

# Progress Report

2013 - 2014



**NETHERLANDS  
BRAIN BANK**

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The cover photo shows paraffin sections of brain tissue of 8  $\mu\text{m}$  in thickness. After sections have been cut, they are mounted on glass slides and (immuno)histochemically stained for further evaluation.

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# Introduction

It is with great pleasure that I present the 2013-2014 progress report of the Netherlands Brain Bank. 2013-2014 were important years for the NBB, when, together with five Dutch university medical centers, we started an extensive national brain donor program for psychiatric diseases and during which we intensified our international collaborations and increased our dissemination of tissue and knowledge.

On October 24, 2013, the psychiatric donor program, NBB-Psy, was officially launched during a public symposium entitled “De Wetenschap Ontleedt’ in de Rode Hoed venue in Amsterdam. The new donor program involved the appointment of six research assistants, whose task it was to personally approach psychiatric patients and their families in clinical research cohorts and through a network of patient organizations, with the purpose of informing them about the possibility of brain donation for research into psychiatric diseases. As a result the yearly number of registrations had doubled to almost 600 in December 2014. A Research & Development department of NBB-Psy was initiated to establish protocols for the isolation of pure glia cells for dissemination.

The annual numbers of autopsies in 2013-2014 were comparable to previous years (90-100), but the annual numbers of tissue applications sharply increased from 100-160 annually. The research carried out with NBB brain tissue samples resulted in 426 publications between 2010 and 2014. During these years, the NBB visited a brain bank conference in China and intensified its collaboration with the Chinese Brain Bank in Hangzhou. In November 2014, the NBB was invited to join the Netherlands state visit to the Republic of Korea to sign a Memorandum of Understanding (MoU) to start a collaboration in brain banking, specifically with the Korean Brain Bank in the new Korean Brain Research institute in Daegu. The NBB has also advised the MRC in the UK on cost recovery systems in brain banking. During the relevant period, the NBB was honoured by visits of Professor David Amaral, director of Autism BrainNet, Professor Tom Hyde, COO of the psychiatric brain bank of the Lieber Institute of Brain Development, and Professor Karl Zilles, an expert in mapping the human brain and co-author on the Science paper ‘BigBrain: An Ultra-

## high-Resolution 3D Human Brain Model<sup>1</sup>

In addition to the 426 publications that resulted from research carried out with NBB brain tissue samples, the NBB has also contributed to publications about brain banking in general. We co-authored a paper about brain banking in *Lancet Neurology*<sup>2</sup>, and we are also proud of the publication of our “Brain Net Europe’s Ethical Code of Conduct for Brain Banking” in December 2014<sup>3</sup>. This Code of Conduct covers basic legal rules and the bioethical principles involved in brain banking. Sources include laws, regulations and guidelines (Declarations, Conventions, Recommendations, Guidelines and Directives) issued by international key organizations. Furthermore, the NBB was asked to edit a Volume of the *Handbook of Clinical Neurology* on “Brain Banking psychiatric and neurological disorders”, together with Professor Maree J. Webster, director of the Stanley medical research Institute, Maryland, USA.

I am greatly indebted to the Netherlands Institute for Neuroscience, the Royal Netherlands Academy for Arts and Sciences, Stichting MS Research, Stichting ParkinsonFonds, Hersenstichting, stichting Zabawas and de Vriendenloterij, as well as to private backers, for their financial support, which is indispensable for the continuation of the NBB.

I also thank the members of the autopsy team for their guidance and round-the-clock help with the autopsies. Many of them are (PhD) students and technicians who have volunteered to help us out despite their own busy programs and work commitments. Equally indispensable are the autopsy assistants and pathologists at VUmc, to whom I would like to express my gratitude for their unstinting willingness to perform the autopsies.

Last but not least, a heartfelt thank you to all our donors and their families, without whom worldwide scientific research of the brain and brain disease would not be possible.

### Inge Huitinga, Director Netherlands Brain Bank

1 Amunts, K. et al. (2013). BigBrain: an ultrahigh-resolution 3D human brain model. *Science*, 340(6139), 1472-1475.

2 Samarasekera, N. et al. (2013). Brain banking for neurological disorders. *The Lancet Neurology*, 12(11), 1096-1105.

3 Klioueva, N. et al. (2015). BrainNet Europe’s Code of Conduct for brain banking. *Journal of Neural Transmission*, 122(7), 937-940.

# Vision and mission

## The vision of the Netherlands Brain Bank

The human brain forms one of the main scientific puzzles and many aspects of its functioning are still waiting to be understood. Innovative research using human brain tissue may lead to major scientific breakthroughs regarding the understanding of the human brain in health and disease and may yield novel therapeutic strategies to treat brain disorders.

## The mission of the Netherlands Brain Bank

The Netherlands Brain Bank (NBB) facilitates cutting edge human brain research by providing the scientific community with the highest quality of post mortem tissue of patients and matched controls in combination with cliniconeuropathological documentation. The NBB adheres to strict ethical guidelines such as informed consent, open access, and non-profit policy, as stated in **BrainNet Europe's Ethical Code of Conduct for brain banking**<sup>4</sup>.

## History

The Netherlands Brain Bank was founded in 1985 by Dick Swaab, initially with the sole purpose of obtaining brain tissue for his Alzheimer research. However, he soon realized that a facility where people could register as brain donors for research purposes would greatly benefit other researchers in neuroscience as well. From the very start, the NBB has thus had an open access policy, accepting applications for brain tissue from researchers from all over the world.

The NBB organization chart can be found in the **Appendix (Figure 17)**.

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4 Klioueva, N. M., Rademaker, M. C., Dexter, D. T., Al-Sarraj, S., Seilhean, D., Streichenberger, N., ... Huitinga, I. (2015). BrainNet Europe's Code of Conduct for brain banking. *Journal of Neural Transmission*, 122(7), 937–940. <http://doi.org/10.1007/s00702014-1353-5>





# Donor program

The aim of the Netherlands Brain Bank (NBB) is to establish and maintain a resource of human brain tissue to facilitate and stimulate post mortem brain research. The NBB focuses on several neurological and psychiatric disorders and therefore welcomes individuals with a disorder as well as healthy controls as brain donors. By registering, a donor gives informed consent to the NBB to perform a rapid autopsy after the donor has passed away, to collect medical information from the donor's physicians, and to distribute brain tissue and anonymized medical information to researchers worldwide.

The registration forms and accompanying informational brochures (informed consent forms) are in line with regulations and guidelines issued by international key organizations, such as the Council of Europe, the European Commission, the World Medical Association and the World Health Organization. The informational brochures and registration forms were reviewed and approved by the Medical Ethics Committee of VU medical center, Amsterdam, where the NBB's autopsies take place. The NBB adheres to BrainNet Europe's Ethical Code of Conduct for brain banking. More information can be found in the NBB's **ethical declaration**<sup>5</sup>.

The NBB has a prospective donor program and actively encourages individuals to register as a brain donor. Besides increasing numbers of donor registrations, this active approach also aims to raise common awareness of the importance of post mortem research.

## **Focus of the NBB donor program**

In line with previous years, in 2013-2014 the NBB focused its donor registration program on diagnoses for which the research community has a high demand for brain material. The NBB is always in need of more control donors, i.e. individuals without any diagnosis related to the brain. In addition, on December 31, 2014, new registrations of individuals with the following diagnoses were explicitly welcomed: psychiatric diagnoses, multiple sclerosis, Parkinson's disease, frontotemporal dementia, Alzheimer's disease (only via VUmc Alzheimer center), Huntington's

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<sup>5</sup> [http://www.brainbank.nl/media/uploads/file/Ethical declaration.pdf](http://www.brainbank.nl/media/uploads/file/Ethical%20declaration.pdf)

disease, Amyotrophic Lateral Sclerosis (ALS), narcolepsy and transsexuality. The NBB has a separate donor program for psychiatric diagnoses, NBB-Psy, which is described in more detail in a **separate subchapter**.

Despite this focus, every registration request is still reviewed on an individual basis, and persons with another diagnosis who are interested in registering as a brain donor are welcomed to contact the NBB to discuss the possibilities. It's also important to note that, though new registrations of a certain diagnosis may no longer be accepted, previously registered donors with that diagnosis can remain registered and are still appreciated as donors.

The registration policy is subject to change. A current list of accepted diagnoses is available on [www.hersenbank.nl](http://www.hersenbank.nl).

## Registrations

On December 31, 2014, 3108 living donors were registered at the NBB. Figure 1 shows these registrations broken down by diagnosis.

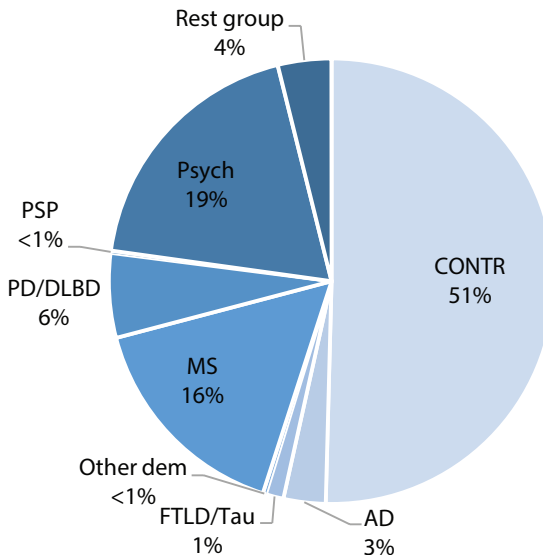


Figure 1 Registered donors on December 31, 2014 (total: 3108)

In 2013 and 2014, a total number of 704 new donors registered at the NBB. Therefore, the increase of registrations that was already notable in 2011-2012 (742 new registrations) has persisted. The most notable difference is that the number of registrations from people with a psychiatric diagnosis is much higher than before. This growth can be explained by the active encouragement of registration through the NBB-Psy project. The distribution of new registrations across other diagnoses has remained comparable to previous years, although registration numbers of people with Alzheimer’s disease (due to the limited registration policy since 2012), MS and Parkinson’s disease have declined somewhat. Registration numbers by diagnosis are displayed in figure 2.

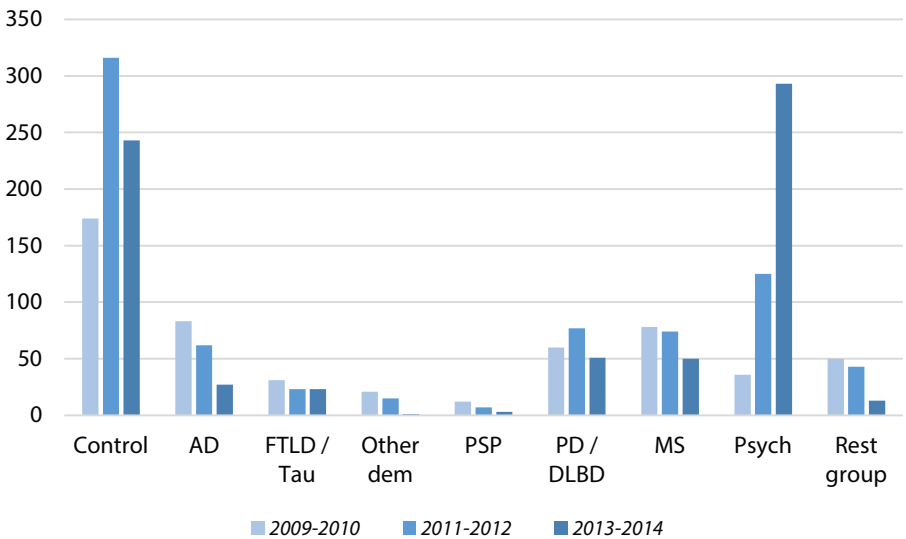


Figure 2 New donor registrations 2009 - 2014

The active donor program of the NBB-Psy project started in late 2013. This is reflected in the large difference in registration numbers compared between 2013 and 2014. Figure 3 shows the registration numbers by diagnosis, separately for 2013 and 2014. There was a sharp increase of registrations of control donors (after relatively few registrations in 2013) and donors with psychiatric diagnoses.

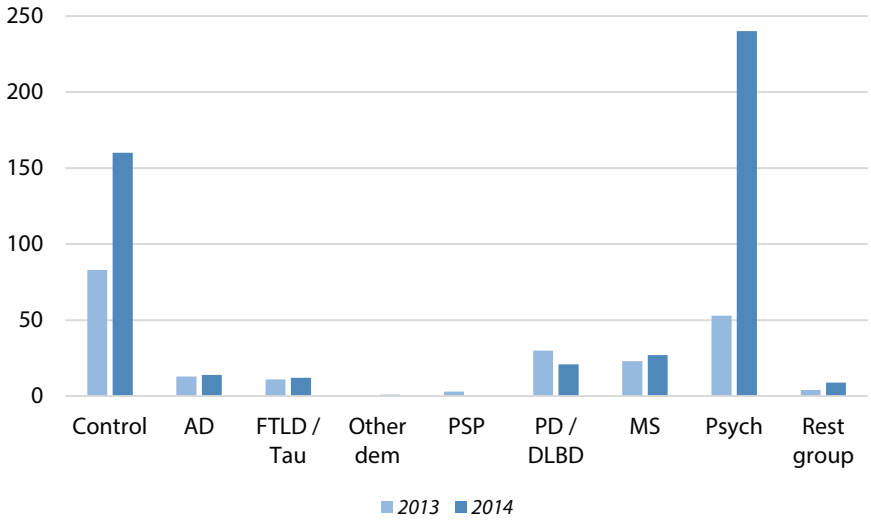


Figure 3 Comparison of new donor registrations in 2013 and 2014

# The Netherlands Brain Bank for Psychiatry (NBB-Psy)

## Aim of NBB-Psy

In 2012 the project ‘The Netherlands Brain Bank for Psychiatry’, abbreviated NBB-Psy, was launched. The aim of NBB-Psy is to recruit brain donors who have been diagnosed with one or more of the following psychiatric disorders:

- Schizophrenia or psychoses
- Bipolar disorder
- Major depression
- Obsessive-compulsive disorder
- Post-traumatic stress disorder
- Autism spectrum disorder
- Attention-deficit hyperactivity disorder

NBB-Psy approaches potential donors with these psychiatric disorders both actively and passively, to inform them about brain donation. To this end, six research assistants were appointed in September 2013. The team of research assistants are supervised by the clinical coordinator. More information on the staff can be found in chapter **Staff and Collaborations**.

## Background

The NBB-Psy project is funded by the Netherlands Organisation for Scientific Research (NWO) with €3,450,000 for five years. The funding was assigned to inform and register potential brain donors and to reimburse the costs of brain autopsies of subjects registered by NBB-Psy. In addition, the funding enables NBB-Psy to collect information about the psychiatric history of both new donors and previously registered donors. The NBB-Psy project is a collaborative effort of the NBB and five University Medical Centers:

- University Medical Center Utrecht (UMC Utrecht)
- Academic Medical Center Amsterdam (AMC)
- VU University Medical Center (VUmc)
- Radboud University Medical Center (Radboudumc)
- Erasmus University Medical Center (Erasmus MC)

In collaboration with the first four university medical centers, participants of their clinical research cohorts were individually informed about the possibility to become a brain donor. These clinical research cohorts included hundreds of people diag-

nosed with the disorders within the scope of NBB-Psy. Since a substantial amount of scientific data of the subjects was collected during cohort participation, there is extensive information about the symptoms, course, severity of the disorders and cognitive functioning. In addition, biomaterials such as DNA and plasma are available. Those data make participants highly valued brain donors for the NBB-Psy program.

Besides collaborating with academic medical centers, we set up a network with the relevant patient and family associations as well. The aim of this network is to inform the members of those associations about NBB-Psy, for example by advertising in their magazines and giving presentations about the project. Our network includes the following patient and family associations: Anoiksis, Ypsilon, Vereniging voor Manisch Depressieven en Betrokkenen (VMDB), Nederlandse Vereniging voor Autisme (NVA), Angst, Dwang en Fobie Stichting (ADF Stichting), Depressie Vereniging, Impuls, Personen uit het Autisme Spectrum (PAS), Nederlandse Vereniging voor Psychiatrie (NVvP) and Balans.

**Strategy of the NBB-Psy donor program**

Potential donors are approached both actively and passively. The main method is the active approach of participants of clinical research cohorts of the participating

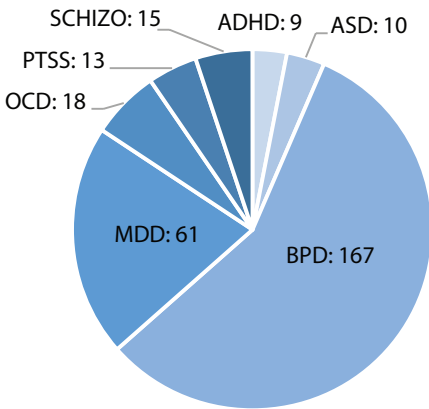


Figure 4 New registrations in 2013-2014 of donors with a psychiatric diagnosis (total: 293)

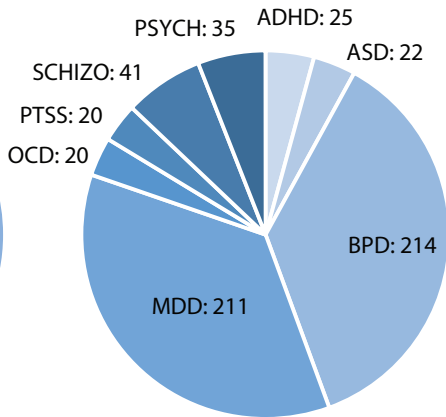


Figure 5 Registered (living) donors with a psychiatric diagnosis on December 31, 2014 (total: 588)

University Medical Centers. All cohort participants are first approached by mail with our brochure and an accompanying letter, and in a later stage also by telephone. If desired, participants receive more information on brain donation via telephone, mail, e-mail or in person.

In addition to the active individual approach, potential donors are also informed passively. This includes placing posters and brochures and presenting information on digital screens in waiting areas of psychiatric clinics. The brochure was developed specifically for NBB-Psy and provides general information on brain donation. It encloses a reply card to request more information.

In 2013-2014, this donor recruitment approach has resulted in 293 new registrations of subjects with one or more of the seven psychiatric disorders that NBB-Psy focuses on. Figure 4 further specifies the numbers of new registrations by diagnosis. Figure 5 shows all registrations of persons with a psychiatric diagnosis (including people who registered before the launch of the NBB-Psy project) on December 31, 2014. The large proportion of depression and bipolar disorder registrations can be explained by the large size of the clinical research cohorts for these diagnoses, combined with a relatively high registration efficiency (percentage of approached cohort participants that have registered as a brain donor) compared to other cohorts.

At the time this progress report was published, the results of the first 18 months of donor recruitment activities in the research cohorts had been analyzed. A manuscript presenting these results is currently in preparation (De Lange et al., in preparation).

## **Collecting donor information**

In addition to active recruitment of new brain donors, the NBB focuses on collecting information about the donor's medical and psychological history. Before 2013, the NBB has mainly gathered this information after donors had passed away, but since 2013, information has been increasingly collected during the donor's life by means of medical questionnaires, diagnostic interviews, and verifying the psychiatric diagnosis directly after registration by requesting the official DSM classification.

## **Medical questionnaire**

A medical questionnaire was developed to gather information on the development and course of possible diseases during life. This questionnaire addresses treatment by specialists, family history of several disorders and diseases, brain injuries and lifestyle. Since May 2013, all new registration forms include the questionnaire. In January 2014, all control donors and donors with a psychiatric diagnosis who had registered before May 2013 were also asked to complete the questionnaire. Subsequently, control donors are asked to update the information every five years, and donors with a psychiatric diagnosis are approached every year. To enable donors to provide online updates, an online questionnaire application was developed.

## **Interview to assess psychiatric symptoms**

We also started to collect data on psychiatric symptoms and disorders. A diagnostic tool, named the M.I.N.I. plus interview (Mini International Neuropsychiatric Interview), has been used by the NBB since September 2013. We strive to interview all control donors and donors with a psychiatric diagnosis in person at one time during life. Donors with a psychiatric diagnosis are interviewed to get detailed information on psychiatric symptoms they do and do not have. Control donors are also interviewed, in order to determine whether they fit the criteria for control donors for comparison with psychiatric donors. If a control donor turns out to have significant psychiatric symptoms, but not enough to justify a psychiatric diagnosis, he or she is more suitable as a control donor for research projects focused on other, non-psychiatric brain disorders. Furthermore, the M.I.N.I. plus interview may reveal psychiatric symptoms that could benefit from treatment, but for which the donor has not yet sought help. In such a case the NBB-Psy team can notify the donor's general physician (with the donor's permission), who may direct the donor to suitable treatment.



For the interview, donors are visited at home or invited to come to the office of one of the NBB-Psy research assistants. To optimize capacity, our team expanded with two students to conduct those interviews. In October 2014, we hosted a so-called ‘M.I.N.I. day’. During this event, donors participated in an interview and followed a tour through the NBB building guided by our staff (figure 6). The M.I.N.I. day was very successful and well-attended and offered the opportunity to interview more people on one day than usual.



Figure 6 Donors get a tour of the NBB during the M.I.N.I. day

### **Verifying the psychiatric diagnosis**

Since 2013, upon registration of a new donor who mentions a psychiatric diagnosis on the registration form, the NBB approaches the donor’s general physician, psychiatrist or psychologist to request the official classification according to the Diagnostic and Statistical Manual of Mental Disorders (DSM). For donors who registered before 2013 and who have participated in the M.I.N.I. plus interview, the official DSM classification is also requested if this is warranted by the interview’s results.

## **Collaboration with cohorts**

In addition to the NBB-Psy cohorts, and in line with previous years, in 2013-2014 the NBB's registration policy for other diagnoses has also focused on several clinical research and / or treatment patient cohorts. People who participate in such cohorts are especially interesting for post mortem research because they have usually been studied longitudinally and therefore a large amount of standardized medical data is already available. The general approach is that the NBB informs the researchers, physicians and / or other professionals involved in the cohorts about brain donation and provides information material. The cohorts, in turn, ask their participants and / or their next of kin to consider brain donation via the NBB.

### **VUmc Alzheimer Center**

In 2013-2014, the previously established collaboration between the NBB and the **VUmc Alzheimer Center**<sup>6</sup> has continued. Since 2012, we have only registered donors with Alzheimer's disease if they are registered at the VUmc Alzheimer Center. 54 NBB donors were included in the VUmc Alzheimer Center cohort on December 31, 2014, mainly with a diagnosis of Alzheimer's disease, but also with other diagnoses. Nineteen of these donors had already come to autopsy at that time. Since 2013, the collaboration was extended and two more clinical research cohorts within the Alzheimer Center were included in the donor and autopsy program of the NBB: the 100-plus study and PAGE-AD.

#### ***100-plus study***

The NBB and the **100-plus study**<sup>7</sup> have collaborated since 2013. The study researches non-demented centenarians in order to identify the processes that maintain cognitive health during aging: how do these persons differ from people who do become demented, usually at a much earlier age? This cohort is separate from the general VUmc Alzheimer Center cohort, which does not include cognitively healthy control donors. The study participants are interviewed and examined during life by the 100-plus study researchers. If they also decide to become a brain donor at the NBB, the brain material is made available exclusively to the 100-plus study. 26 NBB donors were included in the 100-plus cohort on December 31, 2014. Five of these donors had already come to autopsy at that time.

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6 <http://www.alzheimercentrum.nl>

7 <http://www.alzheimercentrum.nl/100plus/>

## **PAGE-AD**

The PAGE-AD project (Pathological substrate of clinical variability in AD) started in 2014 after receiving a grant from the **Memorabel program**<sup>8</sup> of ‘Deltaplan for Dementia’. In most patients with Alzheimer’s disease (AD), memory impairment is the first symptom, but a substantial group of patients present with non-memory symptoms. This may indicate a so-called parietal subtype of AD that is insufficiently understood. The goal of the PAGE-AD project is to endophenotype the parietal AD type by means of neuropathological and histochemical analysis and comparison to typical AD patients and healthy controls. A subset of donors from the general VUmc Alzheimer Center cohort are included in this study.

## **Other cohorts**

In 2014, preparations began for the Netherlands Parkinson Cohort. A research network of eleven hospitals will uniformly gather data from living persons with Parkinson’s disease. These persons will also be asked to register at the NBB to enable post mortem research. Also in 2014, the NBB has started a collaboration with the research project **PreDiva**<sup>9</sup>, aimed at cardiovascular interventions. Study participants were asked to consider registration at the NBB. Furthermore, the NBB collaborates with two specialized nursing homes: **Dijk en Duin**<sup>10</sup> (elderly persons with psychiatric symptoms and/or cognitive and behavioral problems) and **Nieuw Unicum**<sup>11</sup> (multiple sclerosis).

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8 <http://www.zonmw.nl/en/programmes/memorabel-dementia-research-and-innovation-programme/programme/>

9 <http://www.zonmw.nl/nl/projecten/project-detail/prevention-of-dementia-by-intensive-vascular-care-pre-diva/>

10 <https://www.dijkenduin.nl/>

11 <http://www.nieuwunicum.nl/>

## Donor communication

In 2013 and 2014, several updates of the NBB's communication channels and materials were implemented. Since 2014 donors can send paper mail to the NBB free of charge (by means of an 'antwoordnummer'). A new logo and house style were developed in 2012 and the transition was completed in 2013. The NBB's short information brochure was renewed to match the new style, and the text was updated. The websites [www.hersenbank.nl](http://www.hersenbank.nl) and [www.brainbank.nl](http://www.brainbank.nl) were also completely redesigned and now allow for easier updates by means of a content management system. Furthermore, in 2013 a new web-based donor registration database was developed, including the appropriate functionality to keep track of the additional information that is collected within the NBB-Psy program. The online questionnaire application is linked to this database, which means that updates provided by the donor can be implemented in the database directly.

Especially within the NBB-Psy program, several new communication strategies were implemented. The separate websites [www.nhb-psy.nl](http://www.nhb-psy.nl) and [www.nbb-psy.nl](http://www.nbb-psy.nl) were launched in 2013. Another novelty is the use of social media. You can find NBB-Psy on twitter ([@NHBPsy](https://twitter.com/NHBPsy)<sup>12</sup>) and facebook ([NHB-Psy](https://www.facebook.com/NHB-Psy)<sup>13</sup>). Furthermore, NBB-Psy has developed an **informational film**<sup>14</sup> to inform potential donors, psychiatric healthcare professionals and researchers about the program. Finally, in 2014 the first separate NBB-Psy newsletter was developed and distributed. This newsletter introduced the NBB-Psy staff and included interviews with a donor and researcher and an overview of media attention. Through the newsletter, we keep our donors and collaborative network up to date concerning our progress. The NBB-Psy newsletter will be sent every year (in contrast to the general NBB newsletter which is sent every two years).

## Public relations

Like in previous years, the NBB has continued to raise awareness of the importance of research with human brain tissue and the possibility of brain donation. When reaching out to (people involved with) potential new donors, we always emphasize that for good scientific research, donors with neurological or psychiatric diseases and healthy control donors are equally important. We're glad to note that due to the additional resources that were available for NBB-Psy, the NBB was able to invest

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12 <https://twitter.com/NHBPsy>

13 <https://www.facebook.com/NHB-Psy>

14 <https://www.youtube.com/watch?v=Yi4eyMk2pys>

much more time and effort in public relations activities than in previous years, which resulted in a notable increase of media appearances, presentations and attendance of events.

The public relations activities include events organized by the NBB, presence of NBB staff at events and congresses of other organizations, presentations, and coverage in different types of media such as magazines, websites, tv, and radio. Tables 1 - 3 provide an overview of the NBB's public relations activities in 2013 and 2014. Table 1 lists general PR activities and activities focused on non-psychiatric diagnoses. Tables 2 and 3 list the PR activities of the NBB-Psy program, with separate tables for presence at events and congresses (table 3) and other types of PR activities (table 2).

Highlights include the kick-off symposium to promote the official start of NBB-Psy (figure 7), a scientific symposium on the possibilities of research with brain tissue from donors with a psychiatric diagnosis, articles in two national newspapers (Trouw and Volkskrant) and a national magazine (Elsevier), an interview with the NBB's director Inge Huitinga broadcasted on national television (Omroep Max), and the visit of Inge Huitinga to the Republic of Korea to sign a Memorandum of Understanding (MoU) between the NBB and Korea Brain Research Institute (figure 8). The MoU was signed during the state visit, in the presence of President Park Geun-hye of the Republic of Korea and King Willem-Alexander and Queen Máxima of the Netherlands. Dr. Huitinga also attended the state banquet at the Blue House, President Park's executive office and official residence.



Figure 7 Impression of the NBB-Psy kick-off symposium



Figure 8 Dr. Huitinga visits Republic of Korea to sign MoU with Korea Brain Research Institute

**Table 1** Overview of public relations activities and articles on the work of the NBB in 2013 and 2014 (general PR activities and activities focused on non-psychiatric diagnoses)

<b>Date</b>	<b>Title* / description</b>	<b>Medium / information</b>
Jan - Feb 2013	Radio commercial with Inge Huitinga	MS Research (patient organization)
2013/05/21	Interview with Inge Huitinga: 'MS research in brain tissue'	De Telegraaf (daily newspaper)
2013/06/13	Interview with Veronica Popescu (VUmc): 'How to find a brain for MS research?'	De Volkskrant (daily newspaper)
2013/07/11	Book 'Alzheimer en Afscheid' (Alzheimer's and farewell) by Frits van den Haspel	Book written by the husband of a woman who donated her brain to the NBB. For every sold copy, € 2 is donated to the NBB
2013/10/05	Introductory presentation about the NBB by Petra Brom and Bonnie van Huik	MS association region Drenthe
2013/10/10	Information stand at the yearly public event of the Hersenstichting (Dutch brain foundation)	
2013/12/04	'Worldwide MS research with Dutch brain tissue'	Supplement of Telegraaf (daily newspaper)
2014/02/11	Introductory presentation about the NBB by Petra Brom, Bonnie van Huik, Jack van Horsen	MS association region Utrecht
2014/05/28	Inge Huitinga leads expert sessions at world MS day	MS Research world MS day (Oegstgeest)
2014/05/28	'Inge Huitinga about MS in men and women'	Dutch edition of the international MS atlas
2014/10/09	Information stand at the yearly public event of the Hersenstichting (Dutch brain foundation)	
2014/11/05	Round table sessions with Bonnie van Huik, Petra Brom, Mark Mizee	MS Research / MS Vereniging: MS patient day ('dag voor mensen met MS')
Nov 2014	Inge Huitinga visits the Republic of Korea to sign a Memorandum of Understanding (MoU) between the NBB and Korea Brain Research Institute. The MoU was signed during the state visit, in the presence of President Park Geun-hye of the Republic of Korea and King Willem-Alexander and Queen Máxima of the Netherlands. Dr. Huitinga also attended the state banquet at the Blue House, President Park's executive office and official residence.	
2014/11/28	Inge Huitinga participated in talkshow 'Biobanking 2.0'.	Event of BBMRI-NL

\*Original Dutch titles were translated in English

**Table 2** PR NBB-Psy - overview of public relations activities and articles in 2013 and 2014, focused on psychiatric diagnoses

<b>Date</b>	<b>Title* / description</b>	<b>Medium / information</b>
January 2013	The new brain bank initiative in the Netherlands	Newsletter UK Brain Bank for Autism
March 2013	Collecting brain tissue	Elsevier (magazine)
August 2013	Autism in research: the Netherlands Brain Bank for Psychiatry	Engagement with autism (magazine of Nederlandse Vereniging voor Autisme; autism patient organization)
September 2013	New brain bank for psychiatry: program team in search of donors	De Psychiater (magazine for Dutch Psychiatrists)
September 2013	Brains needed! Netherlands Brain Bank launches donor recruitment for brain research	Ypsilon News (magazine of Ypsilon; schizophrenia family organization)
2013/10/24	Kick-off symposium NBB-Psy (De Rode Hoed, Amsterdam)	Including presentations about the goals and importance of NBB-Psy, research with psychiatric brain tissue, personal experience with psychiatric disease, and music. Video recordings of the symposium were made publicly available online.
2013/10/26	'Detectives in the brain'	Trouw (daily newspaper)
October 2013	What goes wrong in the brain of people with a psychiatric disease?	Article on LPGGZ (website of Dutch national mental healthcare platform)
2013/11/09	Searching for many-headed monsters in the brain	Volkskrant (daily newspaper)
2013/11/14	Interview with Inge Huitinga	Studio MAX Live (TV show)
January 2014	Are you a brain donor already?	Ypsilon News (magazine of Ypsilon; schizophrenia family organization)
January 2014	NBB-Psy: the Netherlands Brain Bank for Psychiatry	Article on KenBiS (website of bipolar disorder knowledge center)
February 2014	Interview with Saskia Palmen on NBB-Psy	NTR Science Café (national radio)
March 2014	NBB-Psy: brain tissue	PlusMinus (magazine of VMDB; bipolar disorder patient organization)
March 2014	NBB-Psy: brain tissue for research	Suzan!; (ADHD lifestyle magazine)

\*Original Dutch titles were translated in English



**Table 2** PR NBB-Psy (continued)

<b>Date</b>	<b>Title* / description</b>	<b>Medium / information</b>
April 2014	NBB-Psy needs brain donors	www.depressievereniging.nl (website of depression patient organization)
May 2014	NBB-Psy: brain tissue for research	Originally on www.nodea.nl, now available on www.nedkad.nl (website of fear and depression knowledge center)
June 2014	Are you a brain donor already? Which information should I provide when registering as a brain donor?	Ypsilon News (magazine of Ypsilon; schizophrenia family organization)
June 2014	NBB-Psy: brain tissue for research	Wetenschappelijk Tijdschrift Autisme (Dutch peer-reviewed scientific journal focused on autism)
June 2014	The Netherlands Brain Bank for Psychiatry	Digital newsletter of knowledge center ADHD
June 2014	NBB-Psy: brain tissue for research	Open Geest (magazine of Anoksis; schizophrenia patient organization)
July 2014	NBB-Psy Newsletter	Newsletter made available online and sent to all control donors and donors with a psychiatric diagnosis, and other persons involved with the NBB-Psy project.
July 2014	"Kelly wants to contribute to research" (interview) & "The Netherlands Brain Bank for Psychiatry" (article)	Vizier (magazine of Angst, Dwang en Fobiestichting; patient organization for anxiety disorder, OCD and phobia)
Sep 2014	"The Netherlands Brain Bank for Psychiatry" (invitation for expert group autism)	Engagement met autisme (magazine of Nederlandse Vereniging voor Autisme; autism patient organization)
Sep 2014	NBB-Psy: brain tissue for research	Digital newsletter of Stichting Ovaal (organization for parents of children with autism)
Sep 2014	Are you a brain donor already? What will NBB-Psy do with (my) brain(s)?	Ypsilon News (magazine of Ypsilon; schizophrenia family organization)
Sep 2014	Bipolar Genetics & NBB-Psy: an update	PlusMinus (magazine of VMDB; bipolar disorder patient organization)
Oct 2014	Brain tissue for ADHD research	Impuls Magazine (ADHD patient organization)
Oct 2014	NBB-Psy: brain tissue for research	Vizier (magazine of Angst, Dwang en Fobiestichting; patient organization for anxiety disorder, OCD and phobia)

\*Original Dutch titles were translated in English

**Table 2** PR NBB-Psy (continued)

Date	Title* / description	Medium / information
Nov 2014	Symposium "Psy Brain Tissue Research"	Scientific symposium on post-mortem psychiatric brain research
Dec 2014	The Netherlands Brain Bank for Psychiatry	Newsletter of IMpACT (International Multicentre persistent ADHD Genetics CollaboraTion), sent to all Dutch research participants)

\*Original Dutch titles were translated in English

**Table 3** Presence of NBB-Psy team members at congresses and events

Date	Venue (diagnosis of focus*)	Additional information
May 2013	Annual NESDA-day, Leiden (MDD)	Poster presentation
June 2013	National VMDB day (BPD)	Information stand
June 2013	11th World Congress of Biological Psychiatry, Kyoto Japan (psychiatry in general)	Presentation by Inge Huitinga
July 2013	Chinese Brain Bank, Hangzhou China (psychiatry in general)	Presentations by Saskia Palmen and Inge Huitinga
Sept 2013	National VMDB day (BPD)	Information stand
Sept 2013	Symposium Balans, Utrecht (ADHD)	Poster presentation
Oct 2013	Symposium 'The apple doesn't fall far from the tree', Nijmegen (ASD & ADHD)	Poster presentation
Oct 2013	Annual Autism congress, Utrecht (ASD)	Information stand
Nov 2013	National Ypsilon day, Maarssen (SCHIZO)	Information stand
Dec 2013	Meeting Kenniscentrum Bipolaire Stoornissen, Utrecht (BPD)	Presentations by Saskia Palmen and Inge Huitinga
Dec 2013	National VMDB day, Utrecht (BPD)	Workshop and information stand
March 2014	Lecture Studium Generale, Utrecht (all)	Presentation by Saskia Palmen
March 2014	National VMDB day, den Bosch (BPD)	Information stand
April 2014	Information market ADHD & ASD, Leidschendam (ASD + ADHD)	Posters and leaflets were sent

\*Diagnosis abbreviations are explained in the [List of Abbreviations](#)

**Table 3** Presence of NBB-Psy team members at congresses and events (continued)

<b>Date</b>	<b>Venue (diagnosis of focus*)</b>	<b>Additional information</b>
April 2014	Annual NVvP Spring Congress, Maastricht (psychiatry in general)	Workshop and information stand
April 2014	Peer support and information day on depression, Utrecht (MDD)	Information stand
April 2014	Autism congress RINO Group, Ede (ASD)	Information stand
May 2014	Study day on the overlap between ASD & OCD, Amersfoort (ASD + OCD)	Information stand
June 2014	Lannoo Campus congress 'ADHD Plus!', Utrecht	Information stand
June 2014	National VMDB day, Den Bosch (BPD)	Information stand
Sept 2014	National VMDB day, Den Bosch (BPD)	Information stand
Oct 2014	PsyQ annual ADHD study day, Amersfoort	Presentation by Saskia Palmen
Nov 2014	Impuls theme-evening, Nijmegen (ADHD)	Presentation by research assistant
Nov 2014	Symposium 'Disorders of the Will', Utrecht (psychiatry in general)	NBB-Psy film on brain donation was shown
Dec 2014	National VMDB day, Utrecht (BPD)	Information stand

\*Diagnosis abbreviations are explained in the [List of Abbreviations](#)



# Autopsies & Diagnostics

Between 1985 and December 31, 2014, the NBB has obtained brain material from a total number of 3889 autopsies (Figure 10). The NBB performed 98 autopsies in 2013 and 81 autopsies in 2014. This is a decrease compared to previous years, especially 2010 through 2012. However, it is comparable to the years prior to 2008. Figure 9 shows the numbers of autopsies by disease for the last three two-year periods.

Despite the decline in the number of annual autopsies, the number of PD / DLBD autopsies increased in 2013-2014. This might be an effect of the increase in new PD / DLBD donor registrations that took place in 2011-2012. Furthermore, the number of AD autopsies has markedly decreased. In general, for donors with AD there is quite a short time between registration and death. Therefore, the decrease may be an effect of the limited registration policy for AD that was implemented in 2012. The number of control autopsies has also markedly decreased. Other than that, the decrease seems to be distributed evenly across the remaining diagnosis groups. However, especially due to high numbers of new registrations within the NBB-Psy program, we expect the number of autopsies to increase again in future years.

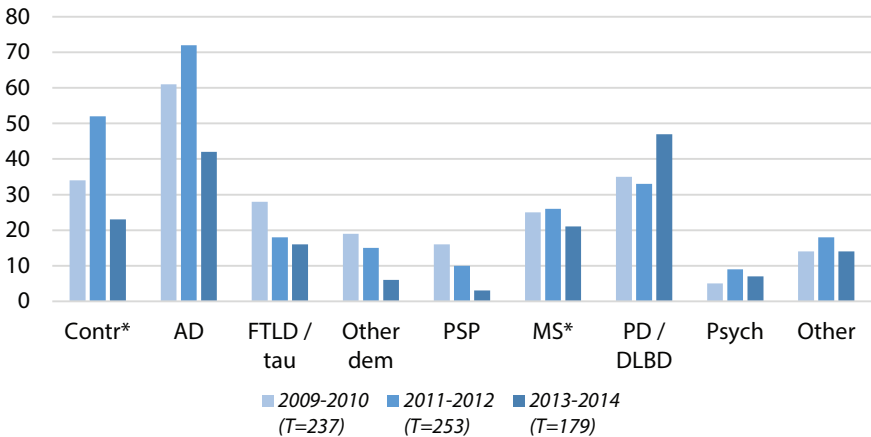


Figure 9 Numbers of autopsies 2009-2014, broken down by diagnosis

\*for 1 control autopsy and 8 MS autopsies in 2014, the clinical diagnosis (instead of final diagnosis) was counted because the final diagnosis had not yet been confirmed.

Figure 10 shows the total number of brain donors (3889) from which the NBB has obtained brain material from 1985 through 2014, broken down by diagnosis.

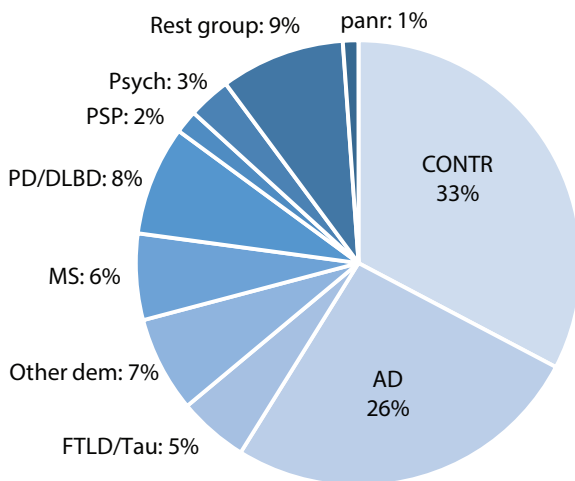


Figure 10 Total number of brain donations since 1985 (3889 on December 31, 2014)

## Post mortem delay

Due to autolytic processes, tissue of the central nervous system quickly decays after death and therefore the NBB aims for rapid autopsies within hours after a donor has deceased. The post mortem delay (PMD: time elapsed from a person's death to completion of the brain autopsy) depends on several factors: time of notification of the donor's death, distance and duration of transportation of the body and the availability of brain bank staff to perform the autopsy around the clock. Because PMD has a strong impact on the quality of the tissue (i.e. RNA, DNA and proteins), the NBB has established rapid autopsy protocols relying on 24/7 availability of staff. The NBB achieves short PMDs; the yearly average is generally between 6 and 6.5 hours, whereas the average PMD of other European brain banks is more than 12 hours in most cases. The NBB's yearly average PMD is very stable and the numbers for 2013 and 2014 are in line with previous years (figure 11).

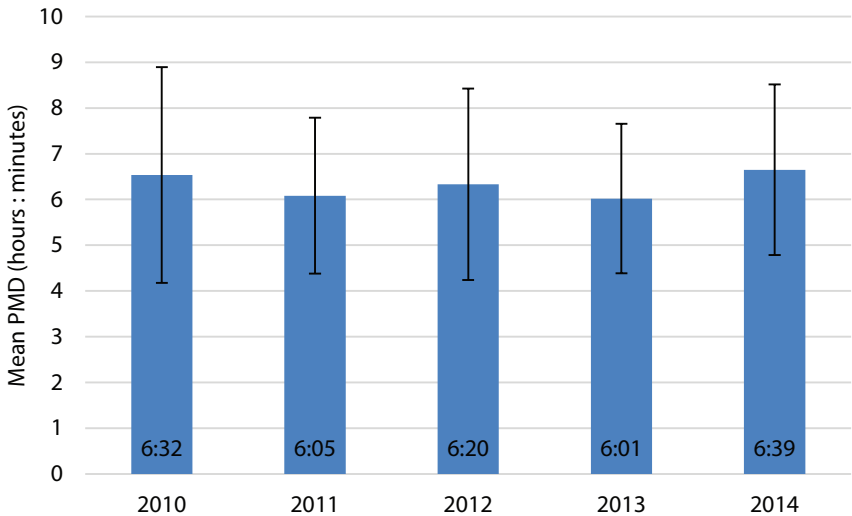


Figure 11 Yearly mean post mortem delay  $\pm$  standard deviation

## **Autopsy procedures**

Concerning the autopsy procedures, a number of new developments took place in 2013-2014.

### **Combining brain donation with organ donation**

In September 2014, for the first time, brain donation via the NBB was combined with organ donation for transplantation purposes. Because this concerned a person who underwent euthanasia, it was possible to coordinate the organ donation beforehand. Therefore, the organ donation process could be completed more quickly than usual, leaving enough time for brain donation afterwards.

If the circumstances allow for more of such combinations in the future, the NBB will encourage this. However, active involvement of the donors' physician(s) is essential, because organ donation for transplantation purposes cannot be arranged by the NBB, but should be initiated by a registered physician involved with the donor. The same applies to tissue donation for transplantation purposes, although the conditions for tissue donation are less strict, allowing the tissue donation to take place after brain donation in some cases. This concerns tissues such as skin, cornea, heart valves, bone and tendon tissue, cartilage, and blood vessels.

Many people who are registered at the NBB are also registered for organ donation. In most cases this does not lead to conflicts because the conditions for organ donation are much stricter than the conditions for brain donation. In cases where organ donation is possible, and the circumstances don't allow this to be completed in time for subsequent brain donation, the brain donation won't take place. Organ donation takes priority because it can save lives in a more direct manner than brain donation for research purposes, which only has long-term effects.

### **Eye dissection**

As the eye is part of the brain, the NBB collects eyes for research as well. The eyes may be used for investigation of (hereditary) eye diseases or to study similarities between tissues from the eye and the brain. In 2009, on initiative of professor Arthur A. Bergen, the NBB included eyes in its donor program. Researchers can request frozen eyes or fresh eyes (from future autopsies) in medium, such as a normal saline solution. In 2013-2014, eyes have been dissected from 34 donors (19% of the total number of autopsies). On December 31, 2014, there were 1080 living donors who had given separate permission for eye dissection, and eyes had been dissected from



112 donors in total since the start of the eye dissections.

### **Post mortem program NBB-Psy**

The NBB uses different dissection protocols for different diagnoses, because the brain regions that have been affected by pathology differ by diagnosis. Since 2014, a new dissection protocol for psychiatric diagnoses has been added. Previously, the brains of donors with a psychiatric diagnosis were dissected according to the control protocol. The new protocol is more extensive: more samples are dissected, and the protocol takes samples for frozen as well as FFPE storage from both hemispheres. Since the neuropathological substrate for the various psychiatric disorders is not yet fully mapped, the possibility for unilateral pathophysiology exists. To prevent a biased acquisition of samples from one hemisphere over the other, and therefore loss of possibly valuable samples, both hemispheres are sampled.

The same protocol is used for each of the seven psychiatric disorders that the NBB-Psy program focuses on. Since 2014, the same NBB-Psy dissection protocol has also been used for autopsies of control donors who are suitable to be used as a control for studies focused on psychiatry. For control donors who are only suitable for comparison in non-psychiatry studies, the original (less extensive) control protocol is still used.

Since 2013, the NBB-Psy team has been setting up a post mortem infrastructure towards the application of novel methods to enrich the brain material:

- Isolation of pure primary microglia and astrocytes;
- Generation of immortalized glial cell lines (microglia and astrocytes) from pure glial cells
- Dissemination of small tissue samples suitable for DNA and RNA isolations, to expand the number of studies that can use the same regions and donor populations
- Generation of induced pluripotent stem cells (iPSCs) from primary skin fibroblasts

### ***iPSCs***

Since 2014, a small skin sample (from the back of the head, adjacent to the cut that is made for removal of the brain) has been taken from control donors and donors with a psychiatric diagnosis. From these skin samples, fibroblasts are isolated to generate iPSCs in the Erasmus Stem Cell Centre (Headed by Prof. Joost Gribnau and

dr.Mehrnaz Ghazvini) for dissemination by NBB-psy. Once generated, iPSC lines can be stored in liquid nitrogen until use. Through the use of established protocols, iPSCs can be differentiated into neural stem cells, and subsequently used to generate donor-specific neurons and glial cells. At the end of 2014, skin fibroblasts from 10 different donors (both psychiatric and control) were successfully processed as described.

### ***Glia isolations***

During 2014, the protocol used for the isolation of pure microglia from post-mortem CNS samples was improved to obtain higher yields in a shorter processing time (4 hours). This protocol will be the standard operating procedure for all Psy autopsies starting from 2015. Microglia will be isolated from both occipital cortex and corpus callosum, and stored as biobank samples. A protocol for the isolation of pure astrocytes will be developed from the start of 2015.

## **Post mortem diagnostics**

After completion of an autopsy the brain tissue is fixed in formalin for four weeks. After fixation, approximately eighteen standard regions of tissue are embedded in paraffin, cut and (immuno)histochemically stained. These sections are evaluated by one of our neuropathologists according to the latest international diagnostic criteria. Together with the clinical diagnosis this provides the final diagnosis. This post mortem diagnostic procedure is essential because the neuropathological diagnosis regularly differs from the initial clinical diagnosis. With the exception of fresh samples for culture purposes, the brain material is available for researchers only after the neuropathological diagnosis has been determined. This ensures that they receive samples of the diagnosis that they have applied for.

To further improve the available diagnostic information, for Parkinson's Disease (PD), Frontotemporal dementia (FTD) and multiple sclerosis (MS), the general diagnostic procedures are supplemented by additional specialized diagnostics. For PD and FTD, the NBB closely collaborates with Dr. W.D.J. van de Berg (Dept. of Anatomy and Neurosciences) and Prof. Dr. J.M. Rozemuller (Dept. of Pathology) from VU medical center Amsterdam. Dr. van de Berg identifies early PD pathology in donors who were still classified as control donors clinically and neuropathologically, and Dr. Rozemuller retrospectively diagnoses cases of FTD according to the most recent scientific diagnostic criteria. For MS, until 2012 the NBB had already retrospectively characterized the full collection of MS lesions tissue blocks for stages of inflammation and demyelination with the aid of a grant of de Vriendenloterij. In 2013 and 2014, this characterization has continued for new MS autopsies. This enables the correlation of pathological, genetic and clinical data, in order to investigate whether specific pathology of MS relates to a specific clinical course and genetic background.

In 2013, Dr. Wouter Kamphorst has retired from his neuropathological work for the NBB after more than 25 years. We are very grateful for his long and dedicated service.



# Tissue supply

## Research institutes

Since 2007, the NBB has used a Material Transfer Agreement (MTA) to ensure the rights and obligations of both the NBB and the tissue recipients. Researchers can only receive tissue when an MTA is in place between the NBB and the researcher's organization. Once both parties have signed the MTA, which is valid for an indefinite period of time unless specified otherwise, any researcher within the institute can apply for tissue. For each individual tissue delivery, an implementing letter is signed, which is considered an appendix of the master MTA. As of December 31, 2014, the NBB has entered into agreement with 141 organizations in total: 124 universities / research institutes (non-profit) and 17 pharmaceutical companies (for profit). In 2013 and 2014, 21 new MTA's were signed: 18 with non-profit organizations and 3 with pharmaceutical companies.

## Number of tissue requests

Since the NBB's tissue sample dissemination procedure was professionalized in 2007, the number of tissue requests for new research projects has varied between approximately 40 and 60 per year. However, in 2014, the NBB received 70 requests for new projects, which is markedly higher (figure 12). Of the 44 new applications received in 2013, 7 were from for profit organizations (pharmaceutical companies). Of the 70 new applications received in 2014, 9 were from for profit organizations.

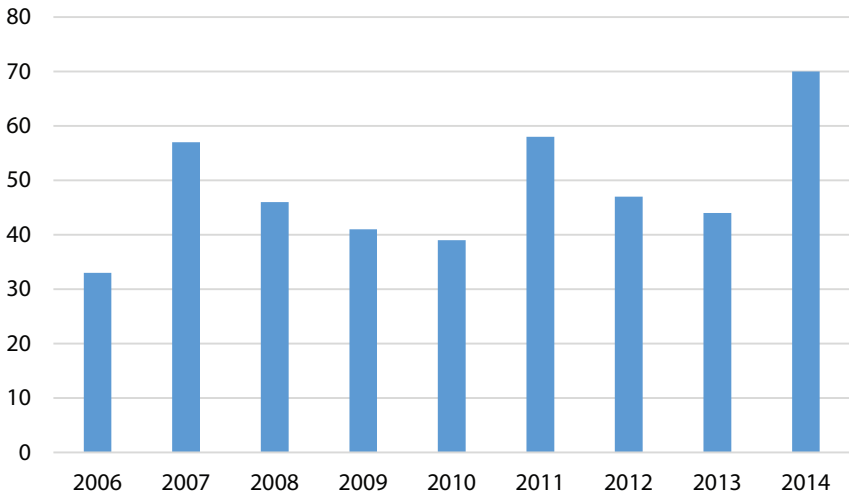


Figure 12 Tissue requests for new projects in 2006-2014

When a researcher requests additional samples for a research line that has already received NBB samples previously, this is called a supplementary application. Figure 13 shows the numbers of supplementary applications that the NBB received in 2013-2014. Of the 63 supplementary applications received in 2013, 9 were from for profit organizations. Of the 90 supplementary applications received in 2014, 12 were from for profit organizations. Two types of supplementary applications can be distinguished: regular supplementary applications and continuous projects. Regular supplementary applications are reviewed on an individual basis. For each regular supplementary application, a separate implementing letter is signed.

In most cases, continuous projects concern requests for fresh tissue samples. Because these samples should be collected from future autopsies, not all samples can be supplied at once. Therefore, one implementing letter is signed at the start of the project (mentioning the total number of samples to be supplied), or multiple implementing letters are signed, each after a fixed interval such as once every quarter or once every year. In figure 13, such projects are counted once per year, even though they may have received samples from many separate autopsies.

Some continuous projects request tissue from the existing stock of NBB tissue multiple times per year. For these projects, implementing letters are also signed quarterly or yearly. In figure 13, such projects are counted once for each separate sample set that

was delivered (once per delivery date).

Some continuous projects receive both fresh samples and samples from the general NBB stock. These projects are counted once per year (for the fresh samples), plus once for each separate delivery date of samples from stock.

Figure 13 also shows the number of new applications in 2013-2014 again. When new and supplementary applications are added up, the NBB received 107 tissue requests in 2013 and 160 tissue requests in 2014.

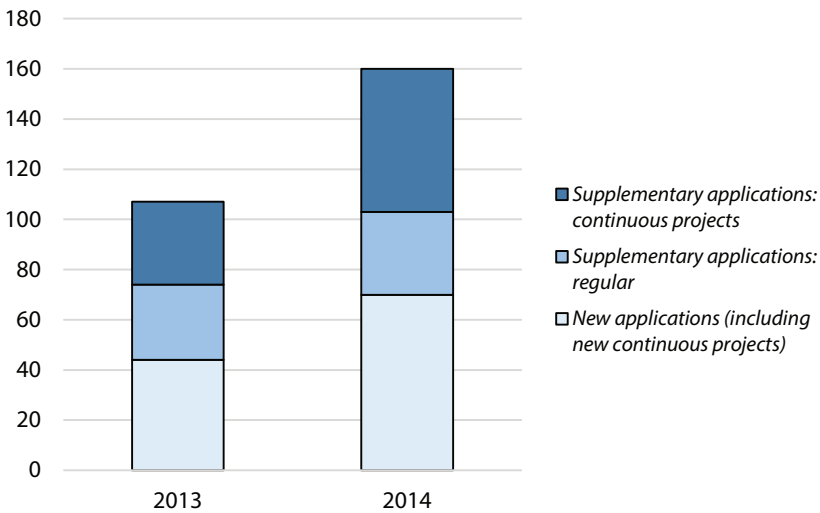


Figure 13 All tissue requests in 2013-2014

In 2013 and 2014 there were 12 cases where tissue inquiries led to requests that could not be approved (mostly due to scarcity of the requested samples combined with suboptimal quality of the research plan) or where approved requests did not lead to transfer of samples (e.g. due to financial problems - rejected grant applications - of the researcher, or difficulties in meeting local requirements for transfer of post mortem human samples). In addition, the NBB received 27 tissue inquiries that did not lead to an actual application. In those cases, information about availability and the application process was sent to the researcher, but the researcher never actually applied for tissue.

The **e-NBB**<sup>1</sup> is the NBB's online tissue database where researchers may view the

<sup>1</sup> <http://www.e-nbb.org/>

available tissue and make their own preliminary tissue selection. Between the launch of the e-NBB in late 2011 and December 31, 2014, 337 users had registered.

### Number of samples supplied to research projects

In 2013, 2497 tissue samples were supplied to researchers, which is markedly less than usual. Although the number of supplied samples in 2007 was comparable (2909 samples), the usual yearly number was around 4500 in 2008-2012. In 2014, however, 4346 samples were supplied again. When this progress report was published, the numbers for 2015 were also already available. In 2015, 5611 samples were supplied, which may indicate that the low numbers of 2013 were incidental. Figure 14 shows the supplied tissue units for the last four two-year periods, broken down by diagnosis.

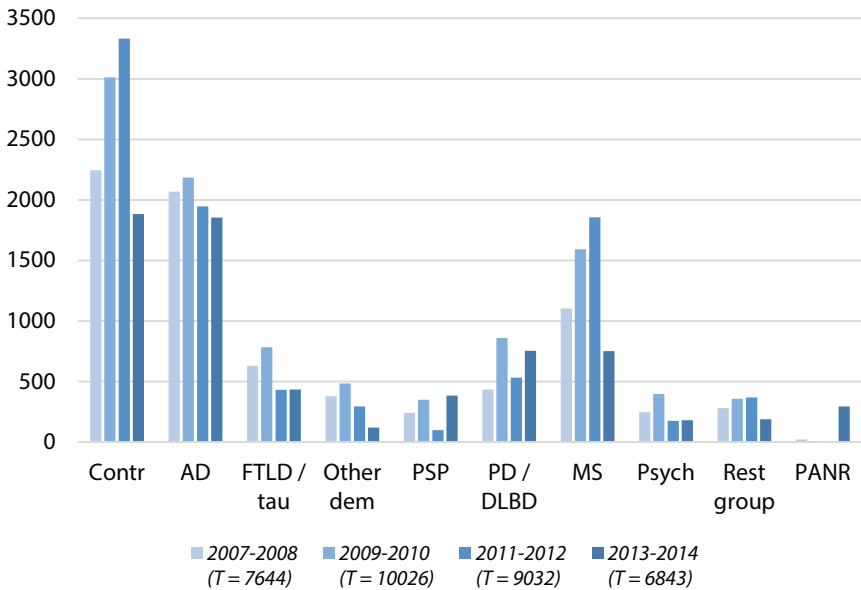


Figure 14 Supplied tissue units in 2007-2014, broken down by diagnosis

When the distribution across diagnoses in 2013-2014 is compared to previous periods, relatively less control and MS samples were supplied (even less than would be expected considering the general decrease in number of supplied samples), and relatively more PSP, AD and PD/DLBD samples were supplied (comparable to the numbers in previous years, despite the general decrease in 2013-2014).

In line with the non-profit / for profit distribution of the research projects that



requested tissue, the majority of tissue samples were supplied to researchers affiliated to universities or other non-profit organizations. In 2013, 475 units (from a total of 2497) were supplied to for profit organizations. In 2014, 511 units (from a total of 4346) were supplied to for profit organizations. These numbers are much higher than those of 2012 (59 units to for profit organizations), but comparable to 2011 (470 units).

The number of supplied samples from donors with a psychiatric diagnosis is still low, due to the very limited availability of these samples. The NBB-Psy project aims to increase the future availability of these samples. To prepare researchers for this, on November 18, 2014, a research symposium was organized by the NBB-Psy team. During the symposium, examples of research with post mortem brain material of donors with psychiatric diagnoses were presented, in order to illustrate the specific possibilities.

Figure 15 shows the number of supplied tissue units broken down by type of storage. In 2013-2014, frozen and FFPE samples remained the type for which demand was highest. The proportion of fresh samples is comparable to previous years, and the proportion of fixed samples has decreased.

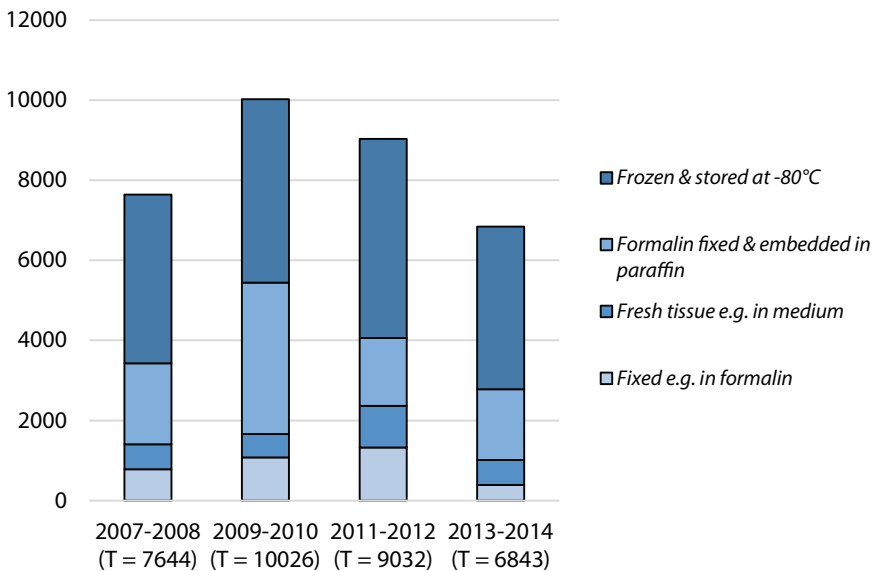


Figure 15 Supplied tissue units by type of storage, 2007-2014



# Finances

The NBB receives structural financial support from the Royal Netherlands Academy of Arts and Sciences (KNAW) and the Netherlands Institute for Neuroscience (NIN), but other than that it is almost completely dependent on grants, donations and the financial contributions from researchers who use NBB material.

## General grants

Grant	2013	2014
Structural contribution from KNAW	€ 224,144	€ 220,000
Structural contribution from NIN	€ 100,000	€ 100,000
Stichting MS Research	€ 106,254	€ 111,096
Stichting ParkinsonFonds	€ 0	€ 36,250
Hersenstichting	€ 11,000	€ 15,000
Stichting Zabawas	€ 0	€ 16,430

## Project-based grants

Funding organization	Project	Period	Amount
NWO (Netherlands Organisation for Scientific Research)	The Netherlands Brain Bank for Psychiatry (NBB-Psy)	15-9-2012 - 15-9-2017	€ 3,450,000*
Vriendenloterij	Characterization of the MS tissue collection of the NBB	1-5-2010 - 1-5-2014	€ 365,000**

The NBB-Psy grant was jointly granted to the NBB and the five participating Dutch university medical centers for setting up the separate NBB-Psy program. The project and its budget are coordinated by the NBB.

The funding from Vriendenloterij was granted to the Netherlands Brain Bank in collaboration with Stichting MS Research, which enabled the Neuroimmunology research group of the Netherlands Institute for Neuroscience to characterize all MS lesions of NBB donors. Now this project has been finished, we are very grateful that in February 2014, the Vriendenloterij has again granted the NBB (in collaboration

with Stichting MS Research) € 295,000 for a new project starting May 1, 2015. In this project, the Neuroimmunology research group will use NBB samples to research the differences in MS between men and women, and the use of body chemicals (sex hormones) to positively influence the disease course of MS.

### **The necessity of grants**

The costs to make tissue available for research are approximately € 800,000 per year. Without the help of patient organizations and other funding agencies, the NBB would not be able to maintain its high standards, and it is only thanks to the received funding that the NBB is able to continue brain banking.

**Stichting MS Research**<sup>1</sup> (MS Research Foundation) has been funding the NBB for many years, resulting in an increase of the number of MS donors and in the availability of MS tissue. Due to the special MRI-guided dissection protocol, the autopsy costs for MS are higher than for other autopsies. Moreover, the clinical history of MS patients is often more extensive and the summarization of the medical information requires a greater effort. Lastly, in-depth neuropathological diagnostics of the MS plaques is time-consuming, but indispensable for good tissue dissemination. MS Research covers the costs of all MS autopsies and of some control autopsies.

The grants of **Stichting ParkinsonFonds**<sup>2</sup> (Parkinson Fund Foundation) cover the costs of some of the Parkinson autopsies and some donor recruitment activities, which would not be possible without this additional funding.

Funding by **Hersenstichting**<sup>3</sup> (Brain Foundation) and **Stichting Zabawas**<sup>4</sup> (Zabawas Foundation) is used to cover costs for donor recruitment, autopsies and administration.

### **Private donations**

Stichting Vrienden van het Herseninstituut (Friends of the Netherlands Institute for Neuroscience Foundation) helps the NBB to reach its objectives by giving financial support.

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1 <http://www.msresearch.nl/>

2 <http://www.parkinsonfonds.nl/>

3 <http://www.hersenstichting.nl/>

4 <http://www.zabawas.nl/>

In 2013, we received € 27,814 in donations through this foundation, and in 2014 we received € 6,731. Financial donations remain vital to the continued existence of the NBB and are thus very welcome. If you wish to help, please make your donation to: Stichting Vrienden van het Herseninstituut, IBAN: NL76INGB0002167378; BIC: INGBNL2A), mentioning “NBB”.

Because the foundation also raises money for the Netherlands Institute for Neuroscience in general, mentioning “NBB” ensures that your donation reaches us. The Foundation is registered at the Dutch Chamber of Commerce under registration no. 41205869.

We are very grateful for all grants and donations. The work of the NBB would not be possible without the support of numerous foundations and patient organizations, and the enthusiastic dedication of individuals.



# Research projects 2013-2014

The abstracts can be downloaded from our website by clicking on the names below or by visiting <http://www.brainbank.nl/research/projects>.

In this list, only the affiliation of the first-mentioned researcher is mentioned. Full affiliation information is included in the abstracts.

## National

The first-mentioned researcher's main affiliation is an organization based in the Netherlands.

**Alkemade**, A., Balesar, R., Zhao, J., Swaab, D.F., and Forstmann, B.U. Amsterdam Brain and Cognition Center, University of Amsterdam. Immunocytochemical characterization of the human subthalamic nucleus.

**Bisschop**, P.H., Dekker, M.J., Osterthun, W., Kwakkel, J., Anink, J.J., Boelen, A., Unmehopa U.A., Koper, J.W., Lamberts, S.W., Stewart, P.M., Swaab, D.F., and Fliers, E. Department of Endocrinology & Metabolism, Academic Medical Center, Amsterdam. Expression of  $11\beta$ -hydroxysteroid dehydrogenase type 1 in the human hypothalamus.

**Bonifati**, V. Department of Clinical Genetics, Erasmus MC, Rotterdam. Characterization of the FBXO7 (PARK15) protein.

**Borgers**, A.J., Fliers, E., Siljee, J.E., Swaab, D.F., Van Someren, E.J., Bisschop, P.H., and Alkemade, A. Department of Endocrinology and Metabolism, Academic Medical Center, University of Amsterdam. Arginine vasopressin immunoreactivity is decreased in the hypothalamic suprachiasmatic nucleus of subjects with suprasellar tumors.

**Borgers**, A.J., Koopman, K.E., Bisschop, P.H., Serlie, M.J., Swaab, D.F., Fliers, E., La Fleur, S.E., and Alkemade, A. Department of Endocrinology and Metabolism, Academic Medical Center, University of Amsterdam. Decreased serotonin transporter immunoreactivity in the human hypothalamic infundibular nucleus of overweight subjects.

**Brouwer**, N., Eggen, B.J., and Boddeke, H.W. Department of Neuroscience, University Medical Center Groningen. Analysis of age-related changes in gene expression in human microglia.

**Bsibsi**, M., Peferoen, L.A., Holtman, I.R., Nacken, P.J., Gerritsen, W.H., Witte, M.E., Van Horsen, J., Eggen, B.J., Van der Valk, P., Amor, S., and Van Noort, J.M. Delta Crystallon, Leiden, and VU University Medical Center, Amsterdam. Demyelination during multiple sclerosis is associated with combined activation of microglia/macrophages by IFN- $\gamma$  and alpha B-crystallin.

**Bugiani**, M., and Van der Knaap, M.S. Departments of Pediatrics / Child Neurology and Pathology, VU University Medical Centre, Neuroscience Campus Amsterdam, Amsterdam.

Unraveling disease mechanisms in genetic white matter disorders.

- Bulk**, M., Van der Graaf, L., Mulders, C., Natté, R., Hassan, W., Dijkstra, J., Van der Voorn, P., Van de Berg, W., Van Buchem, M., and Van der Weerd, L. Departments of Radiology & Human Genetics, Leiden University Medical Center. Pathological correlates of cortical changes in Alzheimer's disease at ultra-high field MRI.
- Chrobok**, N., Bol, J., and Van Dam, A.M. Dept. Anatomy and Neurosciences, VU University Medical Center, Amsterdam. Characterization of tissue Transglutaminase expression in active white and grey matter MS lesions.
- Gorgels**, Th.G.M.F. and Bergen, A.A.B. Netherlands Institute for Neuroscience, Amsterdam, and University Eye Clinic Maastricht, MUMC+, Maastricht. Choroid Plexus and Retinal Pigment Epithelium: Two of a kind?
- Gorgels**, Th.G.M.F. and Webers, C.A.B. University Eye Clinic Maastricht, MUMC+, Maastricht. From genes to glaucoma: identifying glaucoma pathways.
- Grand Moursel**, L., Munting, L., Van der Graaf, L., Van Duinen, S., Van Roon-Mom, W., Van Buchem, M., Van der Maarel, S., and Van der Weerd, L. Departments of Radiology, Human Genetics, and Pathology, Leiden University Medical Center. TGF $\beta$  signalling in HCHWA-D: exploring new therapy targets against CAA.
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- Svedberg, M., and Gulyás, B.,** Department of Clinical Neuroscience, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden. Visualizing amyloid and huntingtin in post-mortem brain slices obtained from Alzheimer's disease and Huntington's disease patients with novel molecular imaging biomarkers and biomarker candidates.
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- Trutzel**, A. et al. Division of Psychiatry Research, University of Zurich, Switzerland. Deficits in synaptic signalling and cytoskeleton organisation in early stages of Alzheimer disease (AD).
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- Tsamis**, K.I., Mytilinaios, D., Njau, S.N., Baloyannis, S.J. Laboratory of Neuropathology, 1st Department of Neurology, Aristotle University, Thessaloniki, Greece. Synaptic alterations of human caudate nucleus in Alzheimer's disease.
- Unger Lithner**, C. and Darreh-Shori, T. Alzheimer Neurobiology Center, Karolinska Institutet, Stockholm, Sweden. The pathological mechanisms of  $\beta$ -amyloid in the brain of Alzheimer's Disease and controls.
- Van den Oord**, E. Center for Biomarker Research and Precision Medicine, Virginia Commonwealth University, Richmond VA, USA. Brain DNA methylation signatures of major depressive disorder.
- Wennström**, M. et al. Clinical Memory Research Unit, Dept. of Clinical Sciences, Lund University, Malmö, Sweden. Are levels of brain miRNA specifically linked to neuroinflammation and synaptic plasticity altered in relation to pathological mechanisms characteristic of AD?
- Wennström**, M. et al. Clinical Memory Research Unit, Dept. of Clinical Sciences, Lund University, Malmö, Sweden. Investigating possible alterations in the NG2 cell population brain tissue from Alzheimer's disease patients and healthy elders.
- Wennström**, M. et al. Clinical Memory Research Unit, Dept. of Clinical Sciences, Lund University, Malmö, Sweden. Using functional cell studies to characterize and map the sensitivity and response to pathology-associated agents of various post-mortem isolated primary human glial cell cultures.
- Willem**, M. Ludwig-Maximilians University Munich, Munich, Germany. Analysis of BACE1 expression and substrate processing in early and late stage Alzheimer's disease.
- Wu**, X., Bao, A., and Swaab, D.F. Department of Neurobiology; Key Laboratory of Medical Neurobiology of Ministry of Health of China; Zhejiang Province Key Laboratory of Neurobiology, Zhejiang Province Key Laboratory of Mental Disorder's Management; Zhejiang University School of Medicine, Hangzhou, China. Is there activity-dependent neurotransmitter respecification in the human hypothalamic suprachiasmatic nucleus between day and night and in depression?
- Xilouri**, M., Papagiannakis, N., and Stefanis, L. Center of Clinical Research, Experimental Surgery and Translational Research, Biomedical Research Foundation of the Academy of Athens, Athens, Greece. The role of Chaperone-Mediated Autophagy in the nervous system in health and disease.
- Yoon**, S.Y., and Kim, D.H. Department of Anatomy and Cell Biology, University of Ulsan College of Medicine, Seoul, Korea. Search for the key pathogenic molecules in Alzheimer's disease brain.
- Zhou, J. Institute of Neuroscience, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, P.R. China. Verification of  $\alpha$ B-crystallin and Hapln2 expression in

brain of patients with Parkinson's disease (**abstract 1**) (**abstract 2**).

**Zhu**, Q.B., Unmehopa, U., Bossers, K., Verwer, R., Balesar, R., Zhao, J., Bao, A.M., and Swaab, D.F. Department of Neurobiology; Key Laboratory of Medical Neurobiology of Ministry of Health of China; Zhejiang Province Key Laboratory of Neurobiology, Zhejiang University School of Medicine, Hangzhou, P.R. China. MicroRNA-132 and Early growth response-1 in the Nucleus Basalis in Alzheimer.

## Pharmaceutical companies

### Asterand UK Acquisition Ltd

- Expression of therapeutic candidate genes in DRGs from control donors
- Correlative analysis of mRNA and protein expression in CNS tissues from MS donors
- Analysis of protein expression in normal and Alzheimer's Disease (AD) human brain
- Analysis of mRNA expression in CNS tissues from ALS donors
- Analysis of gene expression in specific hypothalamic nuclei isolated by Laser Capture Microdissection and analysed via quantitative rtPCR
- Screening a panel of alpha-SYN research antibodies, using FFPE sections from normal donors and those with Parkinson's Disease
- Purification of paired helical filaments from brain cortex samples from donors with early signs of Alzheimer's disease (Braak Stage 3)
- Examination of autoradiographic binding of a proprietary radioligand in frozen sections of different brain regions from normal donors and those with Parkinson's Disease

### AstraZeneca Translational Science Centre at Karolinska Institutet, Stockholm, Sweden

- Establishment and validation of histopathological assays to quantify the levels of the ganglioside GM1 in human brain samples from the Netherland Brain Bank
- Identification and validation of transcripts and proteins in brain tissue derived from Alzheimer's patients with special emphasis on pharmacogenetics

### Charles River Nederland BV

- Collaborative research program with CHDI Foundation (Cure Huntington's Disease Initiative)

### DSM Nutritional Products AG

- A surrogate marker of brain aging: Relationship between telomere length in different brain areas and periphery during aging and disease and role of micronutrients

### EMD Millipore

- Validation of a monoclonal antibody raised against Amyloid Beta nitro-tyrosine 10

### GlaxoSmithKline

- Identification and validation of potential therapeutic targets for Multiple Sclerosis
- Identification of potential therapeutic targets for amyotrophic lateral sclerosis and Huntington's disease
- Identification of potential therapeutic targets for multiple sclerosis

Neurimmune Therapeutics AG

Characterization of therapeutic antibody candidates with respect to binding of pathological protein deposits, in Alzheimer's disease, Huntington's disease and amyotrophic lateral sclerosis.

Novartis Pharma AG

Investigation of IL-17 cytokine and its signaling pathway in MS

Neuroinflammation in AD

Autoradiography studies on orexin receptors in the human brain

Autoradiographic examination of extra- and intracellular markers in Huntington's disease, with special emphasis on visualization of huntingtin aggregates

Pfizer Ltd.

Assessment of ion channel gene expression in human spinal cord

UCB Biopharma SPRL

Evaluation of binding of UCB proprietary molecules to Alzheimer's patients brains for the identification of new therapeutic agents for the treatment of Tauopathies and Alzheimer's disease



# Publications 2010-2014

This chapter lists the articles in which the NBB was involved and that were published between 2010 and 2014. The following two publications concern brain banking in general, and include individual NBB (former) staff members as authors:

Klioueva, N. M., Rademaker, M. C., Dexter, D. T., Al-Sarraj, S., Seilhean, D., Streichenberger, N., ... Huitinga, I. (2015<sup>1</sup>). BrainNet Europe's Code of Conduct for brain banking. *Journal of Neural Transmission*, 122(7), 937–940. <http://doi.org/10.1007/s00702-014-1353-5>

Samarasekera, N., Salman, R. A.-S., Huitinga, I., Klioueva, N., McLean, C. A., Kretschmar, H., ... Ironside, J. W. (2013). Brain banking for neurological disorders. *The Lancet Neurology*, 12(11), 1096–1105.

## Publications of research projects with the NBB as co-author

The other publications in this chapter concern articles that were realized through the use of NBB tissue. The Material Transfer Agreement of the NBB provides guidelines for acknowledgement of the NBB in the Materials and Methods section of publications of data derived from material obtained from NBB donors. However, in cases where the NBB's contribution to a research project is more substantial than usual and includes e.g. intellectual input into study design or specific analyses of tissue or donor data, we request (corporate) co-authorship for (an individual affiliated to) the Netherlands Brain Bank in case of a publication in which NBB material or data are used. For corporate authorship, the NBB can be added to the author list as “Netherlands Brain Bank” or “Netherlands Brain Bank for Psychiatry”. A corporate author is preceded with a ; (not a , ). The affiliation of the Netherlands Brain Bank is: Netherlands Institute for Neuroscience, Meibergdreef 47, 1105 BA, Amsterdam, the Netherlands. The **NBB authorship guidelines**<sup>2</sup> describe this in more detail.

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1 Online publication (ahead of print) in 2014

2 [https://www.brainbank.nl/media/uploads/file/NBB\\_authorship\\_guidelines.pdf](https://www.brainbank.nl/media/uploads/file/NBB_authorship_guidelines.pdf)

Until 2014, the Netherlands Brain Bank was included as a corporate co-author in the following publications:

- Vermunt, M. W., Reinink, P., Korving, J., de Bruijn, E., Creyghton, P. M., Basak, O., Geeven, G., Toonen, P.W., Lansu, N., Meunier, C., van Heesch, S.; Netherlands Brain Bank, Clev-ers, H., de Laat, W., Cuppen, E., & Creyghton, M.P. (2014). Large-Scale Identification of Coregulated Enhancer Networks in the Adult Human Brain. *Cell Reports*, 9(2), 767-779. <http://doi.org/10.1016/j.celrep.2014.09.023>
- Dijkstra, A. A., Voorn, P., Berendse, H. W., Groenewegen, H. J.; Netherlands Brain Bank, Rozemuller, A. J., & Berg, W. D. (2014). Stage-dependent nigral neuronal loss in inci-dental Lewy body and Parkinson's disease. *Movement Disorders*, 29(10), 1244-1251.
- Wong, T. H., Chiu, W. Z., Breedveld, G. J., Li, K. W., Verkerk, A. J. M. H., Hondius, D., Hukema, R.K., Seelaar, H., Frick, P., Severijnen, L.A., Lammers, G.J., Lebbink, J.H., van Duinen, S.G., Kamphorst, W., Rozemuller, A.J.; Netherlands Brain Bank, Bakker, E.B.; International Parkinsonism Genetics Network, Neumann, M., Willemsen, R., Bonifati, V., Smit, A.B., & van Swieten, J. (2014). PRKAR1B mutation associated with a new neurodegenerative disorder with unique pathology. *Brain*, 137(5), 1361-1373. <http://doi.org/10.1093/brain/awu067>
- Nielsen, H. M., Ek, D., Avdic, U., Orbjörn, C., Hansson, O.; Netherlands Brain Bank, Veerhuis, R., Rozemuller, A.J., Brun, A., Minthon, L., & Wennström, M. (2013). NG2 cells, a new trail for Alzheimer's disease mechanisms? *Acta Neuropathologica Communications*, 1(1), 1-13. <http://doi.org/10.1186/2051-5960-1-7>



## Full publication list

The following publications were realized through the use of NBB tissue. The NBB is acknowledged in these articles, but is not included as a co-author.

- Aarsland, D., & Kurz, M. W. (2010). The epidemiology of dementia associated with Parkinson's disease. *Brain Pathol*, 20. <http://doi.org/10.1111/j.1750-3639.2009.00369.x>
- Alberio, T., Bossi, A. M., Milli, A., Parma, E., Gariboldi, M. B., Tosi, G., ... Fasano, M. (2010). Proteomic analysis of dopamine and  $\alpha$ -synuclein interplay in a cellular model of Parkinson's disease pathogenesis. *FEBS Journal*, 277(23), 4909–4919.
- Al-Izki, S., Pryce, G., Hankey, D. J. R., Lidster, K., von Kutzleben, S. M., Browne, L., ... Baker, D. (2014). Lesional-targeting of neuroprotection to the inflammatory penumbra in experimental multiple sclerosis. *Brain*, 137(1), 92–108. <http://doi.org/10.1093/brain/awt324>
- Alkemade, A., Friesema, E. C., Kalsbeek, A., Swaab, D. F., Visser, T. J., & Fliers, E. (2011). Expression of thyroid hormone transporters in the human hypothalamus. *J.Clin.Endocrinol.Metab*, 96(6), E967–E971. <http://doi.org/10.1210/jc.2010-2750>
- Alkemade, A., Unmehopa, U. A., Hessel, E. V., Swaab, D. F., Kalsbeek, A., & Fliers, E. (2012). Suppressor of cytokine signaling 3 in the human hypothalamus. *Peptides*, 35(1), 139–142. <http://doi.org/10.1016/j.peptides.2012.03.004>
- Alkemade, A., Yi, C. X., Pei, L., Harakalova, M., Swaab, D. F., la Fleur, S. E., ... Kalsbeek, A. (2012). AgRP and NPY Expression in the Human Hypothalamic Infundibular Nucleus Correlate with Body Mass Index, Whereas Changes in alphaMSH Are Related to Type 2 Diabetes. *J.Clin.Endocrinol.Metab*, 97(6), E925–E933. <http://doi.org/10.1210/jc.2011-3259>
- Alt, S. R., Turner, J. D., Kloke, M. D., Meijer, O. C., Lakke, E. A., Derijk, R. H., & Muller, C. P. (2010). Differential expression of glucocorticoid receptor transcripts in major depressive disorder is not epigenetically programmed. *Psychoneuroendocrinology*, 35(4), 544–556.
- Amadoro, G., Corsetti, V., Atlante, A., Florenzano, F., Capsoni, S., Bussani, R., ... Calissano, P. (2012). Interaction between NH(2)-tau fragment and Abeta in Alzheimer's disease mitochondria contributes to the synaptic deterioration. *Neurobiol.Aging*, 33(4), 833.e1–e25. <http://doi.org/10.1016/j.neurobiolaging.2011.08.001>
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For more information about the organization structure, please refer to Figure 17: Organization chart of the Netherlands Brain Bank (Appendix).



# List of abbreviations

AD	Alzheimer's disease
ADHD	Attention deficit hyperactivity disorder
ASD	Autism spectrum disorder
BPD	Bipolar disorder
Contr	Non-demented control donors
FTLD/tau	Frontotemporal lobar degeneration/Tauopathy
MDD	Major depressive disorder
MS	Multiple sclerosis
OCD	Obsessive compulsive disorder
Other dem	Other types of dementia
PANR	Pathological report not ready yet
PD/DLBD	Parkinson's disease/Diffuse Lewy body dementia
PSP	Progressive supranuclear palsy
Psych	Psychiatric disorders (unspecified)
PTSD	Posttraumatic stress disorder
Rest group	Other diagnoses
SCHIZO	Schizophrenia
Trans	Transsexuality



# Appendix

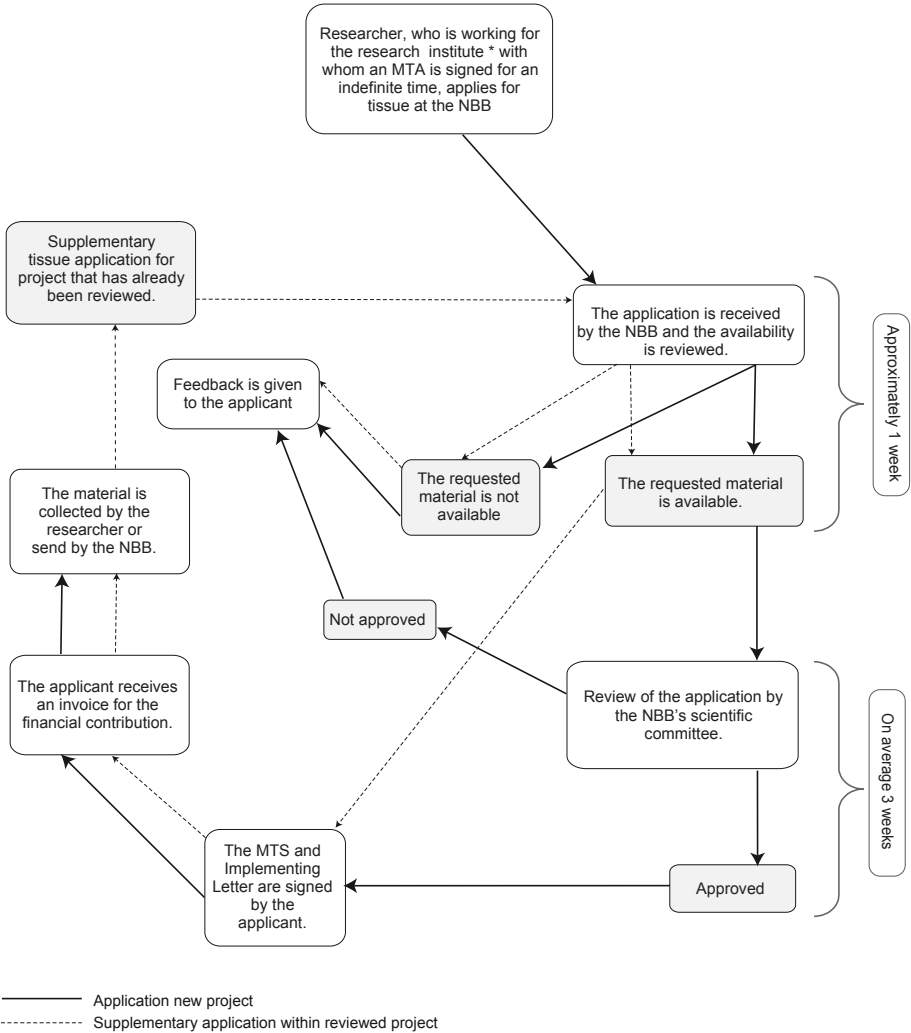


Figure 16 NBB's Procedure of Material Transfer

The research institute is a legal entity with whom the MTA is signed. Therefore, the research institute is a party of the agreement and is called "Recipient" of the Material in the MTA (and not the researcher). In case no MTA for indefinite time has been signed at the institute/organization of the researcher, the NBB will not supply any tissue. First, the authorized person (head manager or managing coordinator) needs to sign the MTA.

**Legend**

- Persons / departments / organizations outside the NBB
- MT Member of management team

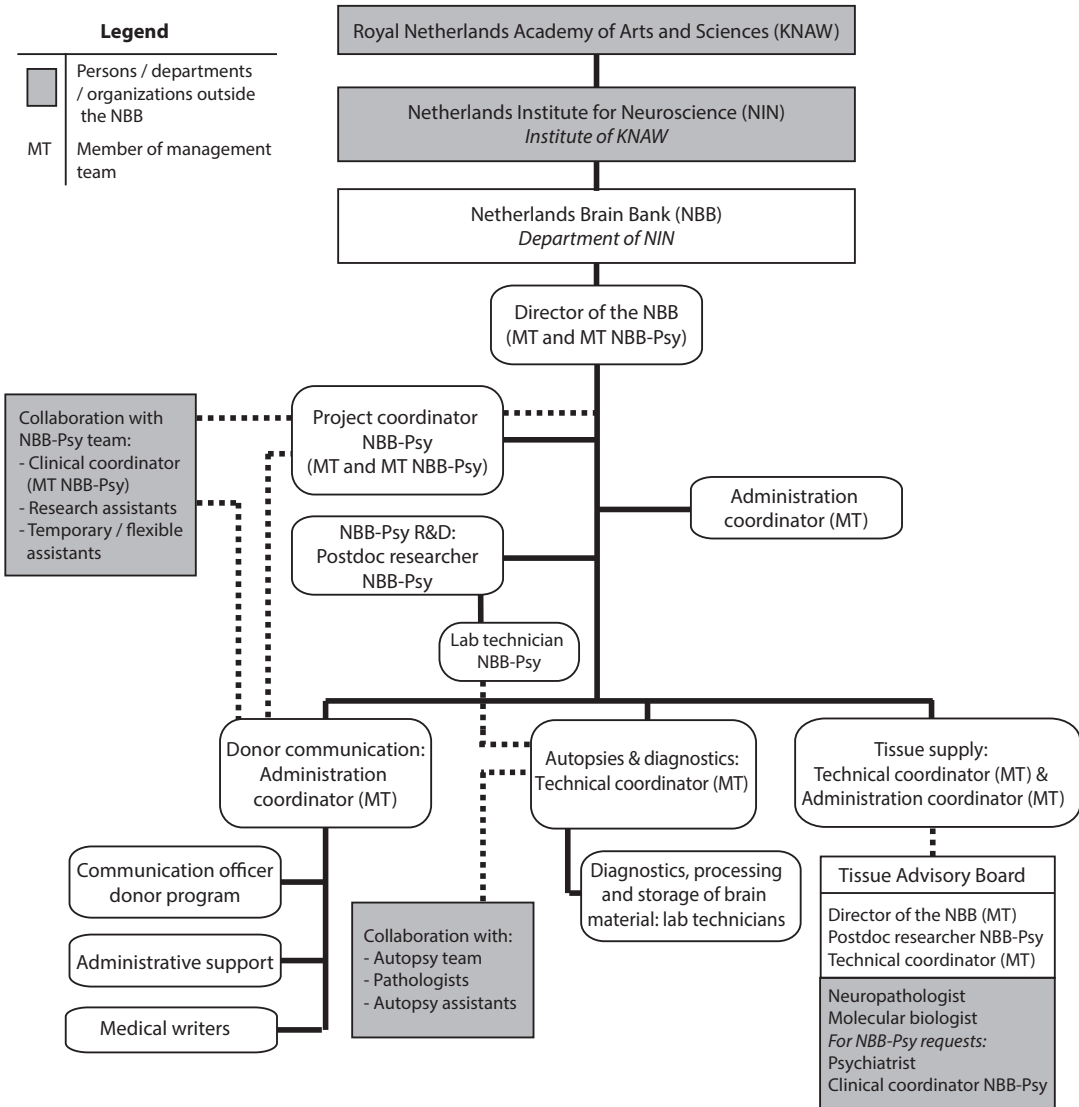


Figure 17 Organization chart of the Netherlands Brain Bank

This chart also shows the main types of activities within the NBB. Therefore, job titles of employees who perform tasks related to multiple types of activities occur more than once.