/support, unemployment, poverty, decreased self esteem, poor adherence to treatment regimen and overall poor quality of life.There is however a dearth of information with regards to this subject matter as well as its correlates in this environment. This study therefore set out to investigate the rate and correlates of self-stigma among outpatients with schizophrenia attending a Nigerian Neuropsychiatric Hospital.
Methods: The study design was a descriptive cross-sectional study. Three hundred and seventy consecutive clinic attendees with a Diagnostic and Statistical Manual of mental disorders (DSM-IV) diagnosis of schizophrenia confirmed with the Structured Clinical Interview for DSM-IV axis I disorders (SCID-I) and aged between 18 and 64 years of age were recruited at the outpatient clinic of the Federal Neuropsychiatric Hospital, Lagos, Nigeria. The respondents were interviewed using a questionnaire that assessed sociodemographic and clinical variables. Self-stigma was assessed using the Internalized Stigma of Mental Illness (ISMI) scale which is a 29 item questionnaire that assesses subjective experience of stigma in those with mental illness. The 18 item Brief Psychiatric Rating Scale (BPRS-18) was used to rate the severity of illness, while a medication use recall questionnaire assessed medication use recall in the 24- hour period prior to data collection as a predictor of medication use behavior. Data was analyzed using SPSS-20 to generate frequency tables, cross tabulation, chi-square tests, t-tests and logistic regression analysis. Ethical approval was sought from the health research and ethics committee of the study centre while a written informed consent was obtained from each subject that participated in the study.
Results: A total of 370 patients participated in the study made up of 181 (48.9%) males and 189 (51.1%) females, and their mean age was 37.87 (±11.24) years. The prevalence of high self-stigma was 16.5%. The associated sociodemographic and clinical variables for high self-stigma were marital status ($P = 0.018$), level of educational attainment ($P = 0.004$), perceived social support ($P = 0.010$), average monthly income ($P = 0.008$), medication side effects ($P = 0.029$), Brief Psychiatric Rating Scale (BPRS) scores ($P = 0.001$) and 24- hour medication use recall scores ($P = 0.011$). Following binary logistic regression analysis, the independent predictors of high self-stigma include having no formal education (OR = 4.010, 95% C.I 1.102-14.592), or achieving only primary education (OR = 3.699, 95% C.I 1.407-9.565), social support (OR = 0.392, 95% C.I 0.172-0.893), experiencing medication side effects (OR = 2.407, 95% C.I 1.088-3.854), low 24- hour medication use recall scores (OR = 0.993, 95% C.I 0.986–1.000), high BPRS scores (OR = 1.147, 95% C.I 1.041-1.265), average monthly income less than $25 per month (OR = 4.608, 95% C.I 1.250–16.990) and average monthly income between $100- 250 per month (OR = 3.797, 95% C.I 1.015–14.197).
Discussion: High self-stigma is prevalent among patients with schizophrenia from this environment and is related to some sociodemographic as well as clinical variables. These factors should be considered during routine care and in the design of intervention programs to reduce self-stigma as a means to improving patient the outcome of patients.

S260. Social skills evaluation of patients with schizophrenia: comparison between treatment resistant, non treatment resistant and normal controls

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Background: Social skills (SS) involve verbal, paralinguistic and non-verbal components of interpersonal relationship. It is well known that SS are compromised in schizophrenia but little is known whether severity of the disorder correlates with impairment in SS. The aim of the present study was to compare patients with Treatment Resistant Schizophrenia (TRS) with patients who respond to antipsychotic therapy (NTRS) and normal controls in terms of SS using an instrument for the evaluation of social skills in normal subjects, the Del Prette Social Skills Inventory (SSI-Del Prette). This instrument evaluates a wide range of social skills comprising five domains or factors, namely: F1: Defense of own rights and self-esteem; F2:Self affirmation and expression of positive affects; F3:Neutral situations in terms of positive and negative affects; F4- Ability to deal with situations of self-exposure; F4- Ability to deal with aggressiveness or anxiety.
Methods: We conducted a cross-sectional study administering the SSI-Del Prette to 62 outpatients with schizophrenia, either TRS ($N = 33$) or NTR ($N = 29$), which were compare with scores of data from general population ($N = 99$). The TRS sample had 24 males and 9 females, had a mean (sd) age of 36.42(7.71) years, age of onset of illness of 18.97 (4.99), duration of illness of 17.45 (7.45) years, 10.52(2.15) of schooling and were all under clozapine treatment. NTRS sample was composed of 14 males and 15 females, had a mean age of 44.69(11.97) years, age of onset of illness of 31.70 (15.09), a duration of illness of 13.52(10.75) years, 10.07 (2.72) years of schooling and were under treatment with various types of non-clozapine antipsychotics. Normal controls sample were 55 males and 53 females, had a mean age of 32.09(10.60) years and 14.49 (2.48) years of schooling. Patients and controls differed significantly in terms of age ($F = 17.52$, $P = 0.001$) and schooling ($F = 56.42$, $P = 0.000$). Therefore an ANCOVA model with age and schooling as covariates followed by post-hoc tests was used to

compare the SSI- Del Prette Inventory domains between patients with schizophrenia and normal controls.
Results: Patients with TRS showed no significantly from NTRS in the five domains the SSI-Del Prette. NTRS showed to have more impairment than controls in three domains of the inventory (*P* values of post hoc tests): F1 (0.02), F2 (0.001) and F4 (0.001). However patients with TRS showed to had significantly more social skills impairments controls in only in two domains: F2 (0,001) and F3 (0.001), with no differences in terms of factors F1(Defense of own rights and self-esteem), F4 (Ability to deal with situations of self-exposure) and F5 (Ability to deal with aggressiveness or anxiety)
Discussion: The SSI-Del Prette was created for the evaluation of social skills in normal subjects. However this inventory seems to be a useful tool for the evaluation of social skills in patients with schizophrenia. Patients with schizophrenia are significantly impaired when compared to normal controls. However patients with TRS showed to be less compromised than patients with NTRS in some domains of the SSI-Del Prette. One hypothesis is that Clozapine may be more efficacious than other antipsychotics in the preservation of certain social abilities.

S261. Relationship of insight with cognitive function, psychopathology and psychosocial factors in patients with schizophrenia

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Background: The purpose of this study is to evaluate the relationships of insight with socio-demographic, clinical, and cognitive parameters in schizophrenic patients.
Methods: Seventy-seven patients with schizophrenia were recruited. All subjects completed the Korean version of the revised Insight Scale of Psychosis (KISP) and Multidimensional Scale of Perceived Social Support (MSPSS). Positive and Negative symptom scale (PANSS), Calgary Depression Scale for Schizophrenia (CDSS), Neurocognitive function tests were also administered.
Results: Patients that are married or currently living together showed significantly higher levels of insight than those who are divorced, separated, or single. Insight also showed positive correlations with CDSS, negative correlations with age of onset, family and friend subscales of MSPSS. Emotional discomfort factor of PANSS showed positive correlations with insight. Total scores of PANSS and neurocognitive functions showed no significant correlations with insight. More severe depressive symptoms, lower perceived social support from friends and family, and younger age of onset were predictor of higher insight.
Discussion: The study suggest that impaired insight might be independent from general psychopathology and cognitive function and more influenced by emotional status and psychosocial environment.

S262. Predictors and outcomes for patients who reduce or discontinue their anti-psychotic treatment after first episode psychosis

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Background: Anti-psychotic medication is the standard treatment for all patients who are diagnosed with a schizophrenia disorder. Even though many patients experience side effects and wish to stop their medication no consensus regarding guided discontinuation exists. This is mostly because most discontinuation trials testing placebo versus anti-psychotics have shown that the relapse rates of patients put on placebo is very high. This has made both clinicians and researchers sceptical to any form of discontinuation or doses reduction. Still there is a discrepancy in the literature between the discontinuation studies and the long term follow-up literature which finds that a large number of patients not treated with ant-psychotic medication are well functioning with manageable symptoms. This study aims to inform clinicians and researchers of characteristics and outcomes for patients who choose to discontinue their medication and to find predictors for successful discontinuation
Methods: As part of a randomized control trial testing the effects of prolonged early intervention in first episode psychosis patients were assessed 18 months after start of treatment in a specialized early intervention team an re-assessed at follow-up five years after start of treatment. A total of 400 patients with a Schizophrenia spectrum disorder (ICD10-F2) were recruited for this study. Excluding those with a schizotypical disorder, 103 were interviewed at the follow-up assessment and had either discontinued their medication or reduced their dose with at least 50%. To evaluate whether the discontinuation were successful the patients were dichotomized on functional level and psychotic pathology at follow-up. Baseline differences on sex, age, psychopathology, functional level, cognition, medication and quality of life were analyzed to find predictors for successful discontinuation. Outcome differences on negative symptoms, cognition and quality of life were assessed to establish whether patients were showing signs of improvement on other domains than those used for the stratification. All statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS) version 22.0 for Windows.
Results: This is an exploratory study aiming to give clinicians and researcher information regarding the course of patients who wish to stop or reduce their medication and how they should advise these patients. The data collection were completed in July 2015 and the analyses are still not finished but all results as explained in the method section will be finished and presented at the 2016 SIRS biennial.
Discussion: There are several limitations in this study. First the design of the overall study were not to asses medicine reduction or discontinuation, but to assess the effect of prolonged early intervention in first episode psychosis therefore many of the measurements one would wish for in these study are not collected, for instance accumulated medicine doses and an exact discontinuation date. With these limitations in mind we wish to discuss the implications for guided discontinuation and what advice clinicians could give to patients wishing to stop their medical treatment.

S263. Cognitive adaptation training helps you live at home: interim results of the Finnish CAT-study

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Background: In Finland, approximately 50 000 people have a diagnosis of schizophrenia. In practice 6% of them reside permanently in mental hospitals (Niemi, 2005). There is a national target to reduce the number of psychiatric hospital beds (Plan for mental health and substance abuse work 2009). However, as hospitals are closed there is a tendency to place schizophrenia patients in different types of sheltered housing instead of supporting them to live independently in the community (i.e. Petersen *et al* 2013). In the Danish OPUS-study 94 patients with first episode schizophrenia were followed and even those who had attended a vigorous rehabilitation program lived about two and a half months in sheltered housing in the fifth year after their diagnosis (Nordentoft *et al* 2010). Thus, with deinstitutionalization we are building up a little monitored system of sheltered housing for schizophrenia patients. This system may increase chronic need for support, it is expensive and marginalizes a large section of people from the community. When service users are asked they usually prefer having their own homes.
Cognitive adaptation training (CAT) is a home-based, manual-driven treatment that utilizes environmental supports and compensatory strategies to bypass cognitive deficits and improve target behaviors and functional outcomes in individuals with schizophrenia. Unlike traditional case management, CAT provides environmental supports and compensatory strategies tailored to meet the behavioral style and neurocognitive deficits of each individual patient. (Meredith *et al*

2009). CAT has been shown to be effective in improving service users' ability to independent living (Velligan *et al* 2006, Velligan *et al* 2008).
Methods: After formal CAT-training the program was implemented in the Kellokoski Hospital community treatment catchment area (approx. 150 000 inhabitants) and used for each consecutive schizophrenia patient treated in the system, in risk of needing a more supportive housing setting and willing to participate in the study. The only exclusion criteria were heavy alcohol and drug abuse and known aggressive behavior. The outcome measurements include both qualitative and quantitative methods: transfer to a different type of housing, need for hospital treatment, psychiatric rating scales, observed measurements and open interviews, and are measured after 4 months after the start of the intervention, at the end of the 9 month intervention and after a 6 months follow-up period.
Ethical permission for the study was given by the Helsinki University Ethical Board.
Results: The study started in March 2013 and is still ongoing. We report here preliminary interim results for the first 20 patients who have completed the study. All the patients had the primary diagnosis of schizophrenia, 12 patients were male (60%), mean age was 36.8+10.3 years, mean GAF-measurement was 44.7+ 12.9 and none of the patients were in remission. When the study started 19 patients lived in their own apartments, one with her spouse, the rest alone; one patient was in a nursing home.
Five patients (25%) discontinued the study, one patient died, the cause of death was not related to the study. 3 patients had to be admitted to hospital treatment and two patients were placed in nursing homes due to the lack of independent living skills. Rest of the patients were able to maintain their previous housing status and did not need any extra support. Only one of the patients was not satisfied with the treatment model, the rest were moderately or very satisfied their treatment. For the conference we can report results for 33 patients and financial calculations of the costs and savings achieved.
Discussion: Using the CAT-model enables schizophrenia patients with severe cognitive defects and psychotic symptoms to live independently. This is appreciated by the patients and saves costs.

S264. Does baseline apathy predict social and vocational outcome at two years follow up in a vocational rehabilitation study?

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Background: Employment rates for people with schizophrenia are low, and improving vocational services and vocational outcome for people with schizophrenia is an ongoing concern. Of the negative symptoms, apathy has an independent negative impact on social and vocational functioning. The current study examines the impact of baseline apathy on social and vocational functioning at post treatment and at two year follow-up, in a vocational rehabilitation study. Adults with psychotic disorders were offered six months vocational rehabilitation augmented by close collaboration between all involved parties, and either cognitive remediation (CR) or cognitive behavior therapy techniques (CBT), both addressing work related issues. We did not expect the interventions to affect apathy, as the interventions do not specifically target apathy, and as apathy tends to fluctuate or decrease slightly over time. We expected baseline apathy to have a negative impact on functioning on all outcome variables.
Methods: Baseline assessments included diagnosis, demographics, symptoms and function. Outcome measures were social functioning assessed with the Social Function Scale (SFS) (without the subscale for work), and vocational functioning measured as hours worked per week at post treatment and follow up.
Independent samples t-test were performed to compare groups. Logistic or hierarchical linear regression analyses were performed to explore predictors of function. Gender, age, education, duration of illness, PANSS positive, and baseline apathy were entered as covariates, as was type of intervention (CR or CBT).
Results: There was no significant difference in apathy according to employment status at baseline, post treatment or at follow up. There were no significant predictors of employment status at post treatment or at follow up. Baseline apathy ($\beta = -.196$, $t = -2.057$, $P = .042$) predicted hours worked post treatment, while the model for hours worked at follow up was not significant. Apathy ($\beta = -.401$, $t = -4.749$, $P < .001$), PANSS positive ($\beta = -.233$, $t = -2.734$, $P = .007$) and gender ($\beta = .276$, $t = 3.620$, $P = .001$) predicted social functioning at post treatment, while baseline apathy ($\beta = -.510$, $t = -5.293$, $P < .001$) was the only predictor of social functioning at follow up.
Discussion: Contrary to our expectations, baseline apathy was no strong predictor of vocational function at post treatment or at follow up, indicating that ongoing support in vocational rehabilitation might compensate for the negative impact of apathy on vocational functioning. Apathy was however a clear predictor for social functioning at both times, lending support to a large body of research showing that apathy has a strong negative impact on function. While one might expect the support in vocational rehabilitation to have a positive impact on some aspects of social functioning, this does not seem to be the case here. It seems that support in the work place does not improve social function outside the work place.

S265. Cognitive adaptation as a nursing intervention for long-term hospitalized patients

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Background: There is a need for evidence-based interventions that contribute to the functional recovery of long-term residential patients. Cognitive Adaptation Training (CAT) is a compensatory approach that aims at creating new routines in the patients' living environment through the use of environmental supports. Previous studies showed that CAT improves functioning in outpatients with schizophrenia when CAT is given by psychologists (Velligan *et al.*, 2002). Long-term residential patients may benefit from CAT as most of them experience difficulties with independently performing everyday tasks due to cognitive deficits. This study aims to evaluate the effect of CAT as a nursing intervention in SMI inpatients who reside in long-term clinical facilities.
Methods: This study is a multicenter cluster randomized controlled trial comparing CAT (intervention group) to Treatment As Usual (TAU, control group). The primary goal is to evaluate the effectiveness of CAT on everyday functioning. The study has a duration of 12 months with follow-up measurements at 15, 18, 21 and 24 months after baseline for the intervention group. Primary outcome measures are the Multnomah Community Ability Scale (MCAS) and the Social and Occupational Functioning Scale (SOFAS).
Results: From one of the three participating institutions 12-month data are available. Repeated measures on this subsample showed no significant differences between the intervention group ($N = 17$) and controls ($N = 21$) over time (SOFAS: $F(37,4) = .33$, $p = .86$, MCAS: $F(37,4) = .99$, $p = .42$). Mean (SE) of SOFAS at baseline were CAT 36.1 (9.6), TAU 36.8 (12.3) and at 12 months CAT 34.1 (5.5), TAU 33.2 (7.5). Mean (SE) of MCAS at baseline were CAT 59.6 (6.7), TAU 57.7 (7.8) and at 12 months CAT 61.6 (7.1), TAU 62.3 (5.8). Data collection of the 12 month measurements at the other two institutions will be finished early 2016.
Discussion: The lack of a statistically significant differences may be due to limited power of these preliminary analyses. Based upon pilot results (Que *et al.*, 2014) we expect that functional outcome will be improved at 12 months and that these improvements will be sustained or further improved after that.

S266. The efficacy of 12 weeks physical health promotion program in patients with major psychiatric disorder

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Background: It was known that taking atypical antipsychotics or negative symptoms of schizophrenia had potential risk factors for weight gain and metabolic diseases in chronic mental illness patients. The purpose of this study was to evaluate the change of body mass index (BMI) and patient satisfaction using physical health promotion

program, and furthermore we tried to find ways for the actual settlement for this program.
Methods: Body weight, BMI, hypertension, diabetes and dyslipidemia were assessed by 100 patients enrolled in Dobong-gu community mental health center, Seoul. 56 patients among them were recruited and were classified into three groups according to BMI and exercise intensity. These groups were composed of exercise regimen of more than 3 times per week, more than one per week and voluntary exercise recommendation. Diet and exercise training by wellness call-center program developed by Lilly were conducted to each of these groups. 12-week program was performed and body measurements, hematological test, Rosenberg Self-Esteem Scale (RSES), Subjective Wellbeing under Neuroleptics (SWUN) and knowledge assessment of nutrition, diet, exercise and weight control were evaluated.
Results: 1) Metabolic diseases were 70 subjects and overweight was 75 patients. 46 patients among these were able to complete a health promotion program and 10 patients dropped out. 2) In all of enrolled patients, significant reduction was observed in weight and BMI and a significant increase was observed in SWUN, knowledge assessment about nutrition and diet, knowledge assessment for weight control and exercise, and high-density lipoprotein. 3) In each of the three groups, significant reduction in body weight and BMI was observed and each knowledge assessment scales were significantly improved after 12 weeks, but weight, BMI, and most of the scale measure were not found in significant differences among the three groups.
Discussion: This study suggests that the physical health promotion program which was conducted by chronic mental illness patients in the community have a significant effect for the reduction of weight and BMI and for the knowledge improvement about nutrition and exercise. And voluntary exercise recommendation by phone interventions was also proved to be effective. These imply that the physical health promotion program in a community mental health center should be an useful model that is applied to physical health of chronic mental illness patients.

S267. Association between family history of psychiatric disorders and long-term outcome in schizophrenia – the Northern Finland birth cohort 1966 study

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Background: Previously, family history of psychiatric disorders has been associated with poorer outcome in schizophrenia. However, there are only few studies on association between family history and long-term social and occupational outcome in schizophrenia. We aimed to investigate the association of family history of psychiatric disorders, especially psychosis, with long-term social, occupational, clinical and global outcome in schizophrenia.
Methods: The study sample comprises of the Northern Finland Birth Cohort 1966 study. Cohort members with psychosis were detected by Finnish national registers. Altogether 69 individuals with schizophrenia spectrum diagnosis participated, approximately at the age of 43, after on average 17 years since onset of illness. The information regarding family history of psychiatric disorders were gathered from registers and interviews. A Strauss-Carpenter Outcome Scale, PANSS and SOFAS were conducted to assess the outcome.
Results: The family history of any psychiatric disorder was associated with more severe positive (median 11.0 vs. 16.0, $P = 0.046$) and emotional (median 13.0 vs. 17.5, $P = 0.041$) symptoms in PANSS. The family history of psychosis was not associated with outcomes.
Discussion: Family history of psychiatric disorders has a small association with positive and emotional symptoms in schizophrenia. After years of illness family history of psychosis does not seem to have effect on outcome of schizophrenia.

S268. Negative symptoms mediate the relationship between social cognition and functioning in schizophrenia: a pilot study

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Background: In spite of significant advances in pharmacological and psychological treatments, schizophrenia still ranks among the leading causes of disability worldwide. People suffering from schizophrenia have significant impairment in major areas of everyday life, such as interpersonal relationships, work or school and even self-care. Enhancing the understanding of factors that hinder real-life functioning is therefore crucial for translating delivered care into more positive outcomes.
Social cognition, defined as the mental operations that underlie social interactions, including perceiving, interpreting, and generating responses to the intentions, dispositions, and behaviors of others, has been implicated in impaired functioning. It is typically broken down into four domains: emotion processing, social perception, attributional bias and theory of mind. Negative symptoms have also been associated with patients' functional outcome; although generally conceptualized as a unitary construct, the most recent literature suggests that these symptoms are heterogeneous and include at least two factors: amotivation and diminished emotional expression. The aim of this study was to analyze the relationships between negative symptoms, social cognition and real-life functioning in people with schizophrenia.
Methods: 12 patients with diagnosis of schizophrenia according to ICD-10 criteria were assessed cross-sectionally regarding relevant dimensions to our study: general psychopathology (Positive and Negative Syndrome Scale), social cognition (Face and Emotion Identification Test, Schema Component Sequencing Test - Revised, Social Perception Scale, Ambiguous Intentions and Hostility Questionnaire, Reading the Mind in The Eyes Test), negative symptoms (Clinical Assessment Interview for Negative Symptoms – CAINS) and general functioning (Personal and Social Performance scale – PSP). Spearman correlations were examined and regression and mediation models (Preacher and Hayes bootstrapping methodology) were performed.
Results: In our preliminary results, emotion processing was the only social cognition dimension significantly correlated with functioning ($rS = .87$) and negative symptoms measured by the CAINS: $rS = -.78$ with amotivation; -.70 with diminished emotional expression and -.78 with total CAINS score (all $P < .01$). Both amotivation and diminished emotional expression, as well as negative symptoms as a whole, correlated with functioning ($rS > .80$, $P < .01$). Emotion processing was a significant predictor of amotivation, diminished emotional expression and total CAINS score (all Beta > -.65, $p < .05$). Both emotion processing (Beta = .71, $P = 0.3$) and amotivation (Beta = -.84, $P = 0.001$) were significant predictors of functioning. Finally, amotivation was found to be a partial mediator of the relationship between emotion processing and functioning (BCA 95% CI = .196 - 7.559).
Discussion: Our results are in partial agreement with previous studies suggesting that emotional processing is the most relevant dimension of social cognition to everyday functioning, despite a possible contribution of theory of mind for such impairment in patients with schizophrenia.
Regarding negative symptoms, amotivation seems to be the dimension of most relevance to functioning. Altogether, negative symptoms seem to be driven by social cognition deficits and, at least partially, negative symptoms may play a role in the deleterious impact of impaired social cognition on functional outcome. The complexity of the crosstalk between negative symptoms, social cognition and functioning will be better addressed in ongoing studies, as a greater understanding of underlying mechanisms is critical to development of effective treatments.

S269. Investigation of the correlates of happiness, life satisfaction and success in schizophrenia

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Background: Previous studies have suggested that, despite marked functional impairments, patients with schizophrenia report levels of subjective well-being that are comparable to healthy controls. However, this paradoxical finding is particularly difficult to reconcile given the disparities in the definitions commonly used to operationalize well-being. Further, subjective well-being is multi-dimensional, but is typically measured as a single, broad construct, thereby providing imprecise and incomplete information. As a result, three important components of subjective well-being - happiness, satisfaction and success – as well as its correlates and factors related to schizophrenia, are not well known. Thus, the present study set out to compare patients with schizophrenia and healthy individuals in their overall levels of subjective happiness, life satisfaction, and sense of success.
Methods: Fifty patients and fifty-six matched controls participated in the study. Clinical status and functioning were assessed, and a series of self-report questionnaires were used to measure levels of happiness, satisfaction, and success.
Results: Mann-Whitney U analyses revealed that, compared to healthy controls, patients with schizophrenia experienced significantly less satisfaction ($U = 941.5$, $p = .009$) and a lower sense of success in life ($U = 982$, $p = .008$). However, the two groups did not significantly differ in their self-reported feelings of happiness ($U = 1096.5$, ns). Additionally, for patients with schizophrenia, subjective feelings of happiness, satisfaction, and success were significantly correlated with higher levels of anticipatory and consummatory pleasure, and with less depression and less avolition. For healthy controls, however, happiness, satisfaction, and success were significantly correlated with higher monthly incomes, better cognitive functioning, younger age, and lower levels of apathy. Further, functional status was significantly correlated with happiness, satisfaction, and success in life for healthy controls, but not for patients.
Discussion: Preliminary analyses suggest that, compared to healthy controls, patients with schizophrenia experience less satisfaction and success in life, but report similar levels of happiness. Additionally, the correlates of happiness, satisfaction, and success differ for patients and controls. These findings suggest that, though related, happiness, satisfaction, and success are separate constructs, defined differently by the two groups. These differences highlight the need to better understand the mechanisms and processes underlying patients' own reflections, opinions, and perceptions of what constitutes and contributes to their happiness, satisfaction, and success in life.

S270. Self-clarity and different clusters of insight and self-stigma in serious mental illness

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Background: Although there are extensive theoretical reviews regarding the self-experience among persons with severe mental illness (SMI), as well as extensive studies on insight and self-stigma interactions, there is limited research that addresses the interactive implications of insight and self-stigma on the self-clarity of persons with SMI. Accordingly, the current study explored the relation between different insight-self-stigma clusters, self-clarity, hope, recovery and functioning.
Methods: 107 persons with SMI consuming psychiatric rehabilitation services in the community were administered four scales: self-concept clarity, self- stigma, insight into the illness, hope and functioning. To explore the associations between the variables and the clusters of insight and self-stigma, the following three step analysis was conducted. First, to explore the relationships between all variables, we performed Spearman correlations. Second, cluster analysis was used to identify homogenous participant groups based on internalized stigma (ISME) and insight (BIS). A two-step cluster method was used, based on the log-likelihood criterion for distance measurement. Finally, in order to examine the validity of the clusters, a series of Kruskal-Wallis and Mann-Whitney tests was conducted comparing the research variables among the clusters. Significance was set at the.05 level, and all tests of significance were two-tailed.
Results: Insight, as measured by a self-report scale was not related to any of the other variables. Self-stigma was negatively associated with self-clarity as well as with hope, recovery and functioning. Three clusters emerged: moderate stigma/high insight ($n = 31$), high stigma/moderate insight ($n = 28$), and low stigma/low insight ($n = 42$). The group with low stigma and low insight had higher mean levels in functioning, hope, self-clarity and recovery than the other two groups. There were no significant differences between cluster 1 (moderate stigma/high insight) and cluster 2 (high stigma/moderate insight) in all the variables beside self-clarity. The group with moderate stigma and high insight had significantly higher mean levels in self-clarity than the group with high stigma and moderate insight.
Discussion: Results reveal that when people with SMI do not have high levels of self-stigma they can poses a positive and clear sense of self accompanied with hope and recovery, even when they have low insight. These findings support the importance of focusing primarily on reducing self-stigma rather than increasing insight. Interventions such as the narrative enhancement and cognitive therapy (NECT) which have shown to be effective in reducing self-stigma are recommended. Notably, this intervention includes narration of a personal story that may be more in accord with narrative insight and the enhancement of self-clarity rather than clinical insight which may be less central to improve psychological outcomes.

S271. Health related quality of life in antipsychotic-treated children and adolescents with psychosis

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Background: Health Related Quality of Life (HRQoL) has rarely been measured in children and adolescents with psychosis. However, in adult populations, schizophrenia is associated with compromised HRQoL in several domains. The few studies of HRQoL in youth with psychosis, has never examined the HRQoL from the youth's perspective. The subjective evaluation in HRQoL is essential in Early Onset Psychosis (EOP), because it can be an important outcome measure from the patients' perspective, also in comparison of the effects and adverse reactions of different antipsychotics. The aim of the present RCT was to investigate whether treatment with aripiprazole vs. quetiapine have differential effects on HRQoL after 12 weeks of treatment.
In addition, we compared HRQoL in children and adolescents with psychosis vs. healthy controls at baseline and after 12 weeks. We also investigated if the severity of the illness, measured by Positive and Negative Syndrome Scale (PANSS), or the Duration of Untreated Psychosis (DUP) was associated with impaired HRQoL at baseline.
Methods: The study is part of the Tolerability and Efficacy of Antipsychotics (TEA) trial, where a total of 113 patients, aged 12-17 years, were randomly assigned 1:1 to a 12 weeks double-blinded treatment with quetiapine 600 mg/day vs aripiprazole 20 mg/day. Of these, 86 patients participated in the HRQoL study. The healthy control group (HC) consisted of 82 healthy youth matched on age and sex. The HRQoL was examined with the generic, 52-item self-

administered questionnaire KIDSCREEN, at baseline and after 12 weeks in both patients and HC.
Results: A total of $n = 86$ patients (schizophrenia ($n = 58$), schizoaffective disorder ($n = 18$), affective psychosis ($n = 4$) and other psychoses ($n = 6$)) were rated on the HRQoL. Mean age was 15.7 years (SD 1.32) years and 30% were males. We found no significant difference in HRQoL between the two groups.
At baseline, HRQoL in patients were significantly lower on all 10 domains compared to HC. For the patient group, HRQoL increased significantly in nine out of ten domains during the 12 weeks treatment period, while in HC group, HRQoL was stable over time. High PANSS Total scores correlated with lower HRQoL on four of ten domains, and high PANSS depression scores correlated with lower HRQoL on five out of ten domains at baseline, but we found no significant correlation between DUP and HRQoL.
Discussion: The present study found no differential effect on HRQoL of 12 weeks treatment with aripiprazole vs. quetiapine ER in youth with psychosis. HRQoL increased significantly in both treatment groups over time, while it was stable in HCs. Illness severity correlated with HRQoL on several domains. HRQoL can be an important supplemental measurement in youth with psychosis, as it can provide the clinicians with a subjective measure disclosing how the patient evaluate the impact of their psychotic illness on their life.

S272. A 24-month follow-up evaluation of quality of life (QOL) as an outcome measure for community treatment orders (CTOs) in central alberta, Canada

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Background: Amendments of the Mental Health Act of Alberta were proclaimed in January 1, 2010 with regards to CTOs to:
– Broaden criteria for certification of persons with serious and persistent mental disorders to permit earlier intervention and treatment.
– Send to family physicians a discharge summary and recommendations for treatment upon discharge of a patient from a facility/hospital.
– Introduce CTOs to encourage individuals to maintain mental health treatment in community and reduce the need for hospitalization.
A CTO is in effect for six months and there is no limit to the number of times it can be renewed.
The value of CTOs remains at issue after years of implementation in several countries. The debate centers around:
– A deontological philosophy versus a utilitarian approach.
– Compulsory community treatment not necessarily more effective than standard care.
The debate led to questioning whether what if any benefits CTOs bestow on the QOL and Health of CTO clients living in Rural Central Alberta.
Aim: Assess from clients' perspectives changes in the QOL and Health among the individuals who were issued a CTO.
Methods: An exploratory qualitative study, utilizing the WHOQOL-BREF. Responding individuals from the baseline survey (2013) were requested to complete a 24 months follow-up questionnaire in 2015. Change in QOL was assessed with descriptive and nonparametric statistical methods due to a small sample size ($n = 10$).
Results: Statistics are presented by the 2013 and 2015 surveys respectively. Respondents considered overall QOL better (M = 4.0, SD = 0.7 (2013) & M = 4.1, SD = 0.7 (2015)) than their overall Health (M = 3.5, SD = 1.1 & M = 3.6, SD = 0.7). Women were more satisfied with their QOL(M = 4.5, SD = 0.7 & M = 4.5, SD = 0.7) than men (M = 3.9, SD = 0.6 & M = 4.0, SD = 0.8) and a slight increase were reported by respondents 35 years and older (M = 4.0, SD = 1.0 & M = 4.2, SD = 0.8). A small increase in overall Health Status occurred among women (M = 2.5, SD = 2.1 & M = 3.5, SD = 0.7) while a slight decrease occurred among males (M = 3.8, SD = 0.7 & M = 3.6, SD = 0.7). The younger age group (< = 34 Years) reported a minor decrease (M = 4.0, SD = 0.7 & M = 3.5, SD = 1.0) in their Health Status while the older age group reported a slight increase (M = 3.0, SD = 1.2 & M = 3.7, SD = 0.6).
In terms of the WHOQOL-BREF domains (scale 0-100), participants were most satisfied with the Environment (72 & 78) followed by the Social Relationships (72 & 77), Physical (68 & 74) and Psychological (68 & 67) Domains. A similar trend of domain increases/decreases occurred among the females, males and older age group.
Discussion: CTO clients are difficult to engage due to psychiatric symptoms, decreased motivation and social mobility.
The results are not reflective of a general CTO population. Nevertheless the results yielded no significant evidence of CTOs benefitting CTO clients in terms of their overall QOL and overall Health Status. These findings substantiate evidence from previous studies that CTOs do not confer considerable benefits on CTO clients. Importantly, the study accounts for a set of factors representing areas of relative vulnerability and strength of the participants. Greatest vulnerabilities were within the Psychological Domain and greatest strengths occurred within the Environment Domain. Compulsory CTO Treatments without consent are not appropriate for everyone. Tragically one respondent succumbed to suicide within a month after completing the 2015 survey. The individual submitted two appeals to the CTO Review Panel during 2014. The Panel upheld the CTO issuance at both appeal hearings. This person resided in a transitional home where recovery is promoted through a psychosocial rehabilitation model of care.

S273. The social functionality of schizophrenic patients and the burden experienced by their caregivers: a sample of Turkey

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Background: Schizophrenia which usually starts at young ages, is seen in both sexes and in all societies, is ongoing with chronic healing and recurrence. Schizophrenia is a chronic mental disorder which severely impair on thinking, emotions, memory, behaviors, movement, interpersonal relationship, functionality and ability of reality evaluation. Schizophrenia doesn't affect only patients mental and physical health but also their relatives suffer emotional, social, economical, physical burden.
Methods: This descriptive study was carried out to determine the social functionality levels of the schizophrenic patients, the burden experienced by their caregivers. The universe comprised of 130 caregivers selected from the Ankara, Gazi, Hacettepe University Hospitals, Atatürk and Dışkapı Yıldırım Beyazıt Training and Research Hospitals, Yenimahalle State Hospital, and the Schizophrenic Patients and Relatives Solidarity Society. For data collection "Patient and Caregiver Identification Form", "Zarit Caregiver Burden Scale" and "Schizophrenic Patients Functional Recovery Scale" were used.
Results: For the normality assumption in data evaluation, the Shapiro-Wilks test, for the significance difference between two means, and one way variance analysis, and for correlation Pearson Correlation Coefficient Test were used. The study results revealed that caregivers' burden level was medium relatives (55.80 ± 15.90), and the patients' social functionality was also medium (49.96 ± 16.34), and there was a negative medium level correlation between the social functionality average points of the patients and the average burden points of the caregiver patient relatives. It was determined that there was statistically important difference between points according to age, education and employment status of the patients, job of working patients, regular drug use and medical visits, caregiver age, civil status, relation with the patient, employment and income level, number of family members, time spent with the patient, knowledge about disease, existence of other mentally ill patients in the family, society membership and regular attendance to family education sessions. Education and employment of patients, regular drug use and medical visits, substance addiction and substance type caused statistically important difference between social functionality levels of patients.
Discussion: In light of these results, psychiatric team member one suggested to plan necessary psychosocial interventions to diminish burden levels of caregivers and psychosocial skill training sessions to improve social functionality levels of patients.

S274. Caregiver burden in schizophrenia: pooled analysis of the involvement evaluation questionnaire data for paliperidone palmitate 3-month formulation

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Background: Schizophrenia-related caregiver burden is often under-recognized and associated with significant psychological and physical stress and increased indirect costs on the caregiver. The pooled analysis of 2 double-blind, randomized, multicenter, phase 3 studies (NCT01529515 and NCT01515423) evaluated the predictors of improvement or worsening of schizophrenia-related caregiver burden following paliperidone palmitate (including 1-month and 3-month formulations) treatment.
Methods: Caregivers (family members/friends who had $\geq$1 hour of contact per week with the patients treated with PP 1-month) were offered to complete the involvement evaluation questionnaire (IEQ; 46 items; each item score: 0-4; total score: sum of all items in module 2 [0-124]).
Results: Total, 1497 caregivers (mean [SD] age: 51.5 [13.02] years) were included: 49.3% were parents and >50% of caregivers spent >32 hours/week in caregiving. Caregivers had significant improvement in IEQ sum scores from baseline to end-of-study ($n = 756$; mean [SD] baseline score: 28.3 [15.34] points; mean [SD] improvement: 8.9 [14.73] points); most improvements seen in worrying (2.6 points) and urging (3.7 points) domains. There was significant relationship between improvement in IEQ sum scores and relapse status ($P < 0.001$), and patient age ($P < 0.05$); age of diagnosis, long-acting injectable (LAI) use at baseline, number and duration of prior psychiatric hospitalizations (< 24 months) had no significant effect on improvement. Caregiver burden improvement was significant in patients on prior oral antipsychotics post switching to LAI with less leisure days being impacted and less hours spent in caregiving ($P < 0.001$).
Discussion: Caregiver burden in family members of patients treated for schizophrenia is considerable. Switching from an oral antipsychotic to an LAI can provide a meaningful and significant improvement in caregiver burden.

S275. Health-related quality of life and burden careviger's of people with severe mental health disorders

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Background: For Severe Mental Health Disorders (SMHD) caregivers, burden lowers health related quality of life (HRQoL) and, it seems to be related to patient's severity of symptoms. For that it is possible that caregivers could show differences in HRQoL and burden according to the level of clinical attention that receives people with SMHD (inpatient, outpatient and rehabilitation) and both measures could improve after a time of clinical intervention, mainly in attentional levels that addressed specifically family therapy.
Methods: Sample: 70 caregivers of persons with SMHD (35 schizophrenia, 21 bipolar and 14 recurrent depression disorders) were included in the study, allocated into three groups (24 inpatient; 27 outpatient and 18 rehabilitation) according clinical attentional levels that receive the person with SMHD. All were assessed for HRQoL (SF-36 Health Survey; Alonso *et al.*, 1995) and Burden (Caregicer Burden Scale of Zarit; Martin *et al*, 1.996,) in two moments (initial and final) with a time interval of six months except for the inpatient level that was of the 61.5 +/- 47.37 days in mean.
Results: Caregivers were mainly women (67.0%) with a mean of age of 55.0 +/-14.6 years. SMHD were mainly men (61.4%) with a mean of age of 44.5 +/-11.3 years. Caregiver's burden did not differ between attentional levels in the two moments assessed. Pain [$F(2,61) = 4.5$; $P = 0.015$], Vitality [$F(2,61) = 6.4$;$P = 0.003$] and Mental health [$F(2,61) = 3.6$;$P = 0.032$] dimensions of HRQoL showed lower scores in rehabilitation level in the initial assessment and, General Health dimension [$F(2,60) = 7.2$;$P = 0.002$] showed lower scores in rehabilitation level at the final assessment. No differences between two assessments were observed in caregiver's burden. Dimensions of emotional role [$F(1,50) = 7.4$;$P = 0.009$] and Mental Health [$F(1,50) = 5.8$;$P = 0.020$] showed a score increase at the final assessment, regardless of attentional level.
Discussion: In our study the burden of caregivers did not differ according the clinical attentional level receiving persons with SMHD, suggesting that symptomatology could not be a main factor interviewing in it, and that other factors should be take into account, such as coping. Our results showed that some dimensions of HRQoL have lower scores in caregivers of persons attended in the rehabilitation level, suggesting that some factors associated with this clinical attendance resources, such as a deficit in community functioning of persons with SMHD receiving this kind of clinical treatment could be underlying it. Moreover, the score of the dimensions of HRQoL related to mental health of caregivers improves in the final assessment, suggesting that interventions carried out in the different levels of clinical attendance, or simply time elapse favor it. All these findings have significant clinical implications, mainly for the design of family interventions since caregivers' role is so relevant for the care of persons with SMHD in our territorial area.

S276. Quality of life and resilience in outpatients with schizophrenia

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Background: Resilience can be defined as the successful adaptation despite risk and adversity and is becoming an important topic in patients with schizophrenia since there is evidence that it increases the probability for long-term recovery in those patients. The aim of this study was to investigate to what extent patients' quality of life (QoL) correlates with both resilience and the severity of illness.
Methods: We recruited patients with schizophrenia on an out-patient basis. Diagnoses were confirmed with the Mini International Neuropsychiatric Interview (M.I.N.I.). Resilience was assessed by the Resilience-Scale (RS-25), and psychopathology was assessed by the Positive and Negative Syndrome Scale (PANSS). In addition, the German version of the Lancashire Quality of Life Profile, the Berliner Lebensqualitätsprofil (BELP), was used.
Results: A total number of 52 patients (27 males, 25 females) with a mean age of 44.1 ± 10.6 years took part in this study. The mean duration of illness was 14.7 ± 10.5 years. The mean PANSS total score was 57.4 ± 18.0, the mean RS-25 score was 132.1 ± 21.6 (range: 25-175), and the BELP subscale overall QoL showed a mean score of 4.73 ± 1.28 (range 1-7). Statistical analysis showed a strong correlation between QoL and resilience ($r = 0.481$, correlation with general life satisfaction) as well as with psychopathology ($r = -0.362$, correlation with general life satisfaction). Resilience, however, correlated significantly with more subscales of the BELP than psychopathology did.
Discussion: Our results show that schizophrenia patients' quality of life correlates strongly with resilience, whereas psychopathology plays a secondary role. Individual resilience thus seems to be an important factor in the long-term recovery of patients with schizophrenia.

S277. Belief and distress in psychotic compared to non-psychotic hallucinators

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Background: Schizophrenia is marked by a disconnection from reality. However, attenuated versions of psychotic symptoms can manifest in otherwise healthy people. In this study, we recruited clairaudient psychics—non-psychotic individuals who experience auditory "messages"— as well as psychotic individuals who experience auditory hallucinations. We enrolled psychotic individuals and nonpsychotic

individuals who do not experience auditory hallucinations as controls. We examined:
1. The phenomenological similarities and differences between nonpsychotic hallucinators (NH), psychotic hallucinators (PH), and psychotic nonhallucinators (PN); 2. The ways the groups differ from each other and healthy controls (NN) in the ways they impose meaning and patterns onto the world.
Methods: We collected data in an interview setting which included Peter's Delusion Inventory (PDI) and the Brief Multidimensional Measurement of Religiosity/Spirituality (BMMRS).
Results: People with psychosis (PN+PH) and those without (NN+NH) do not differ on the number of unusual beliefs they endorse on the PDI ($P = 0.2$), but people who hallucinate (NH+PH) endorsed significantly more than those who do not hear voices (NN+PN, $P = 0.005$). NH do not significantly differ from PH ($P = 0.41$) or PN ($P = 0.16$) on the total number of unusual beliefs, nor do they differ in how preoccupying they find those beliefs ($P = 0.16$ and 0.39 respectively). However, NH psychics were significantly less distressed by their beliefs than both PN ($P = 0.04$) and PH ($P = 0.01$). Furthermore, religiosity and distress were correlated ($r = 0.41$, $P = 0.02$) across subjects; those who were more distressed were more religious.
Discussion: This may be for at least two reasons: 1. People with schizophrenia-like symptoms may be more likely to seek out religion as a coping mechanism; and 2. People with schizophrenia-like symptoms could be more likely to have unusual experiences that are rendered explicable in terms of a higher power. That is not to say that religiosity comes from a predisposition to psychosis, but instead that religiosity and psychosis could stem from a similar predilection for explaining ones' experiences of the world. In this way, religiosity may be a way to combat the disconnect from reality that goes along with psychosis. Future work in these samples, employing cognitive and perceptual tasks will shed further light on the intersections between perception and belief in the genesis of psychosis and spirituality.

S278. Treatment decisionmaking among youth with early psychosis in the US: preliminary findings

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Background: Reducing the duration of untreated psychosis by engaging youth and their families in early interventions that make sense for them is essential for promoting recovery outcomes, but we know little about the goals and priorities of youth and families at the sensitive time surrounding the initial hospitalization for psychosis. While state-of-the-art early interventions provide care for young people that improves their chance of recovery, they do not help the ~½ of the young people who drop-out of care. Preliminary evidence suggests that at least half of the young people initially hospitalized for a psychotic disorder become "lost to follow-up" in the initial months after their hospitalization. There is a gap in the research regarding this group—we know nothing about them. Understanding what personal and contextual factors shape young people's decisions to drop-out or not drop-out of care during the critical time between an initial hospitalization for psychosis and engagement with outpatient services is immensely important. This small, self-contained, prospective, ethnographic, theory-generating study of the decision-making process that young adults (ages 18–30) and their key supporters undergo during the critical 6-month period after an initial hospitalization for a new-onset psychotic disorder.
Methods: This prospective, ethnographic study aimed to follow 24 first-episode psychosis patients from the hospital into the community through one initial inpatient hospital visit followed by up to four, 2–3- hour home visits over the first 6 months post-hospitalization. During this home visit, ethnographic observation, audiotaped interviews with the youth (4 total interviews) and up to 2 key supporters (2 total interviews) were collected. The aim was to assess who followed-up with care and who dropped-out of care, and to use qualitative data analysis to compare the data between them to develop a grounded theory about the personal and contextual (e.g., family, cultural, system-level) factors that emerge as relevant in treatment decision-making at this critical time. Sample: We planned to sample 24 early psychosis patients with the expectation that ~½ of them will drop-out and ~½ will attend follow-up clinical appointments to create 2 groups of ~12 (12 drop-outs and 12 non-drop-outs) to compare and contrast qualitatively. The patient sample also aimed to be 50% African American. Inclusion criteria for first-episode patients: Ages 18–30 years. English speaking. Clinically-documented diagnosis of a nonaffective, psychotic disorder. Exclusion criteria for patients. Known or suspected mental retardation. >3 months of prior antipsychotic treatment or previous hospitalizations for psychosis. Inclusion criteria for key supporter. Identified by the patient. 18 years of age or older.
Results: Preliminary findings include factors that seem to be relevant to youth and their key supporters for decision-making at this critical time. Factors to be discussed in this presentation include personal (e.g., concerns about employment, education and romantic relationships); family-level (e.g., tensions with family post-hospitalization); cultural (e.g., religious explanatory models clash with biomedical models; language barriers); and system-level (e.g., mental health insurance disparities prevent some from seeking further care and can cause crippling deb, lack of clear information about treatment options beyond psychopharmaceuticals).
Discussion: Close attention to social context is essential for improving youth engagement in services. Engagement strategies tailored to the needs, goals, interests, explanatory models, and resources of youth and their families should be set up early in the intervention process and maintained.

S279. Youth mental health services in Italy. an achievable dream?

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Background: The peak of onset of mental disease is from the early teens to the mid-twenties and the incidence and prevalence of mental illness in adolescents and young adults is the highest of any age group (Kessler *et al.*, 2005). Despite this, only a few young people (less than 1/6) with mental disorders access services confirming a paucity of service utilization when mental health problems are beginning to emerge (Singh, 2009). In Italy the main service configuration of distinct Child and Adolescent Mental Health Services and Adult Mental Health Services is a barrier to providing continuity of care with only a small proportion (19%) of adolescents treated by CAMHS move to AMHS (Stagi, Galeotti, Mimmi, Starace, & Castagnini, 2015). Through an extended collaboration between CAMHS and AMHS services, the "Liberiamo il Futuro" (LIF) project was developed to deeper assess adolescents and young adults with psychological problems and to identify Ultra High Risk (UHR) patients. The aim of the present study was to describe the baseline demographic and clinical characteristics of participants in the LIF project.
Methods: LIF is a multicentre project carried out by the contribution of Sapienza University of Rome and six AMHS and six CAMHS located in one of the eight Local Health Districts of Rome, Italy. The study included help-seeking young people aged 12-35 years old who resided in the Rome H area. Patients who score 18 or more on the PQ-92 (Prodromal Questionnaire-92) positive symptoms subscale or evaluated as possibly at risk according to clinical impression were examined with the Structured Interview for Psychosis-risk Syndromes (SIPS) and Schizophrenia Proneness Instrument- Adult (SPI-A) and Child and Adolescents (SPI-CY) to detect if they are at risk for developing a psychosis according to the ultra-high risk (UHR) and basic symptom (BS) criteria. Social and role functioning was assessed using the Global Functioning: Social (GFSS) and Global Functioning: Role scales (GFSR). Axis I diagnoses were evaluated with the SCID-I (age 19-35) and with the K-SADS-PL (age 12-18 years).
Results: 338 individuals and/or their parents or guardians gave written informed consent to participate. Ethical approval was obtained from the local research ethics committee. The mean age was 17.42 years (Median: 16, Mode: 12). One hundred-seventy-three participants were

female (51.2%) and 165 (48.8%) were male. Only 35 (12%) participants had no psychiatric diagnosis. The majority of the sample ($N = 107$, 35%) had an anxiety disorder, followed by mood disorders ($N = 62$, 21%). The mean role/social functioning (measured by GFRS and by GFSS) indicated moderately/mildly impaired functioning. 166 (52%) individuals were assessed with the SIPS and with the COPER and COGDIS criteria. Of these 38.60% ($N = 64$) met UHR criteria, 92 subjects (58.2%) reported BS criteria.
Discussion: Our results showed that psychological problems are very common among help-seeking young people. Psychiatric symptoms are often associated with impaired psychosocial functioning that is a negative predictor of outcome and needs to be targeted with focused treatment. The mean age of our sample highlights the problem of transferring from a child and adolescent service to an adult service at the age of 18. Nevertheless, the help-seeking behaviour of young people is in contrast with the barriers presented by the Italian community mental health system that is modelled around adults' needs. To try to go beyond these barriers is necessary to build a strong, stigma-free and effective system of care for young people up to the mid-20 s modelled on Australian Headspace clinical services. Investing in this direction is an important challenge for the future of the Italian and worldwide psychiatry.

S280. Relationship between director leadership of community mental health center and organizational effectiveness

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Background: After 1990's, it was promoting the transition from long-term hospitalization to community mental center for patients with chronic mental disorder such as schizophrenia in South Korea. The present study was intended to investigate leadership types by the director of community mental health centers and organizational effectiveness of members, and analyze the influence of the leadership on organizational effectiveness.
Methods: The 326 participants in this study were recruited from 32 mental health centers in Gyeonggi province. 217 subjects were responding to the survey (response rate: 67%) and 215 subjects were used in analysis excluding inappropriate 2 cases. Multifactor Leadership Questionnaira-5X was used for director leadership of community mental health center (transformational and transactional leadership). The organizational effectiveness including job satisfaction, organizational commitment, and turnover intention of the members at the mental health centers was investigated. Descriptive statistics to determine the average and standard deviation of the leadership and organizational effectiveness was performed. T-test and one way ANOVA were also used to evaluate the differences between groups and Pearson correlation analysis was conducted to determine the correlation between variables.
Results: The transformational and transactional leadership by the director of mental health centers had a positive correlation with job satisfaction ($r = .383$, $P < 0.01$: $r = .424$, $P > 0.01$) and organizational commitment ($r = .418$, $P > 0.001$: $r = .424$, $P > 0.01$) of organizational effectiveness, and had a negative correlation with turnover intention ($r = -.366$, $P < 0.01$: $r = -.306$, $P < 0.01$). The transformational leadership significantly affected job satisfaction and turnover intention and the transactional leadership influenced only organizational commitment.
Discussion: The present study firstly investigated the influence of the leadership by the directors of community mental health centers on organizational effectiveness in South Korea. The leadership by the director of community mental health centers might affect the organization effectiveness on community mental health centers. Therefore, the director of mental health center had to increase organizational effectiveness by combination with transformational leadership and transactional leadership.

S281. Do routine outcome monitoring results translate to clinical practice? A cross-sectional study in patients with a psychotic disorder

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Background: The use of Routine Outcome Monitoring (ROM) in mental health care has increased widely during the past decade. Little is known, however, on the implementation and applicability of ROM outcome in daily clinical practice. In the Netherlands, an extensive ROM-protocol for patients with psychotic disorders has been implemented over the last years (ROM-Phamous). The current studies investigated to what extent ROM results translate to daily clinical practice. Therefore, we investigated whether clinical problems as identified with ROM were detected and used in the treatment of patients with psychotic disorders.
Methods: Out of the ROM database of 2010 ($n = 1040$), a random sample of 100 patients diagnosed with a psychotic disorder was drawn. ROM-data used in this study included a physical examination, laboratory tests, interviews and self-report questionnaires. Based on these data, the prevalence of positive and negative symptoms, psychosocial problems and cardiovascular risk factors was determined. Next, we investigated whether these problems, as identified with ROM, were reflected in the treatment plans of patients, as an indication of the use of ROM in clinical practice. This study was replicated with data of 2014.
Results: The sample of 2010 consisted of 63 males and 37 females. The mean age was 44 and the mean duration of illness was 17.7 years. The prevalence of positive and negative symptoms, psychosocial problems and cardiovascular risk factors ranged from 11% to 86%. In the majority of cases, problems as identified with ROM were not reflected in the treatment plans of patients. The opposite occurred as well, where problems were reflected in the treatment plans but not identified with ROM. The study of 2014 revealed similar findings.
Discussion: We found a substantial discrepancy between the ROM measurements and the treatment plans, i.e. low rates of detection of symptoms, psychosocial problems and cardiovascular risk factors in the treatment plans, even though these problems were identified with ROM. On the other hand, on some occasions problems were reflected in the treatment plans but not identified with ROM. Thus, ROM and daily clinical practice appear to be two separate processes, whereas ideally they should be integrated. Strong efforts should be made to integrate ROM and consequent treatment activities. Such integration may help to provide patients with adequate and customized care and simultaneously minimize under- and over-treatment.

S282. Bias blaster, a game to beat interpretation bias in patients with psychosis

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Background: People with a psychotic disorder often suffer from social anxiety. Various interventions have been developed to tackle these symptoms, with variable effects. A promising new method is Cognitive Bias Modification (CBM), which is a form of therapeutic training that targets, and ultimately modifies, harmful cognitive biases, as to provide a 'cognitive vaccine' against negative appraisals. A serious game called Bias Blaster was developed, combining the CBM training with gaming elements in order to learn patient with a first episode of psychosis to beat social anxiety
Methods: Interviews with 10 patients with a first episode psychosis treated by the early intervention program of Friesland Mental Health care services were achieved in order to prioritize the most important situations in which patients experience social anxiety.

Secondly a randomized controlled trial was conducted to see whether patients who use Bias Blaster experience less social anxiety after 12 weeks compared to those who don't use Bias Blaster.
Results: Social anxiety occurs in more than half of patients with a first episode of psychosis.
Patients reported giving a speech or speaking in public (10,07%); acting or performing in front of others/an audience (8,38%); going to parties or other social gatherings: 42,68 (7,35%); entering a room when others were already present (6,79%) and suggesting/proposing a request to others (6,33%) as the most fearful situations which were included in the serious game. 80 patients were included in the trial of which 40 received treatment add on using Bias Blaster. First results show significant improvement in patient using Bias Blaster
Discussion: Social anxiety is a major problem in patient with first episode psychosis. Using Bias Blaster, a serious game patients can play whenever they want, seems to be a cheap and approachable intervention with great results.

S283. Person centered psychosis care (PCPC) in an inpatient setting: the implementation process and staff experiences

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Background: Persons with schizophrenia-spectrum disorders might benefit from increased involvement in the care process. To this end, integrated care models have been successfully implemented in outpatient settings. We wanted to develop an inpatient care model inspired by integrated care. Further, we wanted to include central components of person-centered care (as defined by the Gothenburg Center for Person-centered Care) including a focus on the patient's narrative, the creation of partnership between staff and patient, and an agreement between staff and patient concerning the care. The present research project, Person Centered Psychosis Care (PCPC), aims to develop, implement, and evaluate an inpatient care approach that utilizes aspects of integrated care as well as person-centered care. In the present study we will describe the PCPC staff educational intervention, the implementation process that followed, and staff experiences of the intervention and implementation.
Methods: Employing a participatory design, the PCPC staff educational intervention involved one third ($n = 40$) of the staff working at four wards at a clinic providing inpatient care for persons with schizophrenia-spectrum disorders. Facilitators with previous experience in the implementation of person-centered care in somatic settings served as coaches. During six full day workshops, staff learned to apply theoretical concepts of both integrated care and person-centered care to their everyday ward situation and worked in groups to develop ward-level projects with the aim of stimulating patient involvement. Service users took part in the educational intervention. Staff who participated in the educational intervention transferred their new skills to their fellow staff members who had not taken the course. Together they created and tested new approaches to care tasks. This means that all ward staff became involved in the implementation process.
Results: A purposeful sample of staff members (both with and without course participation, $n = 20$) were asked to participate in focus group interviews to relate their experiences of the PCPC staff educational intervention, the transfer to those staff members who did not take the course, and of the implementation process. Focus group interviews with staff are ongoing. The interviews are recorded, transcribed verbatim, and thematically analyzed. Results regarding the implementation process will be presented, with a focus on barriers and facilitators to change.
Discussion: Findings from the focus group interviews will shed light on staff members' experiences of the education intervention, as well as the experiences of staff members who participated in transfer activities but not in the course itself. It is our expectation that the participatory design will facilitate long lasting behavior change in staff, resulting in patients feeling more involved in their care. Future studies will report on patient outcomes (empowerment and care satisfaction) as well as ward level outcomes. If the PCPC-intervention shows positive outcomes for patients and staff, it might be a model that other psychiatric care providers can use to enhance patient involvement and satisfaction with care.

S284. What drives the higher incidence of psychosis in London compared to Palermo?

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Background: Incidence of psychosis seems to be lower in Italy than in other European countries (Tansella *et al.* 1991; Lasalvia *et al.* 2012, Tarricone *et al.* 2012); however there are no studies comparing the incidence of psychotic disorder in Northern and Southern Europe.
Methods: Incidence and socio-demographic data on all psychotic patients presenting for the first time to the mental health services of Palermo were collected over a period of three years.
Palermo incidence rates were compared to South London rates obtained from the AESOP study (Kirkbride *et al* 2006). South London rates were reanalyzed excluding people aged 16-17 years and substance related psychoses. Second generation migrants (people who were born in UK belonging to ethnic minorities) were also excluded to make the sample comparable since migration in Palermo referred to people who were not Italy born. The term migrants was used in the present analysis to indicate non-native born British and Italians respectively.
Incidence rates of overall psychosis, schizophrenia, affective psychoses and other non-affective psychoses were compared in Palermo and in South London by indirect standardization (by age and gender and then by age, gender and migration) to take into account the differences in the population structures between sites. Standardized morbidity ratios (SMRs) and their reciprocal of overall psychoses, schizophrenia, other non-affective psychoses and affective psychoses were calculated.
Results: During the study period two hundred and four patients affected with a first episode of psychosis (FEP) were ascertained in Palermo. South London cases were 195. Standardized incidence rates of overall psychoses were 16.9 (95% CI 14.7-19.4) per 100,000 per year in Palermo and 36.8 (95% CI 31.8-42.3) in South London. Migrants had an increased risk of developing a psychotic disorder both in Palermo OR: 3.12 (95% CI 1.89-4.93) and in London OR: 2.9 (95% CI 2.15-3.93). After standardizing by age and gender the risk of psychosis was significantly higher in South London compared to Palermo for all psychoses 1/SMR = 2.18 (95% CI 1.98-2.39) and for each diagnostic category. After standardizing also for migration the difference in risk of overall psychoses between Palermo and London decreased: 1/SMR = 1.39 (95% CI 1.23-1.56) and no differences in risk were found any longer between Palermo and South London for schizophrenia and other non affective psychoses; there was however an increased risk of affective psychoses in South London compared to Palermo 1/SMR = 3.31 (95% CI 2.52-4.21). This result confirms that migration explains the majority of the difference in incidence rates between Southern Italy and London.
Discussion: This is the first epidemiological study of psychosis ever carried out in Sicily and one of the few from Southern Europe. The risk of psychoses was higher in South London when compared to Palermo. However no significant differences were found in rates of schizophrenia and other non-affective psychoses after taking into account the different proportion of migrants in the two sites suggesting that migration might explain the majority of the difference in the risk of psychosis. However, it did not explain all the difference as there was still an excess of affective psychoses in South London. Further studies are needed to explore the role of other risk factors (Mediterranean diet, vitamin D, social fragmentation, drug use) in influencing the risk of psychosis.

S285. Decide study: effectiveness of shared decision making in treatment planning at discharge of inpatient with schizophrenia: design, tools, clinical and subjective experiences

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Background: Shared decision making denotes a structured process that encourages full participation by patient and provider in making complex medical decisions. There has been extensive and growing interest in its application to long-term illnesses such as diabetes, cancer or cardiac pathology, but surprisingly not in severe psychiatric disorders such as schizophrenia. However, the great majority of schizophrenics are capable of understanding treatment choices and making rational decisions. Although the main justification for shared decision-making is ethical, several randomized controlled trials support its effectiveness in improving the quality of decisions, but robust evidence in objective health outcomes is needed. Hamann *et al* conducted a few years ago a randomized controlled trial with schizophrenic inpatients and found increased knowledge and perceived involvement in decisions about antipsychotic treatment at discharge by the experimental group, but not clear beneficial effects on long term outcomes. The present communication introduces the DECIDE study.
Methods: Randomized controlled trial, prospective, two parallel groups, unmasked, comparing two interventions (shared decision making and treatment as usual). Study population: Inpatients diagnosed of schizophrenia and schizoaffective disorders (ICD-10/ DSM-IV-R: F20 y F25) at Adult Acute Hospitalization Unit at Jerez General Hospital. Objectives: Of the study: To demonstrate the effectiveness, measured as treatment adherence and readmissions at 3, 6 and 12 months, of shared decision making in the choice of antipsychotic treatment at discharge in a simple of schizophrenics hospitalized after an acute episode of their disorder. Of the oral presentation: To present the study design with special emphasis on the decision- making model and the decision tools elaborated. To value the experience after a year and a half developing a clinic-care based in shared decisions making interventions.
Results: We develop 5 SDM sessions model during hospitalization, and 3 after discharge. The 3 first sessions are part of the informative stage with a total duration of 150 minutes. Then a discussion stage takes place, with a total duration of 90 minutes, along two sessions with the physician (and other if required as nurse, family, close friend…). To set up a consensual decision and develop an implementation treatment plan with the help of the records in the decisions diary (also developed by our group). After the discharge there are 3 reinforcement sessions at 3, 6 and 12 months, to consolidate the decision, adapt it if necessary and monitor.
SDM tools our group has develop are evidence-based and follow IPDASi recommendations:
• Antipsychotics General Information (5 pages notebook)
• Antipsychotics Specific Information (18 pages notebook)
• Antipsychotics Side – effects (4 pages notebook and a summary table)
Discussion: Despite the poor implementation of SDM in Mental Health, there are ethical and practical reasons to encourage its use, especially, in patients with severe mental illness. The few empirical studies show that SDM encourages better communication and, possibly, greater patient satisfaction in the decision process, but there is not evidence on health outcomes. The final aim of the study is to assist the implementation of a new model of interaction physician – patient in our health services using data from empirical research. DECIDE study is a Randomized Controlled open Trial, design to assess effect of SDM vs Treatment as usual, after admission in a acute episode of schizophrenia or schizoaffective disorder.
Preliminary data and appraisement with half of sample included show interesting views and perceptions of physicians and users

S286. Decide study: effectiveness of shared decision making in treatment planning at discharge of inpatient with schizophrenia. preliminary data conclusions after 20 months of the study

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Background: Shared decision making (SDM) denotes a structured process that encourages full participation by patient and provider in making complex medical decisions. There has been extensive and growing interest in its application to long-term illnesses such as diabetes, cancer or cardiac pathology, but surprisingly not in severe psychiatric disorders such as schizophrenia. However, the great majority of schizophrenics are capable of understanding treatment choices and making rational decisions. Although the main justification for shared decision-making is ethical, several randomized controlled trials support its effectiveness in improving the quality of decisions, but robust evidence in objective health outcomes is needed. Hamann *et al* conducted a few years ago a randomized controlled trial with schizophrenic inpatients and found increased knowledge and perceived involvement in decisions about antipsychotic treatment at discharge by the experimental group, but not clear beneficial effects on long term outcomes. Ishii *et al* are presently carrying out another randomized controlled trial with first admitted schizophrenics with patient satisfaction at discharge as primary outcome. Our study attempts to replicate and overcome the limitations of Hamann's study and find support to the hypothesis of better adherence to treatment and fewer rehospitalizations when adopting strategies of shared decision making with antipsychotic treatment. Aims and Objectives:? Of the study: To demonstrate the effectiveness, measured as treatment adherence and readmissions at 3, 6 and 12 months, of shared decision making in the choice of antipsychotic treatment at discharge in a simple of schizophrenics hospitalized after an acute episode of their disorder.? Of the oral presentation: To present preliminary conclusions with more of the half of the sample.
Methods: Randomized controlled trial, prospective, two parallel groups, unmasked, comparing two interventions (shared decision making and treatment as usual). Study population: Inpatients diagnosed of schizophrenia and schizoaffective disorders (ICD-10/ DSM-IV-R: F20 y F25) at Adult Acute Hospitalization Unit at Jerez General Hospital A sample of 120 patients for a study period of 36 months, with a recruitment of 24 months, and a follow – up of 12 months.
Results: At discharge, statistically significant increased score in COMRADE both subscales (satisfaction in communication and trust in the decision) in SDM group.? At 3 month-follow-up, intensification of these differences in effect size and statistical significance and trends in health outcomes. We will presents partial results for 6 and 12 months, with trends consistent with that seen in previous reviews, both sub scales of COMRADE, BARS (an adherence objective scale), and admissions.
Discussion: Preliminary data with 60 patients included out of 100 candidates: No differences between excluded and included patients except for days of hospitalization in the last 12 months before intervention. No differences between TAU and SDM groups in basal comparative analysis, except for a trend in psychopathology level. Discharge variables analysis between TAU and SDM shows statistically significant differences in psychopathology and both dimensions of COMRADE (communication and confidence), and days of the admission, which seems to remain along the follow-up. We must be cautious about conclusions and results obtained until we reach the 120 sample subjects but Shared Decision Making is presented as a model that should be taken into account, not only because of ethical or subjective assessment, but also in relation with an improvement of health outcomes.

S287. Neural correlates of faux pas-detection: the role of schizotypal personality traits

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Background: A Faux Pas is an unintended social mishap, mostly attributed embarrassing or funny. Testing the ability to detect faux pas has often been used as a paradigm to investigate social cognition. In contrast to other social cognition paradigms, less is known about the neural correlates of fauxpas detection. While a small number of lesion studies suggest a critical role of medial frontal areas in faux pas detection, almost no functional magnetic resonance imaging studies are available. However, some evidence suggests faux pas detection is impaired in schizophrenia, schizotypal personality disorders and related diseases. Moreover, faux pas detection may be related to shame proneness.
The aim of this project was to investigate faux pas with functional magnetic resonance imaging in a non-clinical population and evaluate the relationship of activations to schizotypal personality traits and shame proneness.
Methods: 25 female subjects (mean age 25,5 years, no history of psychiatric illness) participated in both functional magnetic resonance imaging (fMRI) and personality testing. The fMRI paradigm was a new-developed faux pas paradigm. 50 stimuli (20 faux pas, 20 neutral, 10 visual control baseline) were presented visually. Subjects indicated by button press if a target sentence in their opinion represented a faux pas or not. Personality tests included German versions of the schizotypal personality questionnaire (SPQ-G), shame proneness (Test of Self-Conscious Affect, TOSCA3), NEO-FFI, state-trait humor inventory (STHI-T30), Launay–Slade-Hallucination-Scale (LSHS-R), Digit-span, verbal intelligence and handedness. A 3 T Siemens scanner and SPM software were used for data acquisition and analysis.
Results: Mean SPQ in the sample was 16,3, SPQ was not significantly correlated with performance. Faux pas relative to neutral target sentences activated a bilateral, left lateralised network including lingual and medial predontal regions. In a regression analyses, SPQ total score showed a negative correlation with left superior temporal and medial prefrontal gyri.
Discussion: Brain activation during faux pas comprehension is associated with schizotypal personality traits in brain regions of the social cognition network. The finding is similar to a previous study using ironic stimuli.

S288. White matter connectivity and prefrontal cortical folding alterations in schizophrenia

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Background: In the recent years, cortical folding alterations have emerged as an important neurobiological feature of schizophrenia. However, the neuronal underpinnings of disturbed cortical folding remain unclear. Prominent theories on the morphogenesis of cortical folds (e.g. tension based model by Van Essen) stress the importance of white matter fiber tracts for the development of the cortical folds. Hence, it can be hypothesized that alterations of white matter fiber tracts might be relevant for cortical folding alterations in schizophrenia. Thus, in the present study we aimed to identify white matter fiber tract alterations as a potential basis for disturbed cortical folding in schizophrenia.
Methods: 19 patients with schizophrenia according to DSM IV and 19 age and gender matched healthy subjects were included and underwent high-resolution T1-weighted MRI and diffusion tensor imaging (DTI). Cortical folding was computed using an automated surface based approach (FreeSurfer Software). DTI was analyzed using FSL and SPM 5. Altered radial diffusivity and cortical folding were correlated on a node- by –node basis covering the entire cortex in schizophrenia.
Results: Significantly altered radial diffusivity of the inferior and superior longitudinal fasciculus in the left superior temporal cortex (Koch *et al.* 2013) was negatively correlated with cortical folding of the left dorsolateral prefrontal cortex (DLPFC) in patients, i.e. higher radial diffusivity, as an indicator for disturbed white matter fiber integrity, was associated with lower cortical folding of the left DLPFC. Compared with the healthy controls patients with pronounced alterations of the affected white matter fiber tracts showed significantly reduced cortical folding in the left DLPFC.
Discussion: The superior longitudinal fasciculus (SLF) is a major bundle of the cerebrum connecting parietal and temporal cortex areas with the prefrontal cortex. Our study indicates that a disruption of this tract is an underpinning of altered DLPFC cortical folding in schizophrenia and putatively associated with malfunctioning of the affected parieto-temporo-prefrontal neuronal circuit.

S289. Impact of assertive community treatment in the optimization of pharmacological treatment in patients with severe mental illness

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Background: In order to deinstitutionalize patients with severe mental illness, in 1980 Dr. Stein described in USA the model of Assertive Community Treatment (ACT), characterized as an individualized, intensive and multidisciplinary treatment. This model has been successfully replicated in many countries. The antipsychotic drugs are the mainstream of medical treatment of these disorders. Nevertheless, despite recommendations from different clinical guidelines about not exceeding recommended doses, the clinical practice suggests other things: the use of higher dose, which increases security problems. Benzodiazepines are another group of psychotropic drugs long-term used in patients with severe mental disorders; however, a recent meta-analysis suggests that this type of psychotropic drugs are not suitable for maintenance therapy in psychotic patients, indicating its usefulness in short and specific periods. The aim of this study is to analyse the changes in treatment of these two groups of psychotropic drugs: antipsychotics and benzodiazepines in patients with severe mental disorders, before and after the time of inclusion in a ACT program.
Methods: A retrospective study was designed to include severe mental disorder patients from ACT program with functional impairment and a course of disease for more than two years. The program was scheduled in a Catalonia midlands county mental health centre. Data on benzodiazepines and antipsychotics dose prescribed were obtained from medical records, and a case report form was used. Dose of benzodiazepines was converted to equivalent dose of diazepam, and dose of antipsychotics (oral and long-acting) was converted to equivalent dose of olanzapine. Age, gender, diagnostic and relapse were also registered. Percentages and frequencies are shown for qualitative variables and average, standard deviation or percentiles are shown for quantitative ones. Bivariate analysis was conducted under parametric or no parametric assumptions and differences between entrance and discharge were conducted under paired tests.
Results: 98 patients did 106 entrances to ACT program. 59.2% were males, the age average was 40.1 (SD 12.8) and no differences between age and gender or between age and inclusion diagnostics were obtained. 73 patients (74.5%) had a psychotic disorder (schizophrenia and schizoaffective disorder), 19 (19.4%) had an affective disorder (severe major depression and bipolar disorder), and 6 (6.1%) had other diagnostics (borderline personality disorder, and obsessive-compulsive disorder). Eight patients with a psychotic disorder did entry twice at ACT program.
On benzodiazepines, an overall reduction from 22.0 mg (diazepam equivalents) daily dose to 10.7 mg was observed, and in psychotic patients the reduction was from 17.3 mg to 7.9. Both are statistic

significant (Paired T test, $P < 0.05$). On antipsychotic drugs, the overall reduction was from 26.4 mg (olanzapine equivalents) daily dose to 21.8 mg; in psychotic patients this reduction was from 30.3 mg to 24.4. Here also a Paired T test shown statistic significant differences ($P < 0.05$).
Discussion: Most of the patients with severe mental illness who were included in the ACT program had a schizophrenic spectrum disorder. The ACT program multidisciplinary approach allows a dose reduction of both antipsychotic and benzodiazepine drugs, and specifically in schizophrenic spectrum patients. We conclude that ACT program is useful at optimizing the dosage of psychoactive medication, improving the therapeutic security and reducing pharmacological spending.

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