STUDY PROTOCOL

Protocol Title

Effects of Parent-based Educational Programme for Sleep Problems in Children with Autism Spectrum Disorder: A Randomized Controlled Trial

Protocol Identifying Number: Version 2

Date: 8 May 2020

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Background Information

Sleep is important for healthy development for all children. Previous studies consistently documented that the prevalence rate of sleep problems in children with neuro-developmental disorders such as Autism Spectrum Disorder (ASD) are high (Corkum, Davidson, Tan-MacNeill, & Weiss, 2014; Richdale & Schreck, 2009). Common sleep problems including bedtime resistance, sleep-onset delay, nightwaking and early morning awakening were reported in 53% to 78% in children with ASD (Couturier et al., 2005; Krakowiak, Goodlin-Jones, Hertz-Picciotto, Croen, & Hansen, 2008). Sleep problems in young children were commonly reported across different nationalities and cultures (Lo, 2016; Mindell, Sadeh, Kohyama, & How, 2010). There were few published studies on the prevalence of sleep problems in children in Hong Kong. Ng et al. (2005) reported the prevalence of common sleep symptoms including sleep teeth grinding (20.5%), habitual snoring (10.9%), nocturnal enuresis (5.1%) and witnessed sleep apnea (1.5%) in a sample of 3,047 6- to12- year-old children. However, data on behavioral sleep problems were not collected. Tso et al. (2016) found that only 11% of preschoolers had the recommended 11-12 hours of sleep per day. Associations between sleep deprivation and lower school readiness, more hyperactivity and inattention, and less prosocial behavior were evident. A local study conducted by Doo and Yun investigated sleep problems in preschool children with Pervasive Developmental Disorders (PDD) (Doo & Wing, 2006). They reported that the prevalence of parent-defined sleep problems in various sleep domains ranged from 9.3 to 45.6%, with 67.9% of children having significant problems in at least one sleep domain. The most common problems reported were bedtime resistance and parasomnias.

Previous research has shown the negative impacts of sleep problems in children including typically developing children (Beebe, 2006) as well as specific groups of children with neuro-developmental disorders including ASD (Schneider, Lam, & Mahone, 2016). Analyses of data of three cross-sectional cohorts in a Canadian National Longitudinal Study showed that sleep problems were strong correlate of, and might exacerbate, child emotional and behavioral problem (Reid, Hong, & Wade, 2009). Turnbull and colleagues have done an extensive review on behavioral problems and development of executive functions (EF) in children with behavioral sleep problems (Turnbull, Reid, & Morton, 2013). They proposed that EF might be particularly vulnerable to the effects of these common childhood sleep problems: behavioral problems associated with common sleep problems suggested poor self-regulation in the context of sleep loss, and developing EF skills played important roles in self-regulation. Negative correlates of children's sleep problems identified included inattention and aggressive behavior (Lo, 2016), poor academic performance and bad conduct (Ng et al., 2005), and lower school readiness

(Tso et al., 2016) in samples of Chinese children. On the other hand, child's poor sleep habits were found to bring negative impacts to their parents as well. Parental stress was one of the common outcomes related to children sleep problems (Meltzer & Mindell, 2007). Parents of children with ASD were also known to have challenges in maintaining a positive sense of well-being and self-efficacy (Kuhn & Carter, 2006). There was one study suggesting that the improvement in child's sleep habits relates with improvement in parental sense of competence and satisfaction (Malow et al., 2014).

Previous literature showed that sleep-focused behavioral interventions could result in lasting beneficial effects on sleep with minimal adverse effects (Malow et al., 2012; Meltzer & Mindell, 2007; Vriend, Corkum, Moon, & Smith, 2011). However, few treatment studies have measured changes or improvements in daytime functioning of children with ASD, or mainly based on parent's report as outcome measures of sleep treatment (Turnbull et al., 2013). Data obtained in this RCT would contribute valuable information to the academic knowledge, and propose important implication for relevant treatment to children with ASD.

Study Objective and Purpose

The objective of the current study is to conduct a randomized controlled trial (RCT) for children with ASD, in order to examine the effectiveness of a Parent-based Sleep Educational Programme, with outcomes of parent-report measures and child's performance on tasks involving executive functions. It is hypothesized that parents' sleep quality and child's sleep problems would be improved in the Treatment Group, as compared to Waitlist Treatment-As-Usual (TAU) control. As secondary outcomes, it is hypothesized that parents in the Treatment Group would show improvement in mood, quality of life, parenting stress and competence; while children in the Treatment Group would show improvement in executive functions and daytime functioning.

Study Design

The study is a randomized controlled trial (RCT) aiming to examine the effectiveness of a Parent-based Sleep Educational Programme. Target participants to be recruited are paediatric patients (aged 3 to 6 years old) with a clinical diagnosis of ASD, and their parent (aged 21 or above), who are attending paediatric developmental clinic or clinical psychology service at the Duchess of Kent Children's Hospital at Sandy Bay.

Data on patients' and the family's demographic information will be obtained from the parents. Parent of patients will be invited to complete a set of questionnaires on the child's demographic information and measures on their child including sleep pattern and

sleep problems (Child's Sleep Habits Questionnaire, CSHQ), executive functions (Behavior Rating Inventory of Executive Function – Preschool Version, BRIEF-P) and behavioral and emotional problems (Strengths and Difficulties Questionnaire, SDQ). Parents will also be asked to report their own quality of life (The 12-item Short Form Health Survey, SF-12v2), sleep quality (Insomnia Severity Index, ISI; The Pittsburgh Sleep Quality Index, PSQI), mood symptoms (Depression, Anxiety and Stress Scale - 21 Items, DASS), parental stress level (Parental Stress Scale, PSS), and their sense of competence and satisfaction in childcare (Parenting Sense of Competence Scale, PSOC). Moreover, patients will be assessed using standardized tests on executive functions (Bug Search and Picture Memory Subtests from WPPSI-IV(HK), Statue subtest from NEPSY-2, and Conners K–CPT 2.

Participants will then be randomly assigned into either Treatment Group or Waitlist Group. Parents and Children in both the Treatment Group and Waitlist Group will be interviewed individually by Clinical Psychologist (CP) (Week 0). Parent's specific concerns on the child's sleep issues will be explored. For parents in the Treatment Group, they will receive a Parent Sleep Educational Programme which consists of three weekly group sessions (Week 1-3) conducted by a CP on behavioral intervention for sleep problems. Programme content takes reference from materials developed by the HKU Sleep Research Clinic and Laboratory ("Empowering Parents to Help Children Sleep Better: Parent-based Sleep Education for Children with Autism Spectrum Disorders," 2018) and evidence-based sleep educational materials from the relevant literature (Allen, Howlett, Coulombe, & Corkum, 2016; Autism Speaks Autism Treatment Network, 2019; Yu et al., 2015). Bi-weekly individual telephone support sessions will be conducted by a CP to support the parents and trouble-shoot the difficulties that parents may encounter when implementing the behavioural strategies to manage their child's sleep problems (at Week 1, 3, 5 and 7). For children and parents in the Waitlist Group, they will be placed on waitlist while children continue to receive treatment-as-usual from multidisciplinary team of DKCAC (Paediatrician, Physiotherapist, Occupational Therapist, Speech Therapist, Social Worker etc.) and other available services in the community.

Post-intervention review and assessment at Week 8-10 would be conducted with all parents and children (Treatment Group, Waitlist Group) by CP. Parents will be asked to fill in the same set of questionnaires measures; re-assessment on the standardized tests will also be conducted with the children. Parents in the Treatment Group will also be asked to fill in a post-intervention feedback survey. Parents in the Waitlist group will then be invited to join a Parent Sleep Educational Programme starting from Week 12.

Lastly, a 6-month post-intervention assessment (all instruments and standardized tests) would be conducted for parents and children in the Treatment Group.

Figure 1 shows a schematic diagram of the study design and flowchart.

Outcome Measures

Child-related Measures:

Measure of Sleep

The Children's Sleep Habit Questionnaire (CSHQ) is a parent-report questionnaire designed to assess common sleep problems in children. The 33-item CSHQ evaluates the child's sleep based on behavior within eight different subscales: bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep-disordered breathing, and daytime sleepiness. Parents give responses from a scale of 1-3, with 3 indicating "usually", 2 indicating "sometimes" and 1 indicating "rarely". The scores are added up and a total score of 41 makes an effective cut-off for screening purposes as it correctly identified 80% of the clinical sample in the developers' initial psychometric study. Internal consistency, test-retest reliability, sensitivity and specificity have been demonstrated.

Measure of Emotional and Behavioural Problems

The Strengths and Difficulties Questionnaire (SDQ) is a 25-item screening measure for emotional and behavioral problems in children and adolescents ages 2 to 3, and 4 to 17. It rated on a Likert-type scale and equally divided into five subscales: emotional symptoms, conduct problems, hyper-activity-inattention, peer problems, and prosocial behavior. The sum of the four subscales generates a total difficulties score. Validated Chinese version is available, with satisfactory reliability.

Cognitive Performance

The Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P) consists of 63 items that measure various behavioral manifestations of EF based on parent or teacher ratings, within the context of the child's everyday environment, in children ages 2 to 5 years old.25 The BRIEF-P covers the scales inhibit (I), shift (S), emotional control (EC), working memory (WM), and plan/organize (PO). These scales form three broad indexes: inhibitory self-control (ISC), flexibility (F), and emergent metacognition (EM), as well as one composite score, the global executive composite (GEC). The scale demonstrated high internal consistency reliability and moderate test-retest reliability

The Wechsler Preschool and Primary Scale of Intelligence™ - Fourth Edition (Hong Kong) (WPPSI-IV(HK)) is a measure of cognitive development for preschoolers and young children that's rooted in contemporary theory and research that also places a strong emphasis on child-friendly, developmentally appropriate features and includes new processing speed tasks, the addition of working memory subtests, an expanded factor structure. The Hong Kong edition, published in 2018, is locally validated with local norms. In the Bug Search subtest, children will be asked to use an ink dauber to mark the image of a bug in the search group that matches the target bug. Bug search is conceptually similar to Symbol Search, which involves short-term visual memory, visual-motor coordination, cognitive flexibility, visual discrimination, and concentration. In the Picture Memory Subtest, children will be asked to view a stimulus page of pictures for a specified time, then selects theses pictures from options on a response page. This subtest taps children's visual working memory using the familiarize-recognize paradigm.

The NEPSY-II consists of 32 subtests for use in a neuropsychological assessment with preschoolers, children, and adolescents. The Statue Subtest is designed to assess motor persistence and inhibition for children aged 3- to 6-year-old. Children will be asked to maintain a body position with eyes closed during a 75 second period and to inhibit the impulse to respond to sound distracters.

The Conners Kiddie Continuous Performance Test 2nd Edition™ (Conners K-CPT 2™) assesses attention and inhibition in children ages 4 to 7 years old. Children will be instructed to press the keyboard space bar when target pictures are presented, while inhibiting their response when a specific picture (ball) is presented. Each child's responses would be scored and resulted in performance in four aspects of attention: Inattentiveness, Impulsivity, Sustained Attention, and Vigilance.

Parent-related Measures:

Measures of Sleep

The Pittsburg Sleep Quality Inventory (PSQI) is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval. Nineteen individual items generate seven "component" scores including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The sum of the seven component scores yields one global score, which is used to distinguish good and poor sleepers. Evidence of internal homogeneity, consistency (test-retest reliability), and validity have been demonstrated.

The Insomnia Severity Index (ISI) is a self-rated seven-item questionnaire which asks respondents to rate the nature and symptoms of their sleep problems using a Likert-type scale. The questions relate to subjective qualities of the respondent's sleep, including the severity of symptoms, the respondent's satisfaction with his or her sleep patterns, the degree to which insomnia interferes with daily functioning, how noticeable the respondent feels his or her insomnia is to others, and the overall level of distress created by the sleep problem. Respondents rate each question from 0 to 4, where higher scores indicate more severe symptoms of insomnia. A total score of 0–7 indicates "no clinically significant insomnia," 8–14 indicates "subthreshold insomnia," 15–21 is "clinical insomnia (moderate severity)," and 22–28 indicates "clinical insomnia (severe)." Validity and test-retest reliability has been demonstrated.

Measure of Mood Symptoms and Stress

The Depression Anxiety Stress Scale (DASS-21) is a set of three self-report scales designed to measure the emotional states of depression, anxiety and stress. The Depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia, and inertia. The Anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The Stress scale is sensitive to levels of chronic non-specific arousal and assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient. Parents will be asked to use 4-point severity/frequency scales to rate the extent to which they have experienced each emotion state during the past week. Scores for Depression, Anxiety and Stress scales are calculated by summing the scores for the relevant items. High internal consistency and validity have been demonstrated. The Chinese version which we will use has been validated.

The Parental Stress Scale (PSS) in Chinese is a self-report scale developed by Cheung (2000) based on the Parental Stress Scale developed by Berry and Jones (1995). It measures the level of stress experienced by parents, considering both positive and negative aspects of parenting. It contains 17 items representing pleasure or positive themes of parenthood (emotional benefits, self-enrichment, personal development) and negative components (demands on resources, opportunity costs and restrictions). Respondents are asked to agree or disagree with items in terms of their typical relationship with their child or children and to rate each item on a five-point scale: strongly disagree, disagree, undecided, agree, and strongly agree. The 8 positive items are reverse scored so that possible scores on the scale can range between 18-90. Higher scores on the scale indicate greater stress. The Parental Stress Scale demonstrated

satisfactory levels of internal reliability, and test-retest reliability.

Measures of Quality of Life and Parental Competence

The 12-item Short Form Health Survey (SF-12v2) is a locally validated measure of health-related quality of life (HRQOL) that has been shown to be valid, reliable and sensitive in Chinese adults and adolescents. It consists of 12 items that cover 8 subscales, namely physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). The eight subscale scores can be aggregated into a physical component summary (PCS) score and a mental component summary (MCS) score. Each of the eight SF-12v2 subscale has a scoring range from 0 to 100; a higher score indicates better HRQOL. The PCS and MCS scoring are norm-based with 50 and 10 being the Hong Kong general population mean and standard deviation, respectively.

The Parenting Sense of Competence scale (PSOC) measures parental competence on two dimensions: Satisfaction and Efficacy. It is a 16 item Likert-scale questionnaire (on a 6-point scale ranging from strongly agree [1] to strongly disagree [6]), with nine questions under Satisfaction and seven under Efficacy. Satisfaction section examines the parents' anxiety, motivation and frustration, while the Efficacy section looks at the parents' competence, capability levels, and problem-solving abilities in their parental role.

Study Criteria

Inclusion criteria: Parents/caregivers (aged 21 or above) of preschool children (aged 3 to 6 years old) with a clinical diagnosis of ASD attending paediatric developmental clinic or clinical psychology service at the Duchess of Kent Child Assessment Centre (DKCAC) will be recruited. The clinical diagnosis of ASD would be made by either a Pediatrician or a Clinical Psychologist, using at least one of the following diagnostic tools: Childhood Autism Rating Scale, Second Edition (CARS-2), Autism Diagnostic Observation Schedule, Second Edition (ADOS-2), Autism Diagnostic Interview-Revised (ADI-R) and clinical interview based on diagnostic criteria of ASD depicted in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).

Exclusion criteria: Parent/caregiver of children with diagnosed co-morbid neurological, psychiatric or medical conditions which could have affected their sleep, such as obstructive sleep apnea, epilepsy, childhood anxiety disorder will be excluded.

Statistics

With a priori power analysis for multi-variate analysis of variance (MANOVA) with repeated measures, at an estimated effect size of 0.25, with projected power of 0.8 at the 0.05 error level, the sample size required would be 66. For the current study, around 80 subjects are planned to be recruited based on the estimated number of patients following-up at Duchess of Kent Child Assessment Centre (DKCAC), and the optimal sample size comparable with similar studies conducting RCT with an estimated attrition rate of 10%. Descriptive statistics will be calculated for parent and child characteristics. Categorical variables will be presented as observed frequencies and proportions. Correlational analyses, multivariate analyses of variance (within-subject, between group, mixed) will be conducted. All analyses will be conducted with .05 as level of statistical significance.

Ethics

The current study based on self-reporting questionnaires and commonly used assessment tasks that will pose no harm to the participating subjects.

Data Handling and Record Keeping

All the personal data will be handled and stored by the principal investigator in a safe database server under the participating institute. Paper questionnaires would be stored in a locked cabinet in the participating institute. The principal investigator, the co-investigators and supervisor are responsible for the personal data during and after the study. The data containing personal identifiers be kept for 10 years after publication of the first paper arising from the research project. Anonymized data be kept for 20 years after publication of the first paper arising from the research project.

Financing and Insurance

This is a non-funded project.

Publication Policy

After the analysis of the study findings we aim to have this original study written up in a paper for publication to share the result.

Appendix: Figure 1

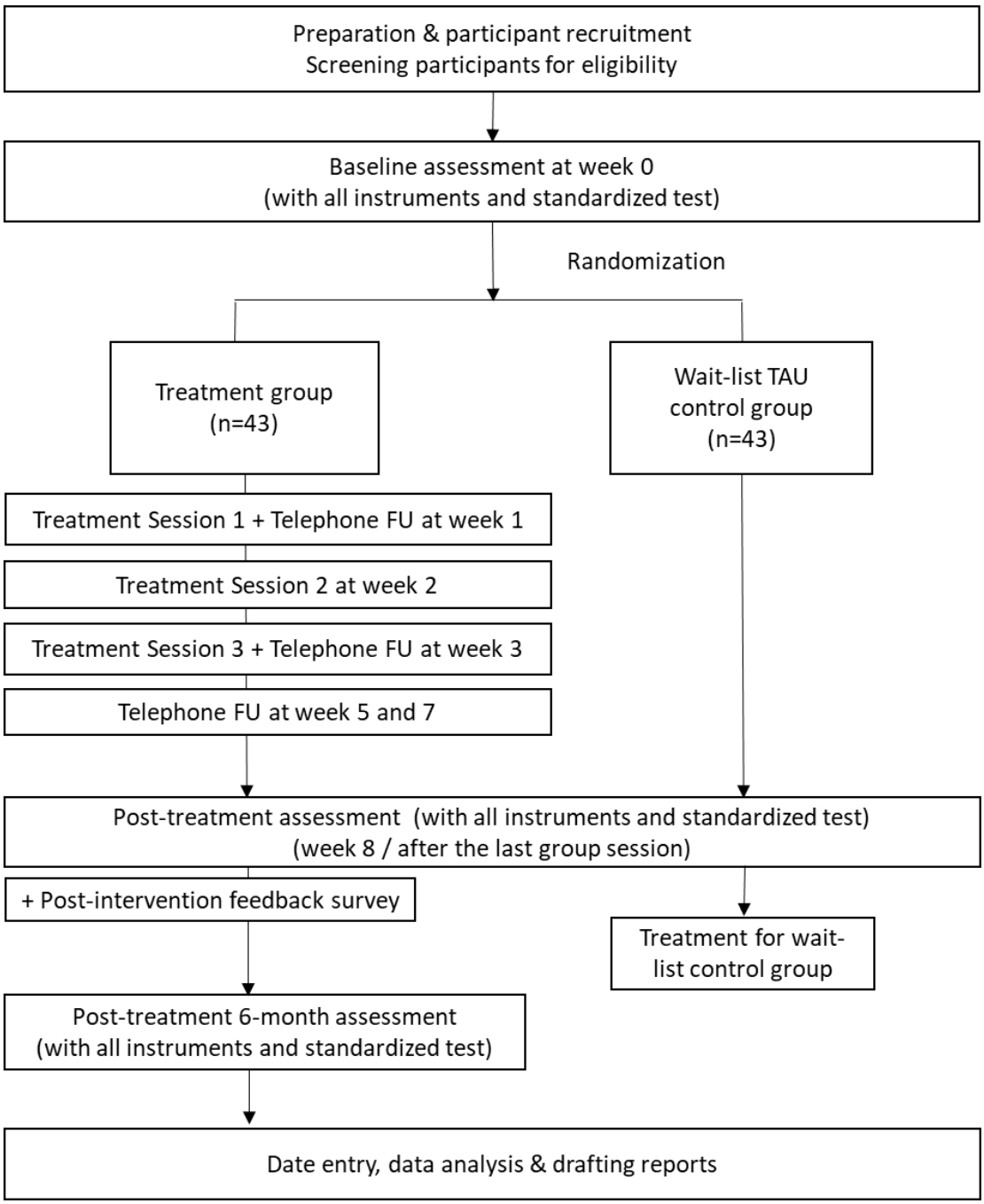

Figure 1. Schematic diagram of the study design and flowchart

References

Allen, S. L., Howlett, M. D., Coulombe, J. A., & Corkum, P. (2016). ABCs of SLEEPING: a review of the evidence behind pediatric sleep practice recommendations. *Sleep medicine reviews, 29*, 1-14.

Autism Speaks Autism Treatment Network, A.-A. (2019). Strategies to Improve Sleep in Children with Autism Spectrum Disorders - a Parent's Guide. Retrieved from https://www.autismspeaks.org/tool-kit/atnair-p-strategies-improve-sleep-children-autism

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

Berry, J. O., & Jones, W. H. (1995). The parental stress scale: Initial psychometric evidence. *Journal of Social and Personal Relationships, 12*(3), 463-472.

Cheung, S.-K. (2000). Psychometric Properties of the Chinese Version of The Parental Stress Scale. *Psychologia, 43*, 253-261.

Corkum, P., Davidson, F. D., Tan-MacNeill, K., & Weiss, S. K. (2014). Sleep in children with neurodevelopmental disorders: a focus on insomnia in children with ADHD and ASD. *Sleep Medicine Clinics, 9*(2), 149-168.

Couturier, J. L., Speechley, K. N., Steele, M., Norman, R., Stringer, B., & Nicolson, R. (2005). Parental perception of sleep problems in children of normal intelligence with pervasive developmental disorders: prevalence, severity, and pattern. *Journal of the American Academy of Child Adolescent Psychiatry, 44*(8), 815-822.

Doo, S., & Wing, Y. K. (2006). Sleep problems of children with pervasive developmental disorders: correlation with parental stress. *Developmental medicine child neurology, 48*(8), 650-655.

Empowering Parents to Help Children Sleep Better: Parent-based Sleep Education for Children with Autism Spectrum Disorders. (2018). Retrieved from http://www.psychology.hku.hk/sleep/asd/index.html

Krakowiak, P., Goodlin-Jones, B., Hertz-Picciotto, I., Croen, L. A., & Hansen, R. L. (2008). Sleep problems in children with autism spectrum disorders, developmental delays, and typical development: a population-based study. *Journal of sleep research, 17*(2), 197-206.

Kuhn, J. C., & Carter, A. S. (2006). Maternal self-efficacy and associated parenting cognitions among mothers of children with autism. *American Journal of Orthopsychiatry, 76*(4), 564-575.

Lo, M.-J. (2016). Relationship between Sleep Habits and Daytime Sleepiness, Inattention, and Aggressive Behavior among Taiwanese Kindergarten Children. *Clinics Mother Child Health, 13*(247), 2.

Malow, B. A., Adkins, K. W., Reynolds, A., Weiss, S. K., Loh, A., Fawkes, D., . . . Clemons, T.

(2014). Parent-based sleep education for children with autism spectrum disorders. *J Autism Dev Disord, 44*(1), 216-228. doi:10.1007/s10803-013-1866-z

Malow, B. A., Byars, K., Johnson, K., Weiss, S., Bernal, P., Goldman, S. E., . . . Glaze, D. G. (2012). A practice pathway for the identification, evaluation, and management of insomnia in children and adolescents with autism spectrum disorders. *Pediatrics, 130*(Supplement 2), S106-S124.

Meltzer, L. J., & Mindell, J. A. (2007). Relationship between child sleep disturbances and maternal sleep, mood, and parenting stress: a pilot study. *Journal of Family Psychology, 21*(1), 67.

Mindell, J. A., Sadeh, A., Kohyama, J., & How, T. H. (2010). Parental behaviors and sleep outcomes in infants and toddlers: a cross-cultural comparison. *Sleep medicine, 11*(4), 393-399.

Ng, D. K., Kwok, K.-l., Cheung, J. M., Leung, S.-y., Chow, P.-y., Wong, W. H., . . . Ho, J. C. (2005). Prevalence of sleep problems in Hong Kong primary school children. *Chest, 128*(3), 1315-1323.

Reid, G. J., Hong, R. Y., & Wade, T. (2009). The relation between common sleep problems and emotional and behavioral problems among 2-and 3-year-olds in the context of known risk factors for psychopathology. *Journal of sleep research, 18*(1), 49-59.

Richdale, A. L., & Schreck, K. A. (2009). Sleep problems in autism spectrum disorders: prevalence, nature, & possible biopsychosocial aetiologies. *Sleep medicine reviews, 13*(6), 403-411.

Schneider, H. E., Lam, J. C., & Mahone, E. M. (2016). Sleep disturbance and neuropsychological function in young children with ADHD. *Child neuropsychology, 22*(4), 493-506.

Tso, W., Rao, N., Jiang, F., Li, A. M., Lee, S.-l., Ho, F. K.-w., . . . Ip, P. (2016). Sleep duration and school readiness of Chinese preschool children. *The Journal of pediatrics, 169*, 266-271.

Turnbull, K., Reid, G. J., & Morton, J. B. (2013). Behavioral Sleep Problems and their Potential Impact on Developing Executive Function in Children. *Sleep, 36*(7), 1077-1084. doi:10.5665/sleep.2814

Vriend, J., Corkum, P., Moon, E., & Smith, I. (2011). Behavioral interventions for sleep problems in children with autism spectrum disorders: current findings and future directions. *J Pediatr Psychol, 36*(9), 1017-1029. doi:10.1093/jpepsy/jsr044

Yu, X., Lam, H., Au, C., Chan, S., Chan, D., & Li, A. (2015). Extended parent-based behavioural education improves sleep in children with autism spectrum disorder. *Hong Kong J Ped, 20*, 219-225.