Systematic Review Project Report: Understanding the Efficacy of Treatment of Sleep Disorders among Children with Neurodevelopmental Disabilities

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Practicum placement for the NeuroDevNet KT Core
For: Dr. Nazeem Muhajarine (field supervisor)
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**Aim of the Systematic Review Report**

As part of a practicum placement with the NeuroDevNet (NDN) Knowledge Translation (KT) Core, a systematic review of available literature on the efficacy of treatment of sleep disorders among children (ages 2-12) with neurodevelopmental disabilities (NDDs). However, due to a number of constraints and changes made by the working group for this project¹, this review has evolved into a somewhat different project that focuses exclusively on Fetal Alcohol Spectrum Disorder (FASD) and sleep. Consequently, this report will delineate the process used to conduct and assess relevant research, discuss its evolution as a project, as well as present available results and offer some suggestions for future actions.

**Rationale**

Children with neurodevelopmental disabilities (NDDs) have chronic conditions that will have an impact on the affected individual and their caregivers throughout the lifespan (Miller, Resky, & Armstrong, 2004). Consequently, it is crucial that “measures [be taken] to reduce the adverse impact of these chronic conditions on children’s health and on their families” (Miller et al., 2004, pp. 1366). In general, children with chronic health conditions are faced with more difficulties and challenges, and these differ from those faced by adults. For instance, Miller et al. (2004) indicate that disruptions in childhood are associated with problems in social/emotional development, education/learning, and behaviour. Furthermore, it must be acknowledged that the impact of chronic conditions is not confined to the individual—as noted above, they can also have and adverse effect on those who live and work with the child (Miller et al., 2004). Finally, the multiplicity and diversity of childhood chronic disorders can easily overwhelm primary physicians and other health-care practitioners, as they must navigate a complex path that includes

¹ The working group includes: Stacey McHenry (practicum student); Dr. Nazeem Muhajarine (field supervisor); Dr. Osman Ipsioglu (clinical consultant), with assistance from Me-Linh Le (health science librarian).
working with the child and family, as well as external institutions and systems such as education (Miller et al., 2004).

One area of functioning that has a major impact on both children and parents is sleep. Currently, very little information exists about the treatment and outcomes of sleep disorders among children (ages 2-12) with NDDs (Jan et al., 2008; Khan et al., 2011), such as Fetal Alcohol Spectrum Disorder (FASD) (Jan et al., 2010), Autism Spectrum Disorder (ASD) (Cortesi, Giannotti, Ivanenko, & Johnson, 2010), and Cerebral Palsy (CP) (Newman, O’Regan, & Hensey, 2006). This gap in the literature on the treatment of children with NDDs and sleep disorders is particularly problematic, as research indicates an increased prevalence of both parasomnias and dyssomnias amongst children with NDDs (Bruni & Novelli, 2010; Owens, 2008). However, due to the intricate relationship between the central nervous system (CNS) and sleep processes, the high rates of sleep disturbances among this population it is not surprising (Jan et al., 2008).

This is a particularly important issue to address, as the known poor outcomes of sleep disorders are vast and complex, often impacting multiple domains of functioning (e.g., mood, physical, cognition) (Owens, 2008). Moreover, children with NDDs are often born with existing neurodevelopmental “vulnerabilities” (Jan et al., 2008), which can be exacerbated by sleep disorders. In fact, Durmer and Dinges (2005) indicate that sleep deprivation has a negative effect on executive function (processes mediated by the prefrontal cortex) including “executive attention, working memory, and higher cognitive functions” (pp. 117), which are areas that are typically already impaired amongst children with NDDs. Sleep disorders can also disrupt functioning in other contexts. For instance, among older children, sleep problems can have a severe impact on academic performance (Dewald, Meijer, Oort, Kerkhof, & Bogels, 2010),
which may already be challenging due to other issues caused by NDDs. Another example is the finding that caregivers of younger children with NDDs and sleep disorders have been found to have higher levels of personal stress, resulting in increased dysfunction in the family functioning and the home environment (Herring et al., 2006). Together, this background provides a strong rationale for future study of the treatment of children with NDDs and sleep disorders.

**Research Question and Methods #1**

Using the PI[E]CO format (population, intervention/exposure, comparison, outcome) format that is often used to guide the development of research questions (Health-evidence.ca, 2006) the primary research question for this systematic review was: Does the treatment of sleep disorders among children (ages 2-12 years of age) with NDDs improve quality of life or sleep outcomes?

In this context, the NDDs of interest are those that are applicable specifically to the focus of NDN and include: Fetal Alcohol Spectrum Disorder (FASD), Cerebral Palsy (CP), Autism Spectrum Disorder (ASD); and NDDs in general.

**Process for Search**

The original framework for the search and review process was to (Health-evidence.ca, 2006): a) define the PI[E]CO; b) search for relevant evidence and store it in RefWorks (reference management database software); c) develop a relevance tool and appraise articles; d) develop a quality/critical appraisal tool and appraise articles; e) synthesize the results to determine if there are actionable messages; f) adapt the information considering how it would work in practice; and g) implement. However, thus far the systematic review has only reached phase C, with a plan in place for next step (quality/critical appraisal). This will be discussed in more detail throughout this report.
Literature Search Strategy

Working in consultation with the working group, a comprehensive search strategy for available literature was devised. The search terms utilized were combined as appropriate and included: This included using appropriate combinations of search terms: neurodevelopmental; disabilities; sleep; sleep disorder; sleep disturbance; child; treatment; fetal alcohol; prenatal alcohol; cerebral palsy; autism. Based on consultation with Ms. Le, it was determined that it was important to keep the search strategy broad in order to capture the limited evidence available.

The next piece of the search strategy involved a database search that included: ClinicalEvidence; Cochrane Library; PubMed; MEDLINE; EMBASE; CINAHL; PsycINFO; Web of Science, Scopus, ERIC, and Sociological Abstracts. In addition, a search of reference lists of key articles and a hand search process of key journals (e.g., Sleep, Sleep Medicine) were also conducted.

Results of literature search. The preliminary literature search of databases (n = 1733) and reference list/hand searching (n = 56) produced a total of n = 1789 articles. After duplicates were removed (n = 546), a total of 1243 articles remained and were saved to the RefWorks database.

Assessment of Studies Using Relevance and Quality/Critical Appraisal Tools

The relevance tool created for this study was constructed through collaboration between the student researcher, Dr. Muhajarine, and Dr. Ipsioglu. Table 1 provides the criteria used for the relevance assessment project. In order to be included in the study, it must meet all of the six criteria defined below.

Table 1: Study criteria for eligibility (inclusion/exclusion)

<table>
<thead>
<tr>
<th></th>
<th>Is the publication date of the study 2001 or later?</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td>Is the study written in English, French or German?</td>
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<tr>
<td>3</td>
<td>Is the study population comprised of individuals with: NDD, FASD, CP, or ASD?</td>
</tr>
<tr>
<td>4</td>
<td>Is the study based on human research?</td>
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<tr>
<td>5</td>
<td>Is the study design: clinical, epidemiological, genetic, imaging or pharmaceutical?</td>
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<tr>
<td>6</td>
<td>Did the study include one of the following outcomes: quality of life, improved sleep, pharmaceutical effect; daytime behaviours; psychological impact; adverse outcomes; or family functioning?</td>
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**Research Question and Methods #2**

Based on time constraints, the working group determined that the SR shift its focus to looking exclusively at the relationship between FASD and sleep disorders. Thus, the new research question became: Does the treatment of sleep disorders among children (ages 2-12 years of age) with FASD improve quality of life or sleep outcomes?

**Methods: SR of FASD Articles**

Rather than conducting an additional search, the RefWorks database was searched using key terms to find all articles pertaining to the specific topic of FASD. The key terms used to search RefWorks included: Fetal Alcohol (n = 141); Prenatal Alcohol (+4) (n =145); FAS (+7) (n = 152); Ethanol (+1) (n = 153); and Melatonin (+6) (n = 159). Thus, the total number of records available on the topic of FASD and related articles retrieved from RefWorks was 159.

**Relevance Assessment Process for FASD Articles**

The student researcher conducted the preliminary relevance assessment. Input from other members of the working group was also provided throughout. The process used to ascertain if the 159 FASD articles was a multistep process. The first step involved reviewing article abstracts to determine if they met relevance criteria (Table 1). If the article did not, it was placed in a “No” folder and coded according to why it was excluded. If the article may meet relevance assessment...
criteria, it was placed in a “Maybe” folder. Of the 159 abstracts reviewed, 133 did not fit the relevance criteria, and 26 were labeled as “Maybe”. Table 2 highlights the rationale for excluding the 133 FASD articles.

Table 2. Excluded FASD Abstracts and Rationale (n = 133)

<table>
<thead>
<tr>
<th># Articles</th>
<th>Reason for Exclusion (based on RA Tool)</th>
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<tbody>
<tr>
<td>23</td>
<td>Date</td>
</tr>
<tr>
<td>4</td>
<td>Language</td>
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<tr>
<td>24</td>
<td>Animal</td>
</tr>
<tr>
<td>4</td>
<td>Population (Pop)</td>
</tr>
<tr>
<td>40</td>
<td>Publication Type (Pub) or Review (Pub-Review)</td>
</tr>
<tr>
<td>5</td>
<td>Study Type (Study)</td>
</tr>
<tr>
<td>33</td>
<td>Outcome</td>
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</table>

The second step of the review process involved retrieving the full-text of articles labeled as “Maybe” and once again applying relevance assessment criteria. Those articles that met the relevance criteria were placed in a “Yes (FT)” folder (n = 3) and were to be included in the systematic review. Those that did not meet criteria were placed in a “No (FT)” folder (n = 10), and were coded according to why they were from the study. Studies that could be considered “Exceptions” were also placed in a folder (n = 13). These “exception” studies either did not meet all criteria or required further evaluation by the systematic review working group to determine inclusion or exclusion status.

Table 3. Excluded FASD FT and Rationale (n = 10)

<table>
<thead>
<tr>
<th># Articles</th>
<th>Reason for Exclusion (based on RA tool)</th>
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</table>

After consultation with a member of the working group, it was determined that all “exception” articles (n = 13) should be excluded from the study (were moved to “No (FT)”) and were coded for exclusion. The rationale for these decisions is provided in Table 4.

Table 4. Excluded FASD Exception Articles and Rationale (n = 13)

<table>
<thead>
<tr>
<th># Articles</th>
<th>Reason for Exclusion (based on RA tool)</th>
</tr>
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<tbody>
<tr>
<td>2</td>
<td>Date</td>
</tr>
<tr>
<td>8</td>
<td>Population (Pop)</td>
</tr>
<tr>
<td>3</td>
<td>Publication (Pub) or Review (Pub-Review)</td>
</tr>
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Results and Future Steps: The FASD and Sleep Consensus Paper Tables

The relevance assessment process produced only three articles that met each of the six relevance criteria. Consequently, the working group determined that it might be beneficial to change directions and focus on a new research product (other than a systematic review in a “traditional” sense). The decision was made to relax relevance criteria and reexamine articles as well as conducting a short supplementary search. The results of this new broader search could then be summarized, placed into tables, and included as part of consensus paper entitled “How to Approach Sleep Disorders in Children with FASD: The 1st Canadian FASD and Sleep Consensus Paper”. The tables were meant to shed light on all available research and supplement the consensus paper. This additional shift required a number of steps to reach its conclusion.
Methods #3: Consensus Paper

Changes to the relevance criteria meant that a reassessment of existing FASD articles must be completed and additional searching of databases, references or hand searching had to be included to ensure all available information was captured. The new relevance assessment criteria can be seen in Table 5.

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<table>
<thead>
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<tbody>
<tr>
<td>1</td>
<td>Is the article population focused on FASD or prenatal alcohol exposure?</td>
</tr>
<tr>
<td>2</td>
<td>Does the article address sleep-related issues?</td>
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</table>

Animal Studies Search

To begin, there were 24 articles from the original FASD database that had been coded as animal studies. An additional search, (including PubMed, Hand Search and Reference List searches) provided an additional 36 articles, for a total of 60. After eliminating articles that were coded as definitively “No” for inclusion, the student researcher and Dr. Ipsiroglu collaborated to determine that 14 animal studies were appropriate for inclusion in the Consensus Statement Tables.

Human Studies Search

In addition to the 135 remaining FASD article from the RefWorks database, 22 other studies were retrieved using PubMed, Hand Search and Reference List searches, for a total of 157 articles. The articles were reassessed using relaxed criteria, and 132 were labeled as “No.” The remaining articles were provided in full-text to Dr. Ipsiroglu for review, and 10 human studies were determined appropriate for the Consensus Statement Tables.

Does the treatment of sleep disorders among children (ages 2-12 years of age) with NDDs improve quality of life or sleep outcomes?
Results: Animal Studies

Tables 5, 6 and 7 provide a list of the 14 animal studies included in the draft consensus table. Note that these are still under review. The table includes information about authorship, study type, objectives, and results/implications. A complete reference list for these studies can be found in Appendix A of this document.
<table>
<thead>
<tr>
<th>Author</th>
<th>Type</th>
<th>Objectives</th>
<th>Results/Implications</th>
</tr>
</thead>
</table>
-Need to examine L/T effects of PAE on development/maintenance of circadian clock/rhythms  
-Understanding of mechanism could lead to possibility of improving symptoms |
| Allen, West, Chen, & Earnest (2004) | Original Article Experimental | Examine if neonatal exposure alters CRs of brain-derived neurotrophic factors (BDNF) content in suprachiasmatic nucleus (SCN) | -Exposure decreased levels BDNF in SCN, produced loss of circadian rhythmicity, lowered hippocampal levels of BDNF  
-BNDF key rhythmic output from SCN circadian clock  
-Exposure during period of rapid brain development can cause permanent changes in SCN circadian clock |
| Allen, West, Chen, & Earnest (2005) | Original Article Experimental | Examine L/T effects of neonatal exposure on circadian behavioural activity | -Found that neonatal exposure can produce permanent changes in circadian regulation of rat activity rhythm and Light/Dark (LD) cycles  
-Combining long-term alterations and changes in SCN (see above) may lead to greater understanding of sleep-wake disturbances, which could be extended to PAE neonates, children and adults |
-Provides information that could be extended from animal model to human studies in terms of mechanisms, genes, etc. Especially related to sleep-wake disturbances and hyper-responsiveness throughout lifespan. |
| Dubois, Houchi, Naassila, Datyest, & Pierrefiche (2008) | Original Article Experimental | Examine respiratory response by juvenile rats to hypoxia in vivo is related to depressed breathing | -Found: PAE during early development may be risk factor for newborn respiratory adaptive mechanisms to low oxygen environment  
-Impact of exposure should be considered when working with individuals with FASD and determining potential treatments and interventions |
Table 6. Consensus Paper FASD Animal Studies (Part 2)

<table>
<thead>
<tr>
<th>Author</th>
<th>Type</th>
<th>Objectives</th>
<th>Results/Implications</th>
</tr>
</thead>
</table>
| Farnell et al. (2008) | Original Article      | Examine if alterations to elements of CRs produce permanent damage to circadian timekeeping system or refigure molecular components | - Exposure during brain growth alters circadian regulation of molecular components of clock mechanism in SCN, cerebellum, and liver  
- Produces alterations in temporal configurations of “gears” of molecular clockwork  
- Could have substantial impact on L/T effects of neonatal exposure and regulation of CRs                                                                 |
| Farnell et al. (2004) | Experimental          | Examine if developmental alcohol exposure alters phase-shifting effects of light pulses on rat activity and circadian rhythm | - Found in other research that exposure produces L/T changes in regulation of circadian behaviour and entrainment of CRs to 24hr LD cycle (mediated by phase shifting or “resetting clock” – extension of this research  
- Developmental exposure to alcohol can alter phase-shifting responses to rat activity rhythm to light  
- When combined with findings from other animal studies, provides evidence for idea that exposure can permanently alter clock mechanism in SCN and regulation of circadian behavior |
| Fukui & Sakata-Haga (2009) | Experimental          | Examine if alcohol exposure impacts brain development on brain brain morphogenesis and CRs         | - Found PAE offspring had: ectopins on cerebral cortex; abnormal distribution of hippocampal mossy fibers and fusion of cerebellar folia.  
- Also has fragile synchronizing systems of CRs in adulthood.  
- Results have similar implications (impact of exposure on CRs) but examined specific brain regions affected by exposure                                                                 |
| Hilakivi (1986)       | Original Article      | Examine effect of PEA on neonatal sleep-wake behaviour and adult consumption of alcohol          | - Found: Exposed had less active sleep and more wakefulness (total sleep time recording); voluntary alcohol consumption of exposed rats was elevated  
- Suggests postnatal sleep activity and neurotransmitting systems that regulate it facilitate more SDs  
- Also suggests that same neurotransmitting systems that regulate sleep may contribute to increased alcohol during adulthood  
- Interesting that regulating systems may have multiple impacts (not just on sleep but on adult behaviour related to alcohol consumption) |
| Hilakivi et al. (1987) | Experimental          | Examine role of genetic factors in effects of PAE on behaviour                                    | - Found that genetic factors may be responsible for differences in susceptibility of rat fetuses to alcohol-induced long-term effects on SD and behaviour  
- Provides additional evidence for notion that PAE can alter regulatory processes, and that these persist into adulthood and have multiple effects (not just on sleep) |
Table 7. Consensus Paper FASD Animal Studies (Part 3)

<table>
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<tr>
<th>Author</th>
<th>Type</th>
<th>Objectives</th>
<th>Results/Implications</th>
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</thead>
</table>
| Sakata-Haga et al. (2006) | Original Article Experimental | Examine effects of alcohol exposure during 3rd trimester brain growth spurt on circadian clock | - Alcohol exposure in third trimester impacts ability to synchronize CRs to light cues  
- Disruptions in circadian regulation may cause abnormal behavioural rhythmicity (i.e., feeding or sleep patterns). These disruptions frequently found in FASD population. |
| Sakata-Haga, as reported in Guerri et al. (2005) | Review of Original Research | Overview of evidence about relationship between circadian system and PAE | - Exposed rats from all developmental stages suffered from fragile synchronizing system of CRs  
- Implications for Interventions: Environmental manipulations may be effective; exposed rats can maintain CRs under stable light conditions (vulnerable to changes); orderly life may diminish CR disruption; melatonin or light therapy may be viable treatment option for human FASD population  
- Better understanding (future research) on underlying mechanisms of fragile system could make it possible to alter and extend this type of research to the human population and increase treatment efficacy |
| Stone et al. (1996) | Original Article Experimental | Examine effect of PAE in adulthood | - Found: PAE results in selective and long-lasting sleep deficits/SDs; using paradoxical sleep as measure can predict memory impairment (characteristic of FASD); glucose may help decrease memory deficits related to alcohol exposure  
- One of few studies that specifically examines adult consequences, uses paradoxical sleep as measure, and discuses potential positive treatment effect of glucose |
| Earnest, Chen, & West (2001) | Review | Examines existing research on PAE and SD using animal models. Emphasis on regulation of CRs (and lack thereof among alcohol exposed rats | - Speculation and growing evidence that SCN (where circadian clock located) is directly affected by PAE  
- Evidence that damage to SCN can cause deregulation of circadian clock (and “timekeeping” function)  
- Research suggests that development exposure can interfere by producing short sleep-wake cycles and changes in release of specific neurochemicals (e.g., neuropeptides) by damaged SCN cells  
- Suggestion that the relationship between damage to SCN cells and system strongly related to behavioural and adaptive disorders in FASD population (including SDs) |
**Results: Human Studies**

Tables 8 and 9 provide a list of the 10 human studies included in the draft consensus table. Note that these are still under review. Each table includes information about authorship, type of study, study objectives, and results/implications. A complete list of reference for these studies can be found in Appendix B of this document.
<table>
<thead>
<tr>
<th>Author</th>
<th>Type</th>
<th>Study/ Objectives</th>
<th>Results / Implications</th>
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| Goril & Shapiro (2010) | Abstract           | Case-Series/Descriptive Examine prevalence of SD in children with FASD            | - Slow-wave sleep and wakefulness elevated, REM sleep decreased relative to norms  
- Some evidence for increased SD among pop  
- Did not include information on where “norms” obtained and used very small broad sample (n = 9), ages 5-18                                                                                      |
| Ipsiroglu et al. (2010)| Abstract           | Qualitative/Descriptive Needs assessment to created standardized survey/algorithm for children with FASD | - Analysis (caregivers, key workers, social workers, PhD/MD) provided information that allowed for preliminary development of screening tool for sleep disturbances.  
- Standardized version of screening tool could be implemented in national/international epidemiological study of FASD and SD among children                                                                 |
| Stade et al. (2008)    | Abstract           | Cross-Sectional Examine prevalence of SD in children with FASD                    | - Found SD in terms of sleep onset delay, sleep duration, and other sleep disturbances (i.e., frequent waking, night terrors, daytime fatigue)  
- Further evidence for high prevalence of SD  
- Highlights need for health practitioners and caregivers to have additional information about interventions                                                                 |
| Stade et al. (2010)    | Abstract           | Cross-Sectional Examine characteristic of sleep among Canadian children with FASD | - Extension of previous study (n = 100, vs. n = 325)  
- Replication produced similar results and has similar implications  
- Highlights need to move from theory to practice                                                                                                               |
| Pesonen et al. (2009)  | Original Article   | Cohort Study/Prospective Examine if small body size at birth or prenatal exposure to alcohol or tobacco associated with poor sleep or increased SD | - PEA 2.9x more likely to have short sleep and 3.6x more likely to have low sleep efficiency (at age 8)  
- Accounted for potential confounds (sex, gestational length, pre- / perinatal complications, BMI, asthma, allergies, SES)  
- Suggests poor sleep (short sleep duration and low sleep efficiency) related to prenatal conditions such as PAE  
- Future research could use methodology (strong) and including multiple measures to focus on PAE/FASD alone.                                                                 |
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<tr>
<th>Author</th>
<th>Type</th>
<th>Study/Objectives</th>
<th>Results/Implications</th>
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</table>
| Steinhausen & Shore (1996) | Original Article | Cohort- Prospective/Longitudinal Examine long-term outcomes of children with FAS (psychopathology, behaviour, learning) | -Rates of sleep disorders were significant in preschool period, and persisted to adolescence, with greatest prevalence/initiation in school period  
- Maternal alcohol consumption associated with increased (and multiple) psychiatric, behavioural and cognitive impairments that can negatively impact QOL  
- Some methodological issues (subsets and measures not consistent)  
- Could be basis of specific study with stronger methodology focusing on sleep and broaden study population to FASD                                                                                                                                 |
| Stone et al. (2010) | Original Article | Cohort - Prospective/Longitudinal Examine impact of maternal substance use on SD of children exposed to various substances (cocaine, opiates, marijuana, alcohol, nicotine) | - Inconsistent with all other related studies, found that only nicotine had significant positive correlation with sleep disturbances from birth to age 12  
- Requires in-depth analysis to determine if methodological issues, Measures, or possible confounds played a role in this contradictory finding                                                                                                                                 |
| Wengel et al. (2011) | Original Article | Case-Control Examine impact of sensory processing deficits on SD among children with FASD, as well as additional information about sleep in this population | - Vs. controls, PAE children have higher rates of SD overall and on all outcome measures (comprehensive) except sleep-disordered breathing  
- Vs. controls have significantly more sensory problems  
- “Pilot” study with small sample size, but significant results suggest the key role of sensory processing in SD in this population. Indicates that further research could assist with determination of more specific interventions (i.e., those that address sensory deficiencies) |
| Troese et al. (2008) | Original Article | Case-Series/Descriptive Examine relationship between PAE and SD amongst infants | - PAE correlated with: poor alertness, irritability, increased sleep fragmentation, decreased active sleep, increased sleep-related movements  
- Did not account for key confounds (i.e., 54% also used tobacco)  
- Calls for future research on relationship between PAE, SD, and sleep-related movements                                                                                                                                                                                                 |
| Jan et al. (2010)   | Review           | Clinical Observations/Expertise Concrete strategies for working with children with FASD | - Includes: sleep promotion activities, changes in sleep environment, preparing children for sleep, sleep scheduling, sleep hygiene for children and caregivers                                                                                                                                                                                                 |
Conclusions and Future Directions for the Systematic Review of the Efficacy of Treatment of Sleep Disorders Among Children with NDDs

This systematic review report has demonstrated the evolution of the systematic project from the onset to the end of the practicum. Not only did it showcase the methodological complexity of this type of project, it also revealed the need for flexibility when conducting research in this context. However, it has also provided information that could be valuable in a KT context, and after further review the Consensus Paper Tables may be a valuable supplement to the first Canadian consensus paper on FASD. The fact that this paper is being written, in and of itself, is a strong indicator that research on the topic of sleep disorders and FASD (and other NDDs) is required to fill the existing gap in the literature and it is hoped that this research project can contribute to that in some way.

In terms of the results, the focus of the animal studies tends to be on disruptions to the circadian rhythm system caused by prenatal alcohol exposure. These studies also aimed to identify the particular neurological mechanisms that were affected by alcohol during development and impacted sleep. For example, a number of studies focused on the impact of damage to the suprachiasmatic nucleus, a key element of the sleep system. Shifting to human studies, it appears that most available articles were descriptive in nature (e.g., prevalence, sleep characteristics among children with FASD). Another limitation of these studies is that many (n = 4) were abstracts rather than full published articles. However, well-crafted articles such as that by Wengel et al., (2011) that use a more rigorous design and provides evidence for the relationship between deficits in sensory processing (characteristic of FASD) and sleep disturbances suggest that this is about to change.
This project has also laid that groundwork for future research in this area. There is currently a database of over 1200 articles on topics relating to NDDs, CP, ASD, and FASD that can be accessed to extend this work into other specific disorders or into NDDs as a whole. Another project could be the completion of a systematic review that focuses only on FASD and reviewed only the 3 articles that met inclusion criteria in the original search strategy. A final suggestion might be to create summary tables (similar to those for the consensus paper) for each of the different populations address. This might be most effective if similar challenges arise in the analysis of data related to other disorders, and may be a useful way to integrate KT into the systematic review process. Although there is much research to be conduction on the efficacy of treatments for NDDs, this project has been a step in the right direction, highlighting the limitations, issues and successful approaches that may become relevant in future research on this project and those related to interventions in these populations in general.
References


http://www2.cochrane.org/reviews/en/protocol_16D1F96C82E26AA20020CBEFC2B00ABA.html


APPENDIX A
References for Animal Study Tables
References: Animal Studies


APPENDIX B
References for Human Study Tables
References: Human Studies


