Sleep Medicine 38 (2017) 130–134

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Brief Communication

Sleep phenotypes in infants and toddlers with neurogenetic syndromes

Emily A. Abel [a], Bridgette L. Tonnsen [b, *]

[a] Department of Human Development and Family Studies, Purdue University, West Lafayette, IN, USA
[b] Department of Psychological Sciences, Purdue University, West Lafayette, IN, USA

ARTICLE INFO

Article history:
Received 12 May 2017
Received in revised form
18 July 2017
Accepted 21 July 2017
Available online 1 August 2017

Keywords:
Sleep
Angelman syndrome
Williams syndrome
Prader–Willi syndrome
Infants

ABSTRACT

Background: Although sleep problems are well characterized in preschool- and school-age children with neurogenetic syndromes, little is known regarding the early emergence of these problems in infancy and toddlerhood. To inform syndrome-specific profiles and targets for intervention, we compared parent-reported sleep problems in infants and toddlers with Angelman syndrome (AS), Williams syndrome (WS), and Prader–Willi syndrome (PWS) with patterns observed among same-aged typically developing (TD) controls.

Methods: Mothers of 80 children (18 AS, 19 WS, 19 PWS, and 24 TD) completed the Brief Infant Sleep Questionnaire. Primary dependent variables included (1) sleep onset latency, (2) total sleep duration, (3) daytime and nighttime sleep duration, and (4) sleep problem severity, as measured by both maternal impression and National Sleep Foundation guidelines.

Results: Sleep problems are relatively common in children with neurogenetic syndromes, with 41% of mothers reporting problematic sleep and 29% of children exhibiting abnormal sleep durations as per national guidelines. Across genetic subgroups, problems are most severe in children with AS and WS, particularly in relation to nighttime sleep duration. Although atypical sleep is characteristically reported in each syndrome later in development, infants and toddlers with PWS exhibited largely typical patterns, potentially indicating delayed onset of sleep problems in concordance with other medical features of PWS.

Conclusions: Our findings suggest that sleep problems in neurogenetic syndromes emerge as early as infancy and toddlerhood, with variable profiles across genetic subgroups. This work underscores the importance of early sleep screenings as part of routine medical care of neurosyndromic populations and the need for targeted, syndrome-sensitive treatment.

1. Introduction

Children with neurogenetic syndromes are at high risk for comorbid sleep problems, including increased sleep latency, frequent and prolonged night waking, and short sleep duration [1]. Sleep problems in preschool- and school-age children with neurogenetic syndromes have been well documented, occurring in up to 86% of children [2], and are known to impact child behavior [3] and parental stress [4]. In healthy developing infants, sleep problems have been associated with a number of negative outcomes including impaired cognitive development [5], emotion dysregulation [6], and attention problems [7]. However, despite the pervasive rates of sleep problems and debilitating impact of sleep on child and family functioning, few studies have examined sleep problems in neurogenetic syndromes during infancy and early childhood. The paucity of research in this area substantially limits our knowledge of when and how sleep problems emerge, constraining targeted and effective early treatment options.

To address this need, the present study evaluated parent-reported sleep problems in infants and toddlers with three low-incidence neurogenetic syndromes, namely Angelman syndrome (AS; prevalence 1:10,000–20,000 [8]), Prader–Willi syndrome (PWS; 1:7500–10,000 [8]), and Williams syndrome (WS; 1:15,000–30,000 [8]), relative to typically developing (TD) controls. In later childhood and adulthood, sleep problems in AS

* Corresponding author. Department of Psychological Sciences, Purdue University, 703 Third Street, West Lafayette, IN 47907, USA.
E-mail address: btonnsen@purdue.edu (B.L. Tonnsen).

http://dx.doi.org/10.1016/j.sleep.2017.07.014
1389-9457/

include reduced total sleep time [9], increased sleep onset latency [10], and frequent and prolonged night waking [11]. In contrast, PWS is associated with excessive daytime sleepiness [2], sleep apnea, reduced sleep quality [1], and early waking [12]. Individuals with WS are generally reported to exhibit the mildest sleep concerns among the considered syndromes, with increased sleep onset latency, decreased sleep efficiency [13], daytime sleepiness [13,14], and more frequent night arousals and wakings [14]. Although sleep problems are expected across these syndromes, variations in topography and severity in childhood thus suggest that infant profiles may similarly vary across groups, requiring syndrome-specific plans of care.

The goals of this study were to (1) compare early childhood sleep profiles across infants and toddlers with and without neurogenetic syndromes, including sleep latency, duration, night waking, and global parent impressions, with those of same-aged typically developing (TD) controls and (2) examine the magnitude of sleep problems relative to established national guidelines.

2. Methods

2.1. Participants and procedure

Participants included 80 infants and toddlers with AS (n = 18), WS (n = 19), PWS (n = 19), and TD (n = 24). Data were drawn from the Early Phenotype Survey, an ongoing longitudinal study of early development in low-incidence neurogenetic syndromes. Families were recruited through web-based support groups and social networks, including the Angelman Syndrome Foundation and Registry (www.angelman.org) and Williams Syndrome Association and Registry (www.williams-syndrome.org/registry). All recruitment, consent, and procedures were approved by the Institutional Review Board at Purdue University. Families were required to primarily speak English for enrollment, and the TD group was excluded if they were born at <37 weeks; had significant surgeries that may impact sleep, or had a family history of developmental delay, intellectual disability, or other neurogenetic conditions. Groups were matched for age and sex (% male: AS = 53%, PWS = 42%, WS = 58%). Eighteen percent of syndromic participants were born preterm (AS: n = 3, PWS: n = 6, WS: n = 1), consistent with higher rates of preterm birth in these populations. Analyses repeated without preterm infants generally yielded similar effect sizes, and any inconsistencies are reported in-text. Groups did not differ across socio-economic variables, as detailed in Supplemental Table 1.

Parents reported child genetic status and completed syndrome-specific screening questions, with 74% of cases confirmed with genetic report (AS = 63%, PWS = 89%, WS = 68%). AS subtypes included maternal deletion (83%, n = 15), UBE3A mutation (11%, n = 2), and uniparental disomy (6%, n = 1). PWS subtypes included paternal deletion (68%; n = 13) and maternal uniparental disomy (32%, n = 6). Medications to target sleep and seizures were most common in the AS group (sleep = 3, seizure = 9; PWS sleep = 0, seizure = 1; WS sleep = 0, seizure = 0).

2.2. Measures

Biological mothers completed the Brief Infant Sleep Questionnaire (BISQ) [15], a 12-item parent-report measure of sleep-related behaviors previously validated against both actigraphy and parent-report sleep diaries [15]. Mothers were instructed to complete the BISQ on their child's sleep over the past week. Primary dependent variables included (1) nighttime sleep onset latency in minutes (Item 7), (2) total sleep duration per 24 h (Items 3 and 4), (3) daytime (Item 4) and nighttime sleep duration (Item 3), and (4) whether mothers rated sleep as a “very serious problem” rather than “a small problem” or “not a problem at all” when asked “Do you consider your child's sleep a problem?” (Item 10). We also determined whether total sleep duration fell outside of “recommended” sleep duration ranges set by the National Sleep Foundation [16] (4–11 months: 12–15 h; 1–2 years: 11–14 h; 3–5 years: 10–13 h).

2.3. Statistical analyses

Analyses were performed in SAS 9.4 (SAS Institute, Cary, NC) using nonparametric methods appropriate to small samples and outliers. We contrasted sleep in TD versus each syndromic group using Wilcoxon–Mann–Whitney tests (sleep latency, duration, and waking variables) and Fisher's exact tests (categorical parent impressions and national guidelines) using $\alpha < 0.05$. Effect sizes are reported using Cohen's d or odds ratios, as appropriate. We also calculated a Levene's homogeneity of variance statistic for each continuous pairwise comparison to determine whether variability in sleep parameters differed by group. Next, we conducted several supplemental analyses to contextualize our primary findings, including (1) pairwise syndromic comparisons, (2) post-hoc within-group analysis of AS-specific factors (eg, subtype, medication use) that may have contributed to group differences, and (3) within-group comparisons of age across participants with and without clinically indicated sleep concerns (Wilcoxon–Mann–Whitney tests). See Supplemental Tables 2–4.

3. Results

3.1. Sleep latency

Table 1 includes primary analyses contrasting each syndrome group to TD controls. Across syndromic groups, parents reported a median sleep latency of 15 min, relative to 30 min in controls. Relative to TD controls, sleep latency was significantly shorter in PWS ($d = 0.95$) and marginally shorter in AS ($d = 0.43$). Supplemental pairwise comparisons (Supplemental Table 2) indicated that the PWS and AS groups did not differ from each other. Variability in sleep latency did not differ by group (Supplemental Table 3).

3.2. Sleep duration

The median sleep duration was 720 min (12 h) per 24 h across syndromic groups, with both the AS ($d = 1.22$) and WS ($d = 0.62$) groups displaying atypically short total nighttime sleep and the AS group also exhibiting greater variability in sleep duration relative to TD controls. Pairwise contrasts indicated marginally less nighttime sleep in AS than WS. When preterm infants were excluded, the PWS group displayed atypically longer total sleep ($d = 0.75$), while the WS group difference approached significance in nighttime sleep ($d = -0.56$).

3.3. Night waking frequency and duration

Across syndromic groups, the median number of parent-reported night wakings was one, lasting approximately 5 min in total. The AS group exhibited atypically long night wakings ($d = 0.70$), with waking durations over three times as long as in controls. The AS group also exhibited greater variability in duration