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Complete List of Authors:	Hanlon-Dearman, Ana; Manitoba FASD Centre, SSCY Centre Chen, Maida; Seattle Children's Hospital, Division of Pulmonary and Sleep Medicine Carmichael Olson, Heather; Seattle Children's Research Institute
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Understanding and Managing Sleep Disruption in Children with FASD

Running Title: Sleep Disruption in Children with FASD

Ana Hanlon-Dearman, MD, FRCPC, FAAP
1. Pediatrics and Child Health, College of Medicine, Faculty of Health Sciences, University of Manitoba, Winnipeg, MB
2. Manitoba FASD Centre, Winnipeg, MB

Maida Lynn Chen, MD
3. Department of Pediatrics, Pulmonary and Sleep Medicine Division, University of Washington School of Medicine, Seattle, WA

Heather Carmichael Olson, PhD
4. Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA
5. Center for Child Health, Behavior and Development, Seattle Children's Research Institute, Seattle, WA

Word Count:

Correspondence:
Dr. Ana Hanlon-Dearman
Manitoba FASD Centre
Specialized Services for Children and Youth (SSCY) Centre
1155 Notre Dame Avenue
Winnipeg, Manitoba
R3E 3G1
Ph. #: 204-258-6630
Fax #: 204-258-6798
Email: ahdearman@rccinc.ca

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ABSTRACT

Accumulating evidence has revealed high rates of sleep disruption among children with Fetal Alcohol Spectrum Disorder (FASD). Multiple animal and clinical studies have found a clear association between sleep problems and prenatal alcohol exposure (PAE), and recent research is beginning to characterize the types and extent of sleep disruption in FASD. Nevertheless, sleep disruption in children with FASD often goes unrecognized or is treated without referring to an evidence base. Children's disrupted sleep interferes with parental sleep and increases caregiver burden, which is of particular importance for families raising children with FASD, a group with very high levels of caregiving stress. The literature supporting an association between sleep problems and deficits in emotional, behavioral, and cognitive function in children is compelling, but needs further investigation in children with FASD. This paper will review the current state of knowledge on sleep in FASD and recommend a rational approach to sleep interventions for affected children and their families.

Key Terms: FASD, sleep, pediatrics, prenatal alcohol exposure, maternal alcohol use

INTRODUCTION

Fetal Alcohol Spectrum Disorder (FASD) is characterized by lifelong neurodevelopmental disabilities arising from prenatal exposure to alcohol (PAE)[1-4]. The prevalence of FASD has generally been estimated to be 9-10 cases per 1,000 live births in the U.S.[5,6], though there are more recent estimates using active case ascertainment in school studies that range as high as 2-5% of younger school children in the U.S.[7,8] , with much higher estimates in high risk subgroups such as children in care[9]. FASD is considered a major public health problem[10,11] that is global in extent[7,11,12]. FASD is known to have frequent sequelae, including social adaptive dysfunction[13], adverse impact on caregiver and family function[14], and high societal costs[10,15-19]. There is also increasing concern about elevated rates of physical health problems in this clinical population and their long-term impact [15,20]. Opportunities to maximize functioning and reduce morbidity in FASD are, therefore, critical for affected individuals, their families, and communities.

In children with FASD, sleep problems from infancy through the school years are commonly experienced by families, yet are poorly understood by health care providers[21-23]. While the frequency of sleep problems in developmentally typical children is often quoted as about 25%, the frequency of sleep problems in children with FASD has been observed as high as 85% in keeping with other children with developmental disabilities[24,25]. For example, sleep problems are reported to occur in 50-80% of children with Autism Spectrum Disorder[26] and up to 70% of those with ADHD[27]. Various characterizations of the sleep disturbances seen in children with FASD have included sleep onset delays, shorter sleep, more frequent night wakings, as well as atypical

features including elevated rates of parasomnias and sleep anxiety[21,24] The complexity of both the sleep disturbance and resultant impact on daytime behavior and learning is significant for both the child and their caregivers[28]. With a high rate of FASD represented in children in care, and a high level of documented caregiver stress, the further impact of night dysregulation on family functioning and the risk for potential destabilization of a care placement is significant[29]. Recognizing these sleep disorders in this high risk group and offering effective treatment strategies offers an opportunity to improve child behavior, reduce caregiver stress, stabilize social placement, and increase child and caregiver resilience.

Contributors to sleep difficulties in children with FASD are multifactorial, including: 1) hypothesized physiologic changes resulting from the neurotoxic effects of PAE on sleep architecture, circadian physiology, and respiratory control; 2) lasting sequelae in health and daytime function for chronically sleep disrupted/deprived parents and affected children; and 3) impact on interpersonal relationships restructured by emotional, behavioral, and cognitive perceptions of a “difficult” sleeper. Sleep difficulties are potentially modifiable when attempting to maximize neurodevelopmental potential and health in each individual with FASD. However, addressing these sleep difficulties must consider the many factors influencing sleep, the sleep environment, and the child/individual experiencing these difficulties within their family. A management approach which integrates current scientific understanding of the impact of PAE on sleep, neurobehavioral patterns, and the needs of the child and family offers the strongest opportunity for effectively addressing these complex difficulties.

The purposes of this review are to characterize what is known about sleep challenges in children with FASD, explore pathophysiologic mechanisms, discuss the

impact of sleep problems within this population, and recommend a rational approach to sleep treatment and support for these children and their families. This review will present the most current research on sleep mechanisms in FASD and will contextualize this research with established knowledge and expert clinical experience.

MECHANISMS OF SLEEP DISRUPTION RELATED TO PRENATAL ALCOHOL EXPOSURE

Preschool or school-aged children with PAE, including those who are not yet diagnosed with FASD, may experience sleep difficulties related to PAE. These may be further compounded by post-birth events, including trauma. Co-occurring prenatal exposures may also have an effect[30,31,32]. The mechanisms underlying the teratogenic effects of PAE on sleep are complex. Descriptive studies using animal models or humans have explored the connection between PAE and sleep disruption in order to delineate possible underlying physiologic mechanisms. An understanding of the impact of PAE including altered sleep architecture, fragmentation, and shorter sleep duration has emerged from such research.

Correlational data from studies of infants with a history of PAE, who may or may not be diagnosed with FASD, have described the impact of PAE on physiologic mechanisms of self-regulation. Early electroencephalographic (EEG) studies of these infants, assessed both prospectively in pregnancy and via retrospective maternal report of gestational alcohol use, showed adverse changes in neonatal state regulation including problems in sleep, sleep cycling, and arousal[30-35]. Work published in the Lancet (1976) was the first to describe disorganized and hypersynchronous voltage patterns in

the EEGs of infants of alcoholic mothers.[36] Later work continued to describe a characteristic EEG pattern across all stages of sleep, with significantly higher voltage than the patterns seen in healthy non-exposed infants.[33] Follow-up work demonstrated that the EEG differences were prolonged, independent of gestational age, and not related to neonatal withdrawal from alcohol[34]. More recent work correlated the early presence of these EEG differences in infants with PAE with subsequent motor and cognitive development later in childhood[35,37].

Newer research has revealed altered arousal responses during sleep in alcohol-exposed infants[38]. A recent large, well-designed longitudinal study in Finland has extended the study of sleep and PAE into childhood, where associations between low birth weight, prenatal exposure to alcohol and tobacco, and sleep duration and efficiency (based on actigraphy, or measurement of sleep movement) were examined in 8-year-olds (N=289)[39]. PAE was associated with shorter sleep duration and poorer sleep efficiency, even after controlling for birth weight and tobacco exposure. In this study, no assessments of daytime function or diagnosis of conditions in the category of FASD were undertaken[39].

Data from experimental animal models of PAE have demonstrated possible mechanisms of alcohol's teratogenic effect on sleep processes and allowed consideration of these issues apart from the impact of other prenatal or postnatal influences. These data suggest that sleep compromise is under both neurological and genetic control, is impacted by PAE, and that problems persist across the lifespan. These data have also characterized the sleep disturbance seen with PAE. Comparing alcohol-exposed rat pups to controls, disturbances in sleep-wake patterns have been found including shorter sleep and sleep fragmentation[40,41]. Rat models of the full Fetal

Alcohol Syndrome (FAS) have demonstrated changes in sleep architecture with significant reductions in REM sleep. Studies using alcohol-exposed rats have shown a shortened circadian sleep-wake cycle, as well as abnormal circadian neurotrophin expression in the suprachiasmatic nucleus which regulates circadian rhythmicity[42-46]. Subsequent work has suggested that impacts on circadian rhythmicity may be long-term, and that PAE may exert a metabolic effect on clock regulatory genes in the hypothalamus[43,47-49] which may predispose exposed individuals to nocturnal sleep fragmentation[37,41-43]. In a 2016 study of binge pattern PAE on adult rats, impaired slow wave sleep with increased slow-wave/fast-wave transitions were demonstrated; furthermore, this sustained sleep fragmentation was associated with memory impairments in these adult mice[50]. Of importance, previous work has suggested the selective sleep deficits found in young adult rats with concurrent deficits in spatial memory could be attenuated with treatment, though human implications are less clear[51]. Finally, blunted ventilatory responses to hypoxia in juvenile rats with PAE have also been demonstrated, suggesting that increased risk for significant sleep-disordered breathing (SDB) could occur[46,52,53].

There are data from animal and human studies which provide potential mechanisms of the links between the teratogenic effects of PAE with clinical findings of SDB and disrupted sleep among children with FASD. Both SDB and sleep disruption encompass a broad range of disorders with varying etiologies, but a few potential pathophysiologic possibilities warrant further discussion as they specifically pertain to children with PAE.

First, central respiratory modulation and respiratory muscle coordination may be impacted in those with PAE via abnormalities in the midline cerebellum[54]. Animal models

and neuroimaging studies have demonstrated the effect of PAE on in utero development of the cerebellar vermis[10,49,55]. Cerebellar anomalies have been described among individuals with FAS, and those with conditions on the broader fetal alcohol spectrum[56]. Mechanisms by which cerebellar compromise may play a role have been illustrated by examining children with lesions in the cerebellar vermis who show a markedly higher incidence of apneas and increased risk of sudden death from presumed SDB[57]. Abnormalities in those same areas of the cerebellum may thus predispose children with PAE to challenges with central respiratory control and coordination.

Second, SBD among those with FASD could also be related to airway obstruction due to a combination of anatomic and neuromuscular differences in the upper airway. Airway patency is challenged during sleep due to inherently decreased neuromuscular tone in the upper airway muscles, predisposing them to collapse [58]. When coupled with midface anomalies, which are known to occur in those with classically described FAS, repeated episodes of airway obstruction are at high risk of happening leading to SDB[1,2,10]. Taken together, these studies suggest the possibility that those with FASD experience respiratory abnormalities during sleep arising from cerebellar abnormalities and/or upper airway obstruction. Respiratory abnormalities, from central nervous system impairment and/or SDB, may additionally result in repeated cortical arousals during sleep, which also leads to sleep fragmentation[59].

Third, neuroimaging and animal research suggest that children with FASD may also be predisposed to teratogenic damage to the suprachiasmatic nucleus, presumed to play a critical role in ‘the circadian clock’[42]. PAE in mice has also been shown to decrease levels of γ-aminobutyric acid (GABA), an important neurotransmitter in sleep-wake stability[60]. A dysfunctional circadian system and/or disrupted GABA circuits

may lead to frequent nighttime arousals (clinical and subclinical) as well as to insomnia, perhaps because awake and sleep states are not appropriately recognized at a neurological level.

In summary, sleep can be fragmented by the impact of PAE through a variety of potential mechanisms, the effects of which may be compounded if these teratogenic insults are combined.

CHARACTERIZING SLEEP PROBLEMS IN CHILDREN WITH FASD

Several research groups in the 1990s identified sleep problems among children with FASD as part of an initial characterization of a neurobehavioral profile for this set of neurodevelopmental disabilities. An early longitudinal study in Germany (1998) examined a clinical sample of individuals with FAS (N=158) at preschool, school-age and adolescence[61]. Using questionnaires and clinical interviews, “sleep disorders” were generally noted as a common clinical problem and, importantly, many participants showed newly manifested sleep disorders at school-age. No details were given about types and exact frequency of sleep disorders, nor were validated measures used. The same year, a U.S. study (N=472) found just over 50% of informants identified “sleeping problems” in the clinical phenotype of alcohol affected children, identifying these to be of greater importance than the “hyperkinetic disorders”[62]. A later 2006 U.S. chart review of youth referred for FASD diagnosis (N=2,231) found “sleep disorder” rates ranging from 9.7% (no confirmed PAE) to 52.3% (high risk alcohol exposure)[63]. A 2009 survey of children with FASD in Canada (N=89), aged 8-15 years, found 62% with “sleeping disorders” gathered from clinical interview compared to 11% of controls, making sleep

disorders the most prevalent comorbidity in children with FASD occurring at a similar rate to that of ADHD/ADD[64]. All these studies have established a consistent and significant prevalence of reported sleep problems among children with PAE and/or FASD.

There is emerging research that more precisely describes sleep difficulties in children with FASD. Cross-sectional findings for young children with FASD (N=100) aged 5-8 years, using sleep diaries and caregiver questionnaires, reported reduced sleep duration and frequent night wakings[65]. Studies have consistently described high rates of clinically significant sleep problems in several samples of children with FASD, suggesting that primary difficulties with sleep initiation and maintenance are common[21,24,66,67]. Furthermore, research is describing abnormalities in sleep architecture and efficiency impacting circadian regulation[24,67]

Three recent studies are of note. In 2011, a Canadian study by Wengel, Hanlon-Dearman and colleagues used actigraphy, as well as sleep scores from the validated Children's Sleep Habits Questionnaire (CSHQ), and compared these with sensory processing characteristics in a group of young children (ages 3-6 years) with FASD compared to controls[21]. This study showed a significantly increased rate of sleep disruption and parasomnias in young children with FASD compared with controls and showed that patterns of sleep disruption also correlated with differences in sensory processing[21]. In 2012, Chen, Olson and colleagues compared a representative group of 4-10 year old children with FASD with an age-matched typically developing community sample (N=418)[24]. They also used the CSHQ[68] and, in addition, obtained parent norm-referenced questionnaire reports of concerning daytime behaviors. Both studies found large differences between groups, with high rates of clinically significant sleep problems in the children with FASD compared to controls. Chen et al. reported that a

striking 85% of children with FASD fell above the cut-off for clinically significant sleep problems (CSHQ Total Score ≥41), significantly more than the 35% seen in community matched controls (p <0.001). In addition, subscales concerning for pediatric insomnia were also elevated among children with FASD compared to controls[19,27,28].

Chen et al. (2012) also performed a full overnight sleep study for a small group of these children with FASD and significant sleep problems, all of whom had CSHQ scores >41[24]. Polysomnography in this study was the first to show objective evidence of fragmented sleep among children with FASD, as well as mildly elevated carbon dioxide levels suggesting SDB. These pilot polysomnography data, coupled with CSHQ parent report data from both studies, suggest two broad areas in which children with FASD may commonly have sleep problems: (1) difficulties with sleep initiation/maintenance; and (2) respiratory disturbances.

Most recently in 2016, Goril and colleagues characterized the sleep and circadian rhythm of 36 children and adolescents with FASD, age 6-18 years, using both gold standard assessments of polysomnography and evaluation of dim light melatonin onset (DLMO)[67]. Consistent with prior work, this study described significant sleep disruption in children and adolescents diagnosed with FASD[21,24,69]. Goril and colleagues also described a high rate of parasomnias in children with FASD (which Hanlon-Dearman's much earlier work had suggested) and a variable pattern of melatonin secretion[69]. Previous work has reported an increased rate of atypical nocturnal behaviors among young children with PAE compared to age matched controls, including talking, kicking, or picking and sniffing of bedclothes[22,69]. Given the variable presentation of alcohol toxicity on neurodevelopment, dependent on factors such as dose, timing, and maternal health, this variable pattern of sleep problems and underlying

hormonal mechanisms may be a predictable consequence and is certainly consistent with previous animal literature investigating the effects of alcohol on other hormonal systems[70].

IMPACT OF SLEEP DIFFICULTIES ON DAYTIME FUNCTION AND TREATMENT POSSIBILITIES

Growing data associating difficulties in sleep and daytime function suggest that disrupted childhood sleep is associated with significant deficits in emotional, behavioral, cognitive and academic functioning, and that these impact child health and quality of life among both typically and atypically developing children. Sleep problems are particularly prevalent in atypically developing children, with reported prevalence rates of up to 80%[71-73]. Associations between sleep and daytime function are reported in many pediatric clinical populations, and particularly among those with developmental disabilities. Frequent night wakings among children with developmental disabilities have been associated with self-injurious behavior, hyperactivity, aggressive, and disruptive behavior[71,74,75]. These disturbances have a significant impact on parent and child quality of life. For example, the association between sleep problems and reduced child quality of life in ADHD has been described, independent of severity of ADHD symptoms[76]. In Autism Spectrum Disorder, parent reports have revealed an association between ratings of poor sleep and less optimal child daytime behavior, with moderately strong associations between sleep latency from polysomnography and ratings of affective problems and aggressive behavior[77-79]. Significantly, sleep problems are related to child behavioral dysregulation, such as externalizing problems and executive dysfunction.

These also represent the most challenging areas of daytime function for children with FASD[80,81].

Data on restricted sleep and SDB (Sleep Disordered Breathing which includes Obstructive Sleep Apnea; OSA) shed further light on the connection between sleep and daytime function at school and at home. There is evidence that OSA, currently the best studied model of sleep fragmentation in children, is associated with poor school performance, neurocognitive deficits such as deficits in self-regulation, daytime inattention and hyperactivity, behavior problems, mood instability, and decreased growth[82-85]. For children with OSA lower scores have been found on measures of phonological processing, executive functioning, and visual attention[86]. Of interest, as many studies have shown, individuals with FASD commonly have problems in these areas of function[2,3,10,24,80,81,87]. Surprisingly though, there has only been one study so far using polysomnography in children with FASD to examine the possibility of SDB and other clinically significant objective sleep study parameters[24]. This is unfortunate, because treatment of SDB leads to notable decreases in health care utilization, and likely improves child quality of life[88]. It is important to note there is a promising and significant treatment opportunity for children with FASD who also show SDB.

Many studies have documented challenges in daytime learning and behavior among children with FASD. But none, to our knowledge, have examined difficulties in daytime function in relation to sleep problems. This is a critical gap in research on FASD. In other clinical populations, sleep fragmentation has been linked to deficits in attention, response inhibition, and working memory[89-92], all areas of neuropsychological impairment well-documented among children with FASD[64,93,94]. For this paper, new exploratory findings from the Chen et al. (2012) sample revealed that daytime behavioral

deficits in children with FASD, particularly in inhibition and working memory as assessed with the Behavior Rating Inventory of Executive Function (BRIEF) questionnaire[95], were moderately and significantly correlated with sleep problems as measured by CSHQ Total score. Strikingly, these new exploratory analyses suggest that children with FASD and more severe sleep complaints tend to have greater impairment in executive function as revealed in an objective parent report. Though studies have not yet clearly linked daytime behavior with sleep in children with FASD, integrating treatment for sleep disorders in an attempt to optimize daytime behaviors should be considered for most children with FASD. Treatments for various sleep problems span the gamut of low to high risk, and should not be taken lightly given the current lack of empirical evidence base for this clinical population. However, the strength of the association between improved sleep and improved behavior in typically developing children makes it quite plausible that successful sleep treatments for those with FASD could result in improvements in daytime behavior.

SLEEP PROBLEMS IN FASD AND ASSOCIATIONS WITH PSYCHOSOCIAL RISK AND CAREGIVER IMPACT

The association between prenatal adversity and poor quality sleep among offspring has become increasingly recognized and described[39]. The “developmental origins” hypothesis relates adverse changes in the intrauterine environment (such as PAE, poor nutrition, or multiple stressors) to later outcomes of mental health or other chronic disorders[39]. Dysregulation of the hypothalamic-pituitary-adrenocortical (HPA) axis related to these changes is suggested as a final common pathway between early

experiences of adversity (including PAE), and poor sleep quality and diurnal regulation[96]. High rates of cumulative risk and adverse caregiving experiences have been well described in children with FASD, who often experience multiple home placements and other types of psychosocial disruption[13,97]. In the broader literature on sleep, children's cultural/racial background and increased psychosocial risk have been associated with differences in sleep patterns and parental sleep expectations[98]. Proximal measures of risk, such as chaotic living conditions, are salient to sleep problems[99]. The more distal factor of socioeconomic status (SES) may moderate the impact of sleep disruption on daytime functioning, with those experiencing higher SES somewhat protected from negative impact and those with lower SES more affected[100-102].

Disrupted sleep in children increases caregiving burden and negatively impacts parental sleep in both typical[103,104] and atypically developing populations[76,105-107]. Fortunately, treatment of children's sleep disturbance helps improve family quality of life. Outcome studies of sleep interventions used with younger children resulted in improved caregiver sleep, as well as improved mood and marital satisfaction after treatment[108]. Improvement in caregiving stress and adult distress is especially important for families raising children with FASD, as there are very high levels of stress and psychological distress among parents of children in this clinical population[14,109]. In FASD, caregiving stress appears directly related to the child's functional impairments[110]. Sleep problems are an important area of functional impairment in FASD. Interventions targeting sleep problems clearly have potential to improve the lives of both parents and children.

TREATMENT RECOMMENDATIONS FOR PEDIATRIC SLEEP CARE IN FASD: A RATIONAL APPROACH

Families are frequently overwhelmed by the complex neurobehavioral and medical challenges of FASD, including the impact of sleep difficulties[65,109]. Families may be further frustrated because children's sleep difficulties are not thoroughly assessed by primary care providers. In turn, providers may not know how to respond to pediatric sleep difficulties and particularly behavioral sleep difficulties[23]. A rational approach to treating pediatric sleep problems is recommended here.

In the opinion of the authors, the ideal model in pediatric sleep care for children with FASD would be anchored in a multidisciplinary approach with opportunity for screening, evidence based sleep-related intervention (e.g., caregiver sleep education, counseling regarding sleep hygiene), referral to therapies, and specialty referral for further behavioral or medical assessment. This approach also supports long-term health care by using a layered, flexible, and individualized approach. A multidisciplinary approach that recognizes the neurodevelopmental complexity of sleep issues in children with FASD, and the unique stressors on their family and caregivers, has the best potential to optimize sleep management for these children. However, in full recognition of limited resources, many recommendations offered here can still be implemented by providers who do not have the benefit of a multidisciplinary team.

Evidence supporting management of sleep related difficulties for children with PAE is linked to the developmental origins of these difficulties. Comprehensive management must consider several important issues. First is consideration of the "fetal programming" of the child's biological system. Second is the need to address the child's sleep difficulties in context of their neurodevelopmental profile of strengths and weaknesses. Third is the need to address the past and current child care environment. Addressing these three areas will result in an integrated care plan.

While it is beyond the scope of this paper to explore each of these issues exhaustively, the following core ideas and related recommendations are made:

Core idea #1: It is critical to understand the impact of prenatal adversity and the priming impact of PAE on the child's biology ("fetal programming"). Prenatal adversity reflects the maternal environment as well as the child's biological responses. Early dysregulation of the HPA stress system through the impacts of maternal substance use (which can include PAE and/or undernutrition, and early disrupted caregiving experiences) can lead to altered diurnal cortisol secretion patterns influencing both daytime and nighttime self-regulation[96]. Related to this core idea, it has been long observed that early FASD diagnostic assessment is a key protective factor.

RECOMMENDATION ONE – *Access early FASD assessment and diagnosis*: Individuals with confirmed PAE should receive early assessment and diagnosis— ideally by an experienced multidisciplinary team (or appropriate mental health or health care providers, depending on available resources)— followed by recommendations for appropriate interventions, deployed early in life or during the school years. Early intervention can help to positively modulate physiologic self-regulatory systems, including altered diurnal rhythms. However, if diagnosis in infancy or early childhood is not possible, diagnosis and appropriate recommendations should still be pursued at any age.

RECOMMENDATION TWO – *Advocate for healthy families*: Public health interventions and policies supporting pregnant women and families through

optimizing nutrition and food security, screening for substance exposure, supporting both harm reduction and addiction treatment, income and housing support, addressing intimate partner violence, and supporting positive parenting, have cumulative effects on the physiologic health of the infant, child, and adolescent within their community.

Core idea #2: Addressing sleep difficulties in FASD must combine an understanding of the neurodevelopmental consequences of FASD with a comprehensive understanding of developmental processes of sleep regulation. The neurobiology seen in FASD has developmental origins with consequences for behavioral and diurnal regulation. Rational treatment of disordered sleep in FASD must address day/night regulation, behavioral regulation, and biochemical regulation. Sleep is regulated by both circadian systems (regulated externally) and sleep/wake homeostatic systems (regulated internally). Sleep is also a developmental process for all, and principles of sleep training and support are equally important considerations for those with and without developmental disabilities[71,111].

RECOMMENDATION THREE – *Apply principles of sleep hygiene in the sleep management plan*: Classical principles of sleep hygiene are evidence-based principles and address the circadian and regulatory problems seen in individuals with FASD. These principles include stressing regular day and night routines and schedules, control of light exposure during the day and darkness at night, appropriately timed physical activity, and support for self-regulation of arousal and sleep[112]. External schedules should support the coordination of biological light

and temperature rhythms relating to sleep-wake patterns of hormonal secretion and regulation including melatonin and cortisol[112].

RECOMMENDATION FOUR – *Use melatonin appropriately with input of an experienced clinician*: Treatment with exogenous melatonin may be a rational part of a comprehensively developed sleep management plan for those with FASD[67,113]. Use of melatonin should be under the guidance of a clinician experienced in appropriate management and use.

RECOMMENDATION FIVE – *Consider sensory needs of the individual with FASD*: Atypical responses to sensory stimuli may need to be assessed and the environment appropriately modified for the needs of the child or older individual with FASD[21,113] For children, consultation with occupational therapists experienced in assessment and management of a child's sensory needs will contribute to a comprehensive understanding of the child's behavior and sleep. Strategies to support sensory needs may include appropriate changes to an affected individual's environment, modifying sensory stimuli, and self-regulation, in childhood and beyond[21,114]

Core idea #3: *Supporting the parent-child system*: In infancy, and the early childhood and school-age years, quality of the parent-child relationship and certain parent characteristics, especially attachment disorders and affect disorders in the parent (depression and anxiety), have significant and persisting influences on sleep[115]. Maternal depression mediates maternal-infant attachment, and attachment insecurity

has been strongly linked to disordered sleep in young children[116,117]. It has been elegantly observed by Charuvastra and Cloitre (2009) that "the capacity to self-regulate affect and to allow affect regulation by environmental cues and caregivers will contribute directly to a child's ability to initiate and maintain sleep, and reciprocally one of the functions of sleep is to restore the capacity for affective and behavioral self-regulation"[118]. Postnatal risk factors such as instability in the caregiving environment, often seen among those with FASD, can further challenge the parent-child system.

RECOMMENDATION SIX – *Screen for parental mood disorders*: Especially for infants and young children with FASD, screening for parental mood disorders both prenatally and postnatally offers the opportunity for positive intervention that may eventually have a long term impact on the child's sleep[119].

Core idea #4: Working with the family/caregiving environment and professional team: There is significantly increased prevalence of FASD among children in care[120], and stressors associated with raising individuals with FASD can be significant[29]. For individuals who have experienced trauma, particularly those with FASD whose biology may be adversely primed, standard behavioral sleep programs which assume typical capacity to self-regulate in response to treatment, may require modification[118].

RECOMMENDATION SEVEN – *Screen for attachment insecurity and advocate for safe environments*: Recognizing risk factors for attachment insecurity, such as multiple caregiver placements for children in care, and histories of trauma and

attachment disorder, offers further opportunity for intervention to improve sleep problems. This is especially true among those with FASD, who often have histories characterized by high levels of postnatal psychosocial risk. Advocacy for stable and safe environments for the affected individual and family will support emotional and behavioral sleep needs.

RECOMMENDATION EIGHT – *Advocate for appropriate caregiver support*: There is a significant need for caregiver support for sleep deprived parents caring for individuals with FASD, particularly in the early years[29,113]. Given the often complex behavioral and medical needs of those with FASD, sleep management plans are often more complex and take longer to implement. Ensuring that parents are receiving support and respite to address their needs is critical for them to effectively meet the needs of their individual with FASD.

CONCLUSIONS

An adequate amount of good quality sleep is fundamental to maximizing an individual's neurodevelopmental potential and overall well-being, and this is especially crucial in childhood. Youth with FASD experience high rates of often under recognized sleep difficulties that likely impact their daytime functioning— and certainly adversely affect family function. For these youth and their families, sleep difficulties have commonly been a chronic, debilitating problem leading to caregiving burden and stress. Treatment of pediatric sleep disorders for those with FASD can be complex, so a multifaceted, evidence informed, and integrated clinical care plan is needed. Ultimately,

identification and treatment of sleep disorders in those with FASD provides a feasible intervention target with high utility, given the possibility to improve functional outcomes, overall health, and quality of life of both the affected individual and the family[113].

REFERENCES

Chudley, A.E., Conry, J., Cook, J.L., et al. 2005. Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. *CMAJ.*172(5 Suppl):S1-S21.

Stratton, K., Howe, C., Battaglia, F. 1996 *Fetal alcohol syndrome: Diagnosis, epidemology, prevention and treatment.* Washington DC: National Academy Press.

Bertrand, J., Floyd, R., Weber, M., O'Connor, M., Johnson, K.A., Riley, E., Cohen, D.E. 2004. Fetal Alcohol Syndrome: Guidelines for referral and diagnosis. Atlanta, GA: Centers for Disease Control and Prevention.

Olson, H., Ohlemiller, M., O'Connor, M., Brown, C., Morris, C., Damus, K. 2009. A call to action: Advancing essential services and research on fetal alcohol spectrum disorders-a report of the national task force on fetal alcohol syndrome and fetal alcohol effect.

May, P.A., Gossage, J.P. 2001. Estimating the prevalence of fetal alcohol syndrome. A summary. *Alcohol Res Health.* 25(3):159-167.

Sampson, P.D., Streissguth, A.P., Bookstein, F.L., Little, R.E., Clarren, S.K., Dehaene, P., Hanson, J.W., Graham, J.M.,Jr. 1997. Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder. *Teratology.* 56(5):317-326.

May, P.A., Gossage, J.P., Kalberg, W.O., Robinson, L.K., Buckley, D., Manning, M., Hoyme, H.E. 2009. Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. *Dev Disabil Res Rev.* 15(3):176-192.

May, P.A., Baete, A., Russo, J., et al. 2014. Prevalence and characteristics of fetal

alcohol spectrum disorders. *Pediatrics.* 134(5):855-866.

Lange, S., Shield, K., Rehm, J., Popova, S. 2013. Prevalence of fetal alcohol spectrum disorders in child care settings: A meta-analysis. *Pediatrics.* 132(4):e980-995.

Riley, E.P., McGee, C.L. 2005. Fetal alcohol spectrum disorders: an overview with emphasis on changes in brain and behavior. *Exp Biol Med (Maywood).* 230(6):357-365.

Warren, K., Floyd, L., Calhoun, F., Stone, D., Bertrand, J., Streissguth, A. 2005. *Consensus statement on FASD. International statistical classification of diseases and related health problems.* Vol 10th Revision. 2nd ed ed. Geneva: World Health Organization.

Calhoun, F., Attilia, M.L., Spagnolo, P.A., Rotondo, C., Mancinelli, R., Ceccanti, M. 2006. National Institute on Alcohol Abuse and Alcoholism and the study of fetal alcohol spectrum disorders. The International Consortium. *Ann Ist Super Sanita.* 42(1):4-7.

Streissguth, A.P., Bookstein, F.L., Barr, H.M., Sampson, P.D., O'Malley, K., Young, J.K. 2004. Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. *J Dev Behav Pediatr.* 25(4):228-238.

Olson, H.C., Oti, R., Gelo, J., Beck, S. 2009. "Family matters:" fetal alcohol spectrum disorders and the family. *Dev Disabil Res Rev.* 15(3):235-249.

Popova, S., Lange, S., Burd, L., Rehm, J. 2012. Health care burden and cost associated with fetal alcohol syndrome: based on official Canadian data. *PLoS One.* 7(8):e43024.

Popova, S., Lange, S., Burd, L., Rehm, J.. 2015. Cost attributable to Fetal Alcohol Spectrum Disorder in the Canadian correctional system. *Int J Law Psychiatry.*

41:76-81.

Popova, S., Yaltonskaya, A., Yaltonsky, V., Kolpakov, Y., Abrosimov, I., Pervakov, K., Tanner, V., Rehm, J. 2014.What research is being done on prenatal alcohol exposure and fetal alcohol spectrum disorders in the Russian research community? *Alcohol Alcohol.* 49(1):84-95.

Lupton, C., Burd, L., Harwood, R. 2004. Cost of fetal alcohol spectrum disorders. *Am J Med Genet C Semin Med Genet.* 127C(1):42-50.

Popova, S., Lange, S., Burd, L., Chudley, A.E., Clarren, S.K., Rehm, J. 2013. Cost of fetal alcohol spectrum disorder diagnosis in Canada. *PLoS One.* 8(4):e60434.

Popova, S., Lange, S., Shield, K., Mihic, A., Chudley, A.E., Mukherjee, R.A.S., Bekmuradov, D., Rehm, J. 2016. Comorbidity of fetal alcohol spectrum disorder: a systematic review and meta-analysis. *Lancet.* 387(10022):978-987.

Wengel, T., Hanlon-Dearman, A.C., Fjeldsted, B. 2011. Sleep and sensory characteristics in young children with fetal alcohol spectrum disorder. *J Dev Behav Pediatr.* 32(5):384-392.

Ipsiroglu, O.S., McKellin, W.H., Carey, N., Loock, C. 2013. "They silently live in terror..." why sleep problems and night-time related quality-of-life are missed in children with a fetal alcohol spectrum disorder. *Soc Sci Med.* 79:76-83.

Honaker, S.M., Meltzer, L.J. 2015. Sleep in pediatric primary care: A review of the literature. *Sleep Med Rev.*

Chen, M.L., Olson, H.C., Picciano, J.F., Starr, J.R., Owens, J. 2012. Sleep problems in children with fetal alcohol spectrum disorders. *J Clin Sleep Med.* 8(4):421-429.

Robinson-Shelton, A., Malow, B.A. 2016. Sleep disturbances in neurodevelopmental disorders. *Curr Psychiatry Rep.* 18(1):6.

Kotagal, S., Broomall, E. Sleep in children with autism spectrum disorder. 2012. *Pediatr Neurol.* 47(4):242-251.

Cortese, S., Brown, T.E., Corkum, P., Gruber, R., O'Brien, L.M., Stein, M., Weiss, M., Owens, J. 2013. Assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 52(8):784-796.

Blackmer, A.B., Feinstein, J.A. 2016. Management of sleep disorders in children with neurodevelopmental disorders: A review. *Pharmacotherapy.* 36(1):84-98.

Bobbitt, S.A., Baugh, L.A., Andrew, G.H., Cook, J.L., Green, C.R., Pei, J., Rasmussen, C.R. 2016. Caregiver needs and stress in caring for individuals with fetal alcohol spectrum disorder. *Res Dev Disabil.* 55:100-113.

Rosett, H.L., Snyder, P., Sander, L.W., Lee, A., Cook, P., Weiner, L., Gould, J. 1979. Effects of maternal drinking on neonate state regulation. *Dev Med Child Neurol.* 21(4):464-473.

Scher, M.S., Richardson, G.A., Coble, P.A., Day, N.L., Stoffer, D.S. 1988. The effects of prenatal alcohol and marijuana exposure: disturbances in neonatal sleep cycling and arousal. *Pediatr Res.* 24(1):101-105.

Chernick, V., Childiaeva, R., Ioffe, S. 1983. Effects of maternal alcohol intake and smoking on neonatal electroencephalogram and anthropometric measurements. *Am J Obstet Gynecol.* 146(1):41-47.

Havlicek, V., Childiaeva, R., Chernick, V. 1977. EEG frequency spectrum characteristics of sleep states in infants of alcoholic mothers. *Neuropadiatrie.* 8(4):360-373.

Loffe, S., Childiaeva, R., Chernick, V. 1984. Prolonged effects of maternal alcohol ingestion on the neonatal electroencephalogram. *Pediatrics.* 74(3):330-335.

Ioffe, S., Chernick, V. 1988. Development of the EEG between 30 and 40 weeks gestation in normal and alcohol-exposed infants. *Dev Med Child Neurol.* 30(6):797-807.

Havlicek, V., Childaeva, R. 1976. E.E.G. component of fetal alcohol syndrome. *Lancet.* 2(7983):477.

Ioffe, S., Chernick, V. 1990. Prediction of subsequent motor and mental retardation in newborn infants exposed to alcohol in utero by computerized EEG analysis. *Neuropediatrics.* 21(1):11-17.

Troese, M., Fukumizu, M., Sallinen, B.J., et al. 2008. Sleep fragmentation and evidence for sleep debt in alcohol-exposed infants. *Early Hum Dev.* 84(9):577-585.

Pesonen, A.K., Raikkonen, K., Matthews, K., Heinonen, K., Paavonen, J.E., Lahti, J., Komsi, N., Lemola, S., Jarvenpaa, A.L., Kajantie, E., Strandberg, T. 2009. Prenatal origins of poor sleep in children. *Sleep.* 32(8):1086-1092.

Hilakivi, L. 1986. Effects of prenatal alcohol exposure on neonatal sleep-wake behaviour and adult alcohol consumption in rats. *Acta Pharmacol Toxicol (Copenh).* 59(1):36-42.

Hilakivi, L., Tuomisto, L., Hilakivi, I., Kiianmaa, K., Hellevuo, K., Hyytia,, P. 1987. Effect of prenatal alcohol exposure on neonatal sleep-wake behaviour and adult alcohol consumption in the AA and ANA rat lines. *Alcohol Alcohol.* 22(3):231-240.

Earnest, D.J., Chen, W.J., West, J.R. 2001. Developmental alcohol and circadian clock function. *Alcohol Res Health.* 25(2):136-140.

Allen, G.C., West, J.R., Chen, W.J., Earnest, D.J. 2005. Neonatal alcohol exposure permanently disrupts the circadian properties and photic entrainment of the activity rhythm in adult rats. *Alcohol Clin Exp Res.* 29(10):1845-1852.

Fukui, Y., Sakata-Haga, H. 2009.Intrauterine environment-genome interaction and children's development (1): Ethanol: a teratogen in developing brain. *J Toxicol Sci.* 34 Suppl 2:SP273-278.

Sakata-Haga, H., Dominguez, H.D., Sei, H., Fukui, Y., Riley, E.P., Thomas, J.D. 2006. Alterations in circadian rhythm phase shifting ability in rats following ethanol exposure during the third trimester brain growth spurt. *Alcohol Clin Exp Res.* 30(5):899-907.

Dubois, C., Houchi, H., Naassila, M., Daoust, M., Pierrefiche, O. 2008. Blunted response to low oxygen of rat respiratory network after perinatal ethanol exposure: involvement of inhibitory control. *J Physiol.* 586(5):1413-1427.

Agapito, M.A., Zhang, C., Murugan, S., Sarkar, D.K. 2014. Fetal alcohol exposure disrupts metabolic signaling in hypothalamic proopiomelanocortin neurons via a circadian mechanism in male mice. *Endocrinology.* 155(7):2578-2588.

Farnell, Y.Z., Allen, G.C., Nahm, S.S., Neuendorff, N., West, J.R., Chen, W.J., Earnest, D.J. 2008. Neonatal alcohol exposure differentially alters clock gene oscillations within the suprachiasmatic nucleus, cerebellum, and liver of adult rats. *Alcohol Clin Exp Res.* 32(3):544-552.

Dikranian, K., Qin, Y.Q., Labruyere, J., Nemmers, B., Olney, J.W. 2005. Ethanol-induced neuroapoptosis in the developing rodent cerebellum and related brain stem structures. *Brain Res Dev Brain Res.* 155(1):1-13.

Wilson, D.A., Masiello, K., Lewin, M.P., Hui, M., Smiley, J.F., Saito, M. 2016. Developmental ethanol exposure-induced sleep fragmentation predicts adult cognitive impairment. *Neuroscience.* 322:18-27.

Stone, W.S., Altman, H.J., Hall, J., Arankowsky-Sandoval, G., Parekh, P., Gold, P.E.

1996. Prenatal exposure to alcohol in adult rats: relationships between sleep and memory deficits, and effects of glucose administration on memory. *Brain Res.* 742(1-2):98-106.

Kervern, M., Dubois, C., Naassila, M., Daoust, M., Pierrefiche, O. 2009. Perinatal alcohol exposure in rat induces long-term depression of respiration after episodic hypoxia. *Am J Respir Crit Care Med.* 179(7):608-614.

Dubois, CJ, Kervern, M., Naassila, M., Pierrefiche, O. 2013. Chronic ethanol exposure during development: disturbances of breathing and adaptation. *Respir Physiol Neurobiol.* 189(2):250-260.

Verrier, V., Harper, R., Hobson, J. 2005. Cardiovascular physiology: central and autonomic regulation. In: Kryger T, Roth W, Dement, eds. *Principles and Practice of Sleep Medicine*. Maryland Heights, MO: Elsevier Saunders:192-202.

Spadoni, A.D., McGee, C.L., Fryer, S.L., Riley, E.P. 2007.Neuroimaging and fetal alcohol spectrum disorders. *Neurosci Biobehav Rev.* 31(2):239-245.

Rasmussen, C., Horne, K., Witol, A. 2006. Neurobehavioral functioning in children with fetal alcohol spectrum disorder. *Child Neuropsychol.* 12(6):453-468.

Chen, M.L., Witmans, M.B., Tablizo, M.A., Jubran, R.F., Turkel, S.B., Tavare, C.J., Keens, T.G. 2005. Disordered respiratory control in children with partial cerebellar resections. *Pediatr Pulmonol.* 40(1):88-91.

Wills, L., Swift, J., Moller, K. 2006. Craniofacial syndrome and sleep disorders. In: Lee-Chiong T, ed. *Sleep: a comprehensive handbook*: John Wiley and Sons.

Katz, E., Marcus, C. 2005. Diagnosis of obstructive sleep apnea syndrome in infants and children. In: Sheldon S, Ferber R, Kryger M, eds. *Principles and Practice of Pediatric Sleep Medicine*. Maryland Heights, MO: Elsevier Saunders:197-210.

Godin, E.A., Dehart, D.B., Parnell, S.E., O'Leary-Moore, S.K., Sulik, K.K. 2011. Ventromedian forebrain dysgenesis follows early prenatal ethanol exposure in mice. *Neurotoxicol Teratol.* 33(2):231-239.

Steinhausen, H.C., Spohr, H.L. 1998. Long-term outcome of children with fetal alcohol syndrome: psychopathology, behavior, and intelligence. *Alcohol Clin Exp Res.* 22(2):334-338.

Streissguth, A.P., Bookstein, F.L., Barr, H.M., Press, S., Sampson, P.D. 1998. A fetal alcohol behavior scale. *Alcohol Clin Exp Res.* 22(2):325-333.

Bhatara, V., Loudenberg, R., Ellis, R. 2006. Association of attention deficit hyperactivity disorder and gestational alcohol exposure: an exploratory study. *J Atten Disord.* 9(3):515-522.

Green, C.R., Mihic, A.M., Nikkel, S.M., Stade, B.C., Rasmussen, C., Munoz, D.P., Reynolds, J.N. 2009. Executive function deficits in children with fetal alcohol spectrum disorders (FASD) measured using the Cambridge Neuropsychological Tests Automated Battery (CANTAB). *J Child Psychol Psychiatry.* 50(6):688-697.

Stade, B., Khuu, M., Bennett, D., Sandor, P., Stephens, R., Lanceta, M. 2008. Sleep disturbances in children with fetal alcohol spectrum disorder (FASD). Paper presented at: Canadian Pediatric Society 85th Annual Conference; Victoria, BC.

Chen, M., Olson, H., Astley, S. 2006. Sleepless in Seattle: preliminary data suggesting sleep disorders in those with FASD. Research Society for Alcoholism, Fetal Alcohol Spectrum Disorders Study Group.

Goril, S., Zalai, D., Scott, L., Shapiro, C.M. 2016. Sleep and melatonin secretion abnormalities in children and adolescents with fetal alcohol spectrum disorders. *Sleep Med.* 23:59-64.

Owens, J.A., Spirito, A., McGuinn, M. 2000. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep.* 23(8):1043-1051.

Hanlon-Dearman A. *2003. Sleep Characteristics of Young Alcohol Affected Children: A Quantitative and Qualitative Analysis* [Masters of Science, Community Health Sciences]. Winnipeg, Manitoba: Community Health Sciences, University of Manitoba.

Lan, N., Chiu, M.P., Ellis, L., Weinberg, J. 2015. Prenatal alcohol exposure and prenatal stress differentially alter glucocorticoid signaling in the placenta and fetal brain. *Neuroscience*.

Wiggs, L. 2001. Sleep problems in children with developmental disorders. *J R Soc Med.* 94(4):177-179.

Wiggs, L., Stores, G. 1999. Behavioural treatment for sleep problems in children with severe learning disabilities and challenging daytime behaviour: effect on daytime behaviour. *J Child Psychol Psychiatry.* 40(4):627-635.

Berkman, J.M. 2006. Sleep in children with developmental disabilities. *Med Health R I.* 89(3):94-96.

Wiggs, L. 2009. Behavioural aspects of children's sleep. *Arch Dis Child.* 94(1):59-62.

Wiggs, L., Stores, G. 1996. Severe sleep disturbance and daytime challenging behaviour in children with severe learning disabilities. *J Intellect Disabil Res.* 40 (Pt 6):518-528.

Sung, V., Hiscock, H., Sciberras, E., Efron, D. 2008. Sleep problems in children with attention-deficit/hyperactivity disorder: prevalence and the effect on the child and family. *Arch Pediatr Adolesc Med.* 162(4):336-342.

Malow, B.A., Marzec, M.L., McGrew, S.G., Wang, L., Henderson, L.M., Stone, W.L. 2006. Characterizing sleep in children with autism spectrum disorders: a multidimensional approach. *Sleep.* 29(12):1563-1571.

Wiggs, L., Stores, G. 2004. Sleep patterns and sleep disorders in children with autistic spectrum disorders: insights using parent report and actigraphy. *Dev Med Child Neurol.* 46(6):372-380.

Sikora, D.M., Johnson, K., Clemons, T., Katz, T. 2012. The relationship between sleep problems and daytime behavior in children of different ages with autism spectrum disorders. *Pediatrics.* 130 Suppl 2:S83-90.

Mattson, S.N., Riley, E.P. 2000. Parent ratings of behavior in children with heavy prenatal alcohol exposure and IQ-matched controls. *Alcohol Clin Exp Res.* 24(2):226-231.

Astley, S.J., Olson, H.C., Kerns, K., Brooks, A., Aylward, E.H., Coggins, T.E., Davies, J., Dorn, S., Gendler, B., Jirikowic, T., Kraegel, P., Maravilla, K., Richards, T. 2009. Neuropyschological and behavioral outcomes from a comprehensive magnetic resonance study of children with fetal alcohol spectrum disorders. *Can J Clin Pharmacol.* 16(1):e178-201.

Chervin, R.D., Archbold, K.H. 2001. Hyperactivity and polysomnographic findings in children evaluated for sleep-disordered breathing. *Sleep.* 24(3):313-320.

Rosen, C.L., Palermo, T.M., Larkin, E.K., Redline, S. 2002. Health-related quality of life and sleep-disordered breathing in children. *Sleep.* 25(6):657-666.

Beebe, D.W. 2006. Neurobehavioral morbidity associated with disordered breathing during sleep in children: a comprehensive review. *Sleep.* 29(9):1115-1134.

Gottlieb, D.J., Vezina, R.M., Chase, C., Lesko, S.M., Heeren, T.C., Weese-Mayer, D.E.,

Auerbach, S.H., Corwin, M.J. 2003. Symptoms of sleep-disordered breathing in 5-year-old children are associated with sleepiness and problem behaviors. *Pediatrics.* 112(4):870-877.

O'Brien, L.M., Mervis, C.B., Holbrook, C.R., Bruner, J.L., Smith, N.H., McNally, N., McClimment, M.C., Gozal. 2004. Neurobehavioral correlates of sleep-disordered breathing in children. *J Sleep Res.* 13(2):165-172.

O'Connor, M.J., Paley, B. 2009. Psychiatric conditions associated with prenatal alcohol exposure. *Dev Disabil Res Rev.* 15(3):225-234.

Mansfield, D.R., Naughton, M.T. 2004. Sleep apnea and congestive heart failure. *Minerva medica.* 95(4):257-280.

Dahl, R.E. 1996. The impact of inadequate sleep on children's daytime cognitive function. *Semin Pediatr Neurol.* 3(1):44-50.

Gozal, D., Kheirandish-Gozal, L. 2007. Neurocognitive and behavioral morbidity in children with sleep disorders. *Curr Opin Pulm Med.* 13(6):505-509.

Sadeh, A. 2007. Consequences of Sleep Loss or Sleep Disruption in Children. *Sleep Medicine Clinics.* 2(3):513-520.

Anderson, B., Storfer-Isser, A., Taylor, H.G., Rosen, C.L., Redline, S. 2009. Associations of executive function with sleepiness and sleep duration in adolescents. *Pediatrics.* 123(4):e701-707.

Green, C.R., Roane, J., Hewitt, A., Muhajarine, N., Mushquash, C., Sourander, A., Lingley-Pottie, P., McGrath, P., Reynolds, J.N. 2014. Frequent behavioural challenges in children with fetal alcohol spectrum disorder: a needs-based assessment reported by caregivers and clinicians. *J Popul Ther Clin Pharmacol.* 21(3):e405-420.

Kodituwakku, P.W. 2009. Neurocognitive profile in children with fetal alcohol spectrum disorders. *Dev Disabil Res Rev.* 15(3):218-224.

Gioia, G., Ilsquith, P., Guy, S., Kenworthy, L. 2000. Behavior Rating Inventory of Executive Function. Odessa: FL: Psychological Assessment Resources, Inc.

McLachlan, K., Rasmussen, C., Oberlander, T.F., Loock, C., Pei, J., Andrew, G., Reynolds, J., Weinberg, J. 2016. Dysregulation of the cortisol diurnal rhythm following prenatal alcohol exposure and early life adversity. *Alcohol.* 53:9-18.

Olson, H.C., Jirikowic, T., Kartin, D., Astley, S. 2007. Responding to the challenge of early intervention for fetal alcohol spectrum disorders. *Infants & Young Children.* 2007;20(2):172-189.

Jenni, O.G., O'Connor, B.B. 2005. Children's sleep: an interplay between culture and biology. *Pediatrics.* 115(1 Suppl):204-216.

Brown, E.D., Low, C.M. 2008. Chaotic living conditions and sleep problems associated with children's responses to academic challenge. *J Fam Psychol.* 22(6):920-923.

Buckhalt, J.A., El-Sheikh, M., Keller, P. 2007. Children's sleep and cognitive functioning: race and socioeconomic status as moderators of effects. *Child Dev.* 78(1):213-231.

El-Sheikh, M., Buckhalt, J.A., Keller, P.S., Cummings, E.M., Acebo, C. 2007. Child emotional insecurity and academic achievement: the role of sleep disruptions. *J Fam Psychol.* 21(1):29-38.

Moore, P.J., Adler, N.E., Williams, D.R., Jackson, J.S. 2002. Socioeconomic status and health: the role of sleep. *Psychosom Med.* 64(2):337-344.

Meltzer, L.J., Mindell, J.A. 2007. Relationship between child sleep disturbances and maternal sleep, mood, and parenting stress: a pilot study. *J Fam Psychol.*

21(1):67-73.

White, C.P., White, M.B., Fox, M.A. 2009. Maternal fatigue and its relationship to the caregiving environment. *Fam Syst Health.* 27(4):325-345.

Doo, S., Wing, Y.K. 2006. Sleep problems of children with pervasive developmental disorders: correlation with parental stress. *Dev Med Child Neurol.* 48(8):650-655.

Hoffman, C., Sweeney, D., Lopez-Wagner, M., Hodge, D., Nam, C., Botts, B. 2008. Children with autism: sleep problems and mothers' stress. . *Focus on Autism and Other Developmental Disabilities.* 23(3):155-165.

Meltzer, L.J., Mindell, J.A.. 2006. Impact of a child's chronic illness on maternal sleep and daytime functioning. *Arch Intern Med.* 166(16):1749-1755.

Mindell, J.A., Durand, V.M. 1993. Treatment of childhood sleep disorders: generalization across disorders and effects on family members. *J Pediatr Psychol.* 18(6):731-750.

Leenaars, L.S., Denys, K., Henneveld, D., Rasmussen, C. 2012. The impact of fetal alcohol spectrum disorders on families: evaluation of a family intervention program. *Community Ment Health J.* 48(4):431-435.

Paley, B., O'Connor, M. J., Frankel, F., Marquardt, R. 2006. Predictors of stress in parents of children with fetal alcohol spectrum disorders. *J Dev Behav Pediatr.* 27(5):396-404.

Wiggs, L., France, K. 2000. Behavioural treatments for sleep problems in children and adolescents with physical illness, psychological problems or intellectual disabilities. *Sleep Med Rev.* 4(3):299-314.

Bathory, E., Tomopoulos, S.. 2017. Sleep regulation, physiology and development, sleep duration and patterns, and sleep hygiene in infants, toddlers, and preschool-age

children. *Curr Probl Pediatr Adolesc Health Care*.

Jan, J.E., Asante, K.O., Conry, J.L., Fast, D.K., Bax, M.C., Ipsiroglu, O.S., Bredberg, E., Loock, C.A., Wasdell, M.B. 2010. Sleep health issues for children with FASD: Clinical considerations. *Int J Pediatr.*.

Vasak, M., Williamson, J., Garden, J., Zwicker, J.G. 2015. Sensory processing and sleep in typically developing infants and toddlers. *Am J Occup Ther.* 69(4).

O'Connor, T.G., Caprariello, P., Blackmore, E.R., Gregory, A.M., Glover, V., Fleming, P., Alspac Study Team. 2007. Prenatal mood disturbance predicts sleep problems in infancy and toddlerhood. *Early Hum Dev.* 83(7):451-458.

Benoit, D., Zeanah, C.H., Boucher, C., Minde, K.K. 1992. Sleep disorders in early childhood: association with insecure maternal attachment. *J Am Acad Child Adolesc Psychiatry.* 31(1):86-93.

O'Connor, M.J., Sigman, M., Brill, N. 1987. Disorganization of attachment in relation to maternal alcohol consumption. *J Consult Clin Psychol.* 55(6):831-836.

Charuvastra, A., Cloitre, M. 2009. Safe enough to sleep: sleep disruptions associated with trauma, posttraumatic stress, and anxiety in children and adolescents. *Child Adolesc Psychiatr Clin N Am.* 18(4):877-891.

Pearson, R.M., Evans, J., Kounali, D., Lewis,G., Heron, J., Ramchandani, P.G., O'Connor, T.G., and Stein, A. 2013. Maternal depression during pregnancy and the postnatal period: risks and possible mechanisms for offspring depression at age 18 years. *JAMA Psychiatry.* 70(12):1312-1319.

Popova, S., Lange, S., Burd, L., Rehm, J. 2014. Canadian children and youth in care: The cost of Fetal Alcohol Spectrum Disorder. *Child Youth Care Forum.* 43:83-96.