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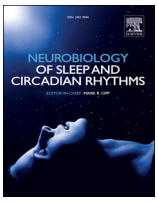

Research Paper

Sleep physiology in toddlers: Effects of missing a nap on subsequent night sleep

Jonathan M. Lassonde [a], Thomas Rusterholz [b,c], Salome Kurth [a,d], Allyson M. Schumacher [a], Peter Achermann [b,e,f,1], Monique K. LeBourgeois [a,*,1]

[a] Sleep and Development Laboratory, Department of Integrative Physiology, University of Colorado Boulder, Boulder, CO, USA
[b] Section of Chronobiology and Sleep Research, Institute of Pharmacology and Toxicology, University of Zurich, Zurich, Switzerland
[c] University Hospital of Child and Adolescent Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland
[d] Division of Pulmonology, University Hospital Zurich, Zurich, Switzerland
[e] Zurich Center for Integrative Human Physiology, University of Zurich, Zurich, Switzerland
[f] Neuroscience Center Zurich, University of Zurich and ETH Zurich, Zurich, Switzerland

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ABSTRACT

The shift from a biphasic to a monophasic sleep schedule is a fundamental milestone in early childhood. This transition, however, may result in periods of acute sleep loss as children may nap on some but not all days. Although data indicating the behavioral consequences of nap deprivation in young children are accumulating, little is known about changes to sleep neurophysiology following daytime sleep loss. This study addresses this gap in knowledge by examining the effects of acute nap deprivation on subsequent nighttime sleep electroencephalographic (EEG) parameters in toddlers. Healthy children ($n=25$; 11 males; ages 30–36 months) followed a strict sleep schedule for ≥ 5 days before sleep EEG recordings performed on 2 non-consecutive days: one after 13 h of prior wakefulness and another at the same clock time but preceded by a daytime nap. Total slow-wave energy (SWE) was computed as cumulative slow-wave activity (SWA; EEG power in 0.75–4.5 Hz range) over time. Nap and subsequent night SWE were added and compared to SWE of the night after a missed nap. During the night following a missed nap, children fell asleep faster (11.9 ± 8.7 min versus 37.3 ± 22.1 min; $d=1.6$, $p=0.01$), slept longer (10.1 ± 0.7 h versus 9.6 ± 0.6 h; $d=0.7$, $p<0.01$) and exhibited greater SWA ($133.3 \pm 37.5\%$ versus $93.0 \pm 4.7\%$; $d=0.9$, $p<0.01$) compared to a night after a daytime nap. SWE for combined nap and subsequent night sleep did not significantly differ from the night following nap deprivation (12141.1 ± 3872.9 μV²*h versus $11{,}588 \pm 3270.8$ μV²*h; $d=0.6$, $p=0.12$). However, compared to a night following a missed nap, children experienced greater time in bed (13.0 ± 0.8 h versus 10.9 ± 0.5 h; $d=3.1$, $p<0.01$) and total sleep time (11.2 ± 0.8 h versus 10.1 ± 0.7 h; $d=1.4$, $p<0.01$). Shorter sleep latency, longer sleep duration, and increased SWA in the night following a missed nap indicate that toddlers experience a physiologically meaningful homeostatic challenge after prolonged wakefulness. Whether toddlers fully recover from missing a daytime nap in the subsequent night necessitates further examination of daytime functioning.

1. Introduction

Brain electrophysiology of recovery from sleep loss has been extensively characterized in adolescents and adults. Slow wave sleep (SWS) and slow wave activity (SWA; power density in the 0.75–4.5 Hz frequency range) of the sleep electroencephalogram (EEG) are well-known physiological markers of sleep pressure, exhibiting a saturating rise with duration of prior wakefulness and an exponential decline with time asleep (Daan et al., 1984). Following sleep loss, recovery sleep is marked by increased SWS and SWA, as well as shorter sleep onset latency and longer sleep duration (Brunner et al., 1993). Although the electrophysiology of adult sleep is predictable according to the two-process model of sleep regulation (Borbely, 1982), large inter-individual differences have been observed in the SWA response to sleep deprivation (Finelli et al., 2000; Rusterholz et al., 2010). This study extends the prior literature by quantifying the neurophysiological response to acute sleep restriction in toddlers.

Nearly all 2-year-olds fulfill part of their 24 h sleep need by taking a daytime nap (Weissbluth, 1995; Thorleifsdottir et al., 2002; Iglowstein et al., 2003; Crosby et al., 2005). In the next few

* Correspondence to: Department of Integrative Physiology, University of Colorado Boulder, 354 UCB, Boulder, CO 8030992.4584, USA. Fax: +1 303 492 6778.
E-mail address: monique.lebourgeois@colorado.edu (M.K. LeBourgeois).
[1] Shared last authorship in alphabetical order.

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years of life, napping declines. By age 5 years, the great majority of children sleep only at night. This shift from a biphasic to a monophasic sleep schedule in early childhood is a naturalistic context for studying sleep homeostasis, as children may nap on some but not all days of the week (Weissbluth, 1995; Crosby et al., 2005). Also, because young children's sleep habits are largely determined by caregivers and modulated by cultural and psychosocial factors (Crosby et al., 2005; Roffwarg et al., 1966; Komada et al., 2011), toddlers may experience daytime sleep restriction for reasons outside their control (e.g., daycare/preschool schedules, family demands). Although recent data show that habitually napping preschool-age children show decrements in behavioral processes (e.g., emotion expression, self-regulation strategies, declarative memory performance) after nap deprivation (Berger et al., 2012; Kurdziel et al., 2013; Giganti et al., 2014), less is known about changes to nighttime sleep neurophysiology following a missed nap in early childhood.

In the present study, we quantified recovery sleep neurophysiology following a missed nap with sleep EEG in a sample of healthy children ages 30–36 months. First, in order to quantify the physiological response to a missed nap, we compared sleep architecture, SWS, and SWA between a night following a nap and a night following a missed nap. We hypothesized that missing a nap would decrease sleep onset latency and increase sleep efficiency, sleep duration, SWS, and SWA. Second, we compared slow-wave energy (SWE; cumulative SWA over time) of a combined nap and subsequent night to that of a night following a missed nap. SWE was used to quantify neurophysiological recovery from a missed nap because it provides a comprehensive quantification of recovery sleep (Dijk and Beersma, 1989; Achermann and Borbely, 1990; Hekkens GAK and Rietveld, 1988) and has been used in similar experimental paradigms in adults (Werth et al., 1996; Campbell et al., 2005). We expected an increase in SWE following a missed nap and explored the extent to which toddlers neurophysiologically recover from a missed nap with one night's sleep (i.e., whether toddlers compensate for a missed nap with a commensurate increase in SWE during nighttime sleep).

2. Materials and methods

2.1. Participants

Participants were 25 healthy habitually napping children ages 30–36 months (11 males; 33.5 ± 1.8 (SD) months) from Boulder, CO or surrounding areas. Details regarding recruitment and study exclusion criteria have been previously published (Berger et al., 2012; LeBourgeois et al., 2013). Briefly, all participants were screened for reported sleep problems/disorders, variable sleep schedules, chronic use of medications affecting sleep, alertness, or the circadian system, a personal or family history of sleep or mental health problems or personal history of developmental disabilities, head injury, chronic illnesses, or low birth weight. Of the 102 children screened, 45 met criteria, 35 were enrolled, and 25 were included in this analysis. Exclusions were due to discomfort with electrodes ($n=4$), EEG artifacts ($n=4$), or failure to complete all 3 sleep EEG assessments ($n=2$). Parents signed a consent form approved by the University of Colorado Boulder Institutional Review Board, and study procedures were performed according to the Declaration of Helsinki. Parents were compensated with $80 cash, and children received small non-monetary gifts throughout the study and a $200 U.S. Saving's Bond.

2.2. Training

Researchers performed ≥ 3 in-home trainings during the week before sleep EEG assessments. These trainings introduced children to study methods, such as wearing a wrist actigraph and attaching electrodes to the face and scalp.

2.3. Protocol

Fig. 1 illustrates a sample protocol for one participant. Children followed an individualized, stable sleep schedule for 5 days before completing each of 2 counterbalanced in-home 24 h sleep EEG recordings. Children did not attend daycare or preschool on these assessment days. The schedule required a minimum sleep opportunity of 12.5 h per 24 h day (including a daily nap opportunity of ≥ 45 min) and was employed to minimize sleep restriction and to optimize circadian entrainment before the sleep assessments. Schedule compliance was verified with actigraphy, sleep diaries, and daily contact with parents. Participants slept in their typical environment throughout the study (i.e., home, daycare, family care). Consumption of caffeine and medications affecting sleep, alertness, or the circadian system were prohibited throughout the study. Assessments were rescheduled if a child was ill within 24 h before the assessment or if their sleep timing deviated > 15 min from the prescribed schedule.

The experimental protocol included 2 counterbalanced sleep conditions: Baseline (afternoon nap and subsequent overnight) and Recovery (overnight following a missed nap). The Baseline Nap was recorded after 4 h of wakefulness (Fig. 1; e.g., Day 6), and both the Baseline and the Recovery Nights were performed 13 h after morning wake time (Fig. 1; e.g., Nights 6 and 13). Children were allowed to sleep until spontaneously waking. Children slept on their normal schedule for ≥ 5 intervening nights between conditions.

2.4. Measures

2.4.1. Sleep EEG

Sleep EEG from derivations C3A2, C4A1, OzA1, and FzA2 (Jasper, 1958), submental electromyogram, and electrooculogram were recorded using a Vitaport 4 EEG recorder (Temec Instruments, Kerkrade, Netherlands) with a sampling rate of 256 Hz. The high-pass filter was at 0.16 Hz and the anti-aliasing low-pass filter (2nd order) at 70 Hz.

2.4.2. Visual sleep stage scoring and sleep cycle definition

Sleep stages were visually scored in 30-s epochs according to standard criteria (Rechtschaffen and Kales, 1968). Sleep onset latency was defined as the duration (min) from lights off to the first epoch of stage 2 sleep. SWS latency and REM latency were defined as the duration from sleep onset to the first epoch of SWS and REM sleep, respectively. Sleep stage percentages were calculated in reference to the sleep period (sleep onset to last epoch of sleep). NREM and REM sleep episodes were defined according to standard criteria (Rechtschaffen and Kales, 1968; Feinberg and Floyd, 1979) and adapted when a “skipped” REM was observed after the first NREM sleep episode. As previously described in studies of children and adolescents (Kurth et al., 2010; Jenni and Carskadon, 2004), NREM episodes were manually divided if (1) the duration of the first NREM sleep episode exceeded 120 min and (2) SWS sleep in the first NREM episode was interrupted for at least 12 continuous min of stage 1 sleep, stage 2 sleep, wakefulness, or movement time. If both criteria were met, the NREM sleep episode was divided at the SWS midpoint. In total, there were 10 cases of skipped first REM episodes; 1 during a Baseline Nap, 3 during a Baseline Night, and 6 during a Recovery Night.

2.4.3. Protocol verification: sleep diary and actigraphy

Throughout the study, parents completed a daily 26-item sleep

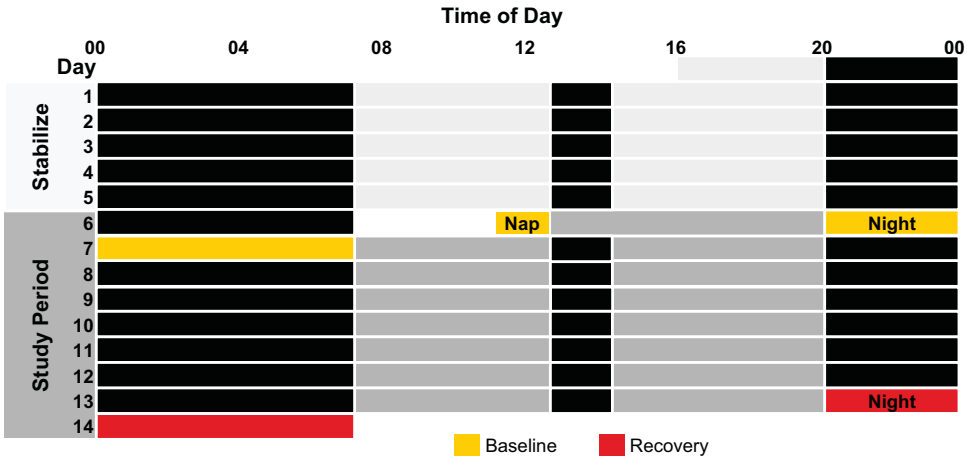

Fig. 1. Sample protocol for an exemplary child following a stabilization (days 1–5) and study period (days 6–14) sleep schedule. Black bars represent time in bed (20:00 bedtime, 07:00 rise time, 12:30-14:00 nap) and grey bars represent time awake. Yellow bars indicate Baseline Nap electroencephalography (EEG) recorded after 4 h of prior wakefulness and Baseline Night EEG recorded 13 h after morning wake time. The red bar represents the Restriction Night EEG recorded after 13 h of prior wakefulness (missed nap).

diary (Akacem et al., 2015), and participants wore an actigraph (model AW Spectrum, Phillips/Respironics, Pittsburg, PA, USA) on their non-dominant wrist for estimation of sleep-wakefulness states based on motor activity. In order to secure the actigraph to the wrist and to reduce skin irritation, children wore colorful lycra-bands around the device (patterns available upon request). Caregivers pressed an event marker button on the actigraph at lights-off (i.e., when child was expected to try to fall sleep) and when their child awakened from nap and nighttime sleep. Actigraphy data were downloaded, examined, and compared to sleep diaries to verify adherence to assigned sleep schedules (Akacem et al., 2015; Acebo et al., 2005). Details regarding our actigraphy scoring and analysis procedures have been published previously (Berger et al., 2012; LeBourgeois et al., 2013). As expected based upon our protocol, paired t-tests revealed no differences in actigraphic sleep variables in the 5 days preceding the Baseline and Recovery assessments (Table 1).

Table 1
Descriptive statistics, *M* (*SD*), for actigraphic sleep measures aggregated across the 5 days preceding the Baseline and Recovery assessments. Statistics (*t*, *d*, *p*) are for group comparisons.

	Condition		Statistics		
	Baseline	Recovery	*t*	*d*	*p*
Nap Lights-Off Time	13:09 (0:32)	13:09 (0:34)	−0.68	0.06	0.50
Nap Wake Time	15:10 (0:44)	15:07 (0:39)	−0.61	0.07	0.55
Nap Time in Bed (min)	120.6 (20.1)	119.5 (23.3)	0.30	0.05	0.77
Nap Duration (min)	94.3 (22.8)	99.4 (19.6)	−1.16	0.24	0.26
Night Lights-Off Time	20:17 (0:30)	20.19 (0:28)	−0.09	0.01	0.93
Morning Wake Time	06:59 (0:33)	07:02 (0:35)	−0.56	0.06	0.58
24 h Time in Bed (h)	12.6 (0.6)	12.7 (0.6)	−0.60	0.10	0.55
24 h Sleep Duration (h)	11.5 (0.5)	11.6 (0.6)	−0.76	0.18	0.46
24 h Sleep Efficiency (%)	89.6 (4.9)	89.9 (3.3)	−0.19	0.05	0.85

2.4.4. Quantitative EEG analysis

Power density spectra were calculated for consecutive 30-s epochs for derivation C3A2 [FFT, Tukey window ($r=0.05$), average of ten 4-s epochs overlapping by 1-s; frequency resolution 0.25 Hz, VitaScore, Temec Instruments, Kerkrade, Netherland; MATLAB, MathWorks Inc., Natick, MA]. Data up to 20 Hz were analyzed, and artifacts were removed semi-automatically. Epochs were excluded when power in the 20–40 Hz and SWA range exceeded a threshold based on a moving average determined over twenty 30-s epochs. Because of sweat artifacts, EEG power density below 1 Hz was excluded for 6 participants, below 1.25 Hz for 2 participants, and below 1.5 Hz for 1 subject. Derivation C4A1 was used for one subject with poor quality data in C3A2 during a recording. Exclusions were applied across all conditions within each subject.

For all recordings, SWA was calculated for the first NREM episode and for total NREM sleep. To control for sleep duration differences between recordings, we analyzed SWA for the greatest common sleep duration [i.e., first NREM episode (37.5 min); total NREM sleep (321.5 min)] across all Baseline and Recovery Night recordings. We used a similar approach for Nap recordings [i.e., first NREM episode (28.5 min); total NREM sleep (36.5 min)]. To control for individual differences in overall EEG spectral power, each subject's SWA in a given recording was normalized with mean SWA during the greatest common sleep duration of NREM sleep (321.5 min) of the corresponding Baseline Night.

SWE was calculated as cumulative SWA over time (μV^2*h; Fig. 2). To account for artifacts, mean SWA per 0.5 h interval was determined based on artifact free 30-s epochs and multiplied by the duration of NREM sleep in this interval. SWE of 0.5 h intervals were cumulated. To control for inter-individual differences in overall EEG spectral power, we also calculated Recovery SWE levels, expressed as a percentage relative to Baseline [(Recovery/Baseline)*100].

2.4.5. Analysis

Statistical analyses were performed with SPSS Statistics Package 22.0 (IBM Corp., Armonk, NY, USA). Distributions of several variables were skewed, thus, we performed both parametric and non-parametric tests. Because the results did not differ between approaches, we present only parametric statistics. To examine the effects of a missed nap on subsequent night sleep, paired *t*-tests (Baseline Night versus Recovery Night) of visually scored sleep measures (i.e., sleep onset latency, sleep duration, sleep stages) and quantitative EEG data (i.e., SWA, SWE) were performed (alpha=0.05; 2-tailed). Paired *t*-tests (alpha=0.05; 2-tailed) were also used to assess differences (Baseline Nap+Baseline Night versus Recovery) in sleep measures, SWA, and SWE. Summary measures are presented as means (*M*) and standard deviations (*SD*). Effect size (Cohen's *d*) was computed for each comparison [$d=(M$Baseline Night–MRecovery Night)/SD pooled or $d=(M$ Baseline Nap and Night–M Recovery Night)/SD pooled]. Effect sizes of $d=0.20$, $d=0.50$, and $d\geq 0.75$ are considered small, medium, and large, respectively (Cohen, 1988).

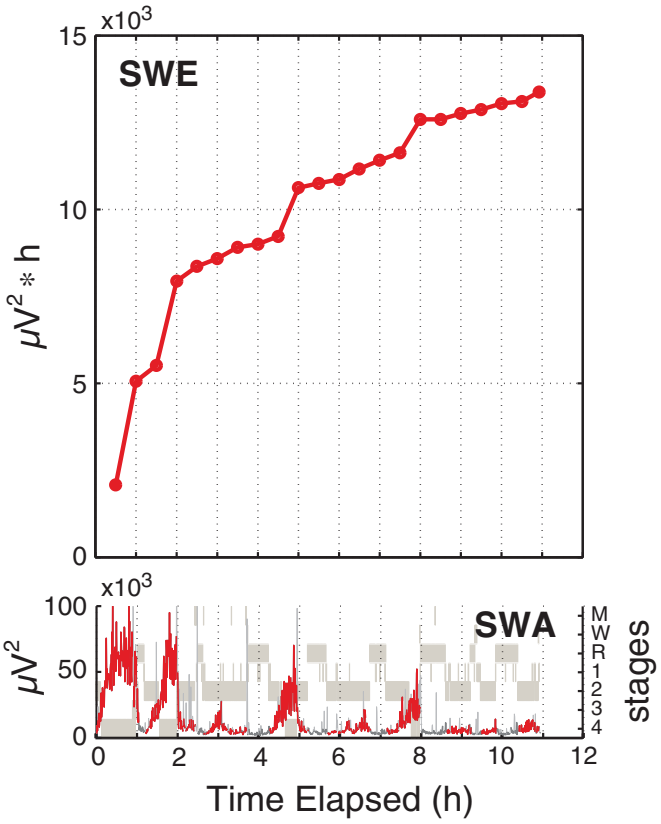

Fig. 2. Representative plots of Slow Wave Energy (SWE) and Slow Wave Activity (SWA) from a night of sleep from a single subject. X-axes show time elapsed since sleep onset. In the lower graph, SWA (EEG power in the 0.75–4.5 Hz; μV^2) is plotted every 30-s in red and is superimposed with sleep stages (M: movement time; W: wake; R: REM; 1–4: NREM sleep stages 1–4) plotted in grey. The upper graph shows the time course of SWE (accumulation of SWA over time; μV^2*h) plotted every half hour. Note how NREM sleep episodes with greater SWA produce a faster accumulation of SWE over the same period, and those with less SWA produce slower accumulation. The end point of SWE represents the total amount of SWE accumulated across the night.

3. Results

3.1. Baseline night versus recovery night

Visually scored and quantitative sleep EEG data are shown in Table 2. As hypothesized, children experienced shorter sleep onset latency, greater sleep efficiency, and longer sleep duration during the Recovery Night than the Baseline Night. Participants also exhibited shorter latency to SWS and spent more total time in SWS. As hypothesized, mean SWA was greater during both the first NREM sleep episode and all NREM sleep episodes in the Recovery Night compared to the Baseline Night (Table 2). Lastly, SWE was ~25% greater during the Recovery Night compared to the Baseline Night (Table 2, Fig. 3). We found no sex differences in the ratio of Baseline Night SWE to Recovery Night SWE.

3.2. Combined baseline nap and night versus recovery night

Children experienced longer time in bed, total sleep time, stage 2 sleep min and %, SWS %, and REM sleep min in the combined Baseline Nap and Night than in the Recovery Night. We found no differences, however, in SWS min, total SWE, or relative SWE between conditions (Table 3, Fig. 3). We detected no sex differences in the ratio of combined Baseline Nap and Night SWE to Recovery Night SWE.

3.3. Individual differences

We observed inter-individual variability in children's capacity to achieve similar levels of SWE in the two 24 h conditions (Figs. 4 and 5). Recovery Night SWE levels ranged from 70% to 124% of the combined Baseline Nap and Night. More than half (60%) of participants achieved less SWE in the Recovery Night than in the combined Baseline Nap and Night.

4. Discussion

This experimental study examined the effects of a missed nap on nighttime sleep EEG in habitually napping healthy 30- to 36-month-old children using a well-controlled, repeated measure design. Results indicate that a missed nap induces changes in sleep architecture and quantitative measures of brain activity indicative of a substantial homeostatic response. Although on average we observed no difference between the SWE of a combined Baseline Nap and Baseline Night compared to that of a Recovery Night, children varied widely in their ability to achieve similar SWE levels between the two conditions.

4.1. Homeostatic response to a missed nap during recovery night

Toddlerhood is a relatively understudied transitional period during which time children gradually drop daytime naps and begin consolidating sleep into one nocturnal episode. Controversy surrounding the costs and benefits of daytime naps in early childhood is increasing (Sinclair et al., 2016), and the topic of when children should stop napping is of great interest in the media, among parents, and within the pediatric sleep community. Data from survey and actigraphic studies indicate nap duration is associated with changes in nighttime sleep, including decreased sleep duration and increased sleep onset latency and sleep disruption (Acebo et al., 2005; Lam et al., 2011). Indeed, a commonly identified concern associated with naps is their interference with subsequent night sleep (Thorpe et al., 2015); however, due to individual variability in developing intrinsic bioregulatory processes (i.e., homoestatic, circadian) and environmental constraints (Jenni and LeBourgeois, 2006), many young children may not be able to obtain the sleep they need only at night. Thus, for these children, daytime sleep may be crucial to satisfying 24 h sleep need and protective of developmental and health consequences associated with sleep loss.

This study examined the relationship between day and night sleep in toddlers using EEG, which is widely considered the gold standard for measuring sleep. Established biological markers of sleep homeostasis (i.e., sleep onset latency, WASO, sleep efficiency, sleep duration, SWS) were included in our analyses of sleep architecture. In our sample, sleep onset latency was reduced from 37 min in the Baseline Night to 10 min in the Recovery Night following a missed nap. Adults experience sleep onset latencies of ~20 min under normal sleep pressure (Ohayon et al. 2004) and sleep onset latencies of ~8 min following restriction to one night of 4 h time in bed (Brunner et al., 1993; Akerstedt et al., 2009). Therefore, it is reasonable to propose that nap deprivation in 2-year-olds poses a physiologically meaningful homeostatic challenge tantamount to acute sleep restriction in adults. We found no significant difference in WASO between the Baseline and Recovery nights in the present study, suggesting that once sleep was initiated in either condition, the presence of a preceding nap had no effect on sleep maintenance. Thus, the difference detected in sleep efficiency between the Baseline and Recovery nights can likely be attributed to disparities in sleep onset latency. This finding suggests that in habitually napping toddlers, daytime sleep gives rise

Table 2
Descriptive statistics, *M* (*SD*), for visually-scored and quantitative sleep electroencephalography (EEG) measures during Baseline Nap, Baseline Night, and Recovery Night assessments. Paired *t*-tests (alpha = 0.05; 2-tailed) compared measures between Baseline and Recovery nights. Statistics (*t*, *d*, *p*) are for group comparisons.

	Baseline Nap	Baseline Night	Recovery Night	Statistics *t*	*d*	*p*
Visually-scored EEG measures						
Total Sleep Time (h)	1.5 (0.6)	9.6 (0.6)	10.1 (0.7)	−2.90	0.73	< **0.01**
Time in Bed (h)	2.1 (0.7)	10.9 (0.5)	10.9 (0.5)	−0.13	0.03	0.90
Sleep Onset Latency (min)	28.6 (20.5)	37.3 (22.1)	11.9 (8.7)	6.62	1.55	< **0.01**
SWS Latency (min)	45.8 (20.5)	51.2 (23.1)	21.2 (8.8)	4.44	1.19	< **0.01**
REM sleep Latency (min)	84.4 (25.8)	110.9 (28.3)	106.7 (43.5)	−2.49	0.62	< **0.01**
WASO (min)	0.9 (1.4)	25.9 (30.3)	19.9 (19.2)	1.37	0.24	0.18
Sleep Efficiency (%)	72.0 (2.5)	88.4 (4.9)	92.5 (3.2)	−4.32	1.00	< **0.01**
Stage 1 (min)	2.34 (2.0)	29.3 (15.2)	27.0 (10.7)	1.09	0.17	< **0.01**
Stage 1 (%)	5.6 (4.1)	5.7 (2.6)	5.3 (2.4)	1.07	0.17	0.30
Stage 2 (min)	50.8 (13.9)	306.9 (32.6)	310.3 (30.2)	−0.55	0.11	0.59
Stage 2 (%)	55.1 (14.3)	50.7 (5.5)	49.5 (5.2)	1.95	0.38	0.06
SWS (min)	26.1 (13.9)	73.3 (20.2)	103.1 (22.0)	−8.33	1.43	< **0.01**
SWS (%)	28.8 (17.4)	12.1 (3.4)	16.4 (3.4)	−6.93	1.24	< **0.01**
REM sleep (min)	13.2 (10.4)	165.2 (30.3)	162.0 (33.1)	0.48	0.11	0.63
REM sleep (%)	12.8 (7.3)	26.6 (4.5)	25.7 (4.5)	2.17	0.45	**0.04**
Quantitative EEG measures						
Mean SWA 1st NREM Cycle (%)	158.1 (40.4)	203.4 (26.6)	234.2 (46.2)	−3.19	0.51	< **0.01**
Mean SWA All NREM Cycles (%)	133.3 (37.5)	93.0 (4.7)	105.8 (15.6)	−4.15	0.92	< **0.01**
SWE (μV²*h)	2654.4 (1263.8)	9486.9 (3013.0)	11,588.0 (3270.8)	−6.64	0.96	< **0.01**
Relative SWE (%)	28.4 (11.4)	100 (0)	124.6 (19.2)	−6.41	1.85	< **0.01**

Note: Slow-wave sleep (SWS); rapid eye movement (REM) sleep; slow-wave activity (SWA); non-rapid eye movement (NREM) sleep; slow-wave energy (SWE).

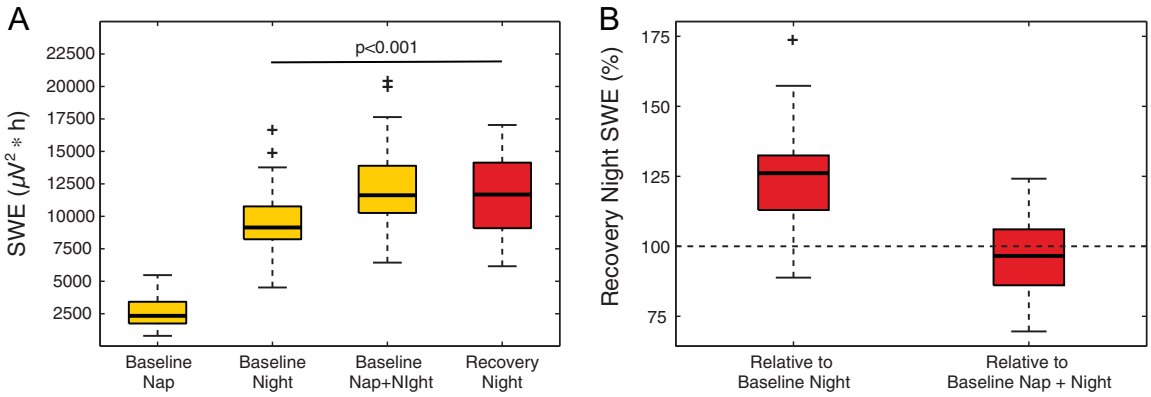

Fig. 3. Boxplots of total slow-wave energy (SWE) by condition (3A) and Recovery Night SWE expressed as a percentage of SWE in the Baseline Night and the combined Baseline Nap and Night (3B). Outliers are denoted by +. Significant post-hoc paired t-test designated by line (3A).

to subsequent nighttime sleep with limited disruption. Lastly, total sleep time and SWS (duration and %) were increased in the Recovery Night compared to the Baseline Night, supporting the notion that missed naps pose a neurophysiological sleep challenge to toddlers.

We also examined the relationship between nap and night sleep using quantitative EEG measures. In our experiment, nap opportunities were presented after 4 h of prior wakefulness. Studies with adults suggest that naps taken after a similar duration of wakefulness have a negligible effect on sleep architecture, SWS, and SWA in subsequent night sleep (Karacan et al., 1970; Knowles et al., 1990, 1986; Campbell and Feinberg, 2005). Contradictory to these findings, one missed morning nap produced a 13% increase in SWA and a 25% increase in SWE during night sleep in our sample of healthy 2-year-olds. These changes are comparable to the 10-20% SWA increase observed in adults following one night of acute sleep restriction to 4 h time in bed (Brunner et al., 1993; Van Dongen et al., 2003). Together, these results also suggest that a missed nap may pose a significant homeostatic sleep challenge to young children. In light of the developmental decline in napping frequency and duration between ages 2 and 5 years, Jenni and LeBourgeois (Jenni and LeBourgeois, 2006) have proposed that sleep pressure accumulates quickly across the day during early childhood, with the rate of buildup declining with age. Our findings support this hypothesis; if 2-year-olds accumulate sleep pressure faster than adults, we would expect to observe a significant homeostatic effect of a morning nap on subsequent night sleep in toddlers, but not in adults.

4.2. Comparison of 24 h SWE: Combined baseline nap and night versus recovery night

We found that SWE of the combined Baseline Nap and Baseline Night sleep was equivalent to that in the Recovery Night. This is consistent with adult data, which suggest that on average, sleep EEG power in the slow-wave range is highly conserved across 24 h regardless of the number of sleep opportunities presented. We did, however, observe large inter-individual variability in the ability of children to achieve similar SWE levels in the two conditions. Individuals' SWE levels in the Recovery condition varied from 70%

Table 3
Descriptive statistics, *M* (*SD*), for visually-scored sleep electroencephalography measures during Baseline Nap and Night and Recovery Night assessments. Paired *t*-tests (alpha=0.05; 2-tailed) compared measures between the combined Baseline Nap and Night and the Recovery Night. Statistics (*t*, *d*, *p*) are for group comparisons.

	Baseline Nap + Night	Recovery Night	Statistics *t*	*d*	*p*
Visually-scored EEG measures					
Total Sleep Time (h)	11.2 (0.8)	10.1 (0.7)	6.03	1.44	< **0.01**
Time in Bed (h)	13.0 (0.8)	10.9 (0.5)	10.66	3.06	< **0.01**
WASO (min)	26.8 (30.2)	19.9 (19.2)	1.57	0.27	0.13
Sleep Efficiency (%)	85.9 (5.3)	92.5 (3.2)	−7.19	1.54	< **0.01**
Stage 1 (min)	31.6 (16.1)	27.0 (10.7)	2.13	0.34	**0.04**
Stage 1 (%)	4.7 (2.3)	5.3 (2.4)	−1.37	0.18	0.18
Stage 2 (min)	357.7 (40.9)	310.3 (30.2)	6.29	1.34	< **0.01**
Stage 2 (%)	53.4 (5.4)	49.5 (5.2)	2.61	0.41	**0.04**
SWS (min)	99.4 (29.3)	103.1 (22.0)	−0.92	0.14	0.37
SWS (%)	14.8 (4.2)	16.4 (3.4)	−3.63	0.58	< **0.01**
REM sleep (min)	178.5 (31.4)	162.0 (33.1)	2.56	0.52	**0.02**
REM sleep (%)	26.6 (4.2)	25.7 (4.5)	−0.01	0.01	0.99
Quantitative EEG measures					
SWE (μV²*h)	12141.1 (3872.9)	11,588.0 (3270.8)	1.67	0.62	0.12
Relative SWE (%)	100 (0)	97.1 (12.8)	1.12	0.32	0.27

Note: Slow-wave sleep (SWS); rapid eye movement (REM) sleep; slow-wave activity (SWA); non-rapid eye movement (NREM) sleep; slow-wave energy (SWE).

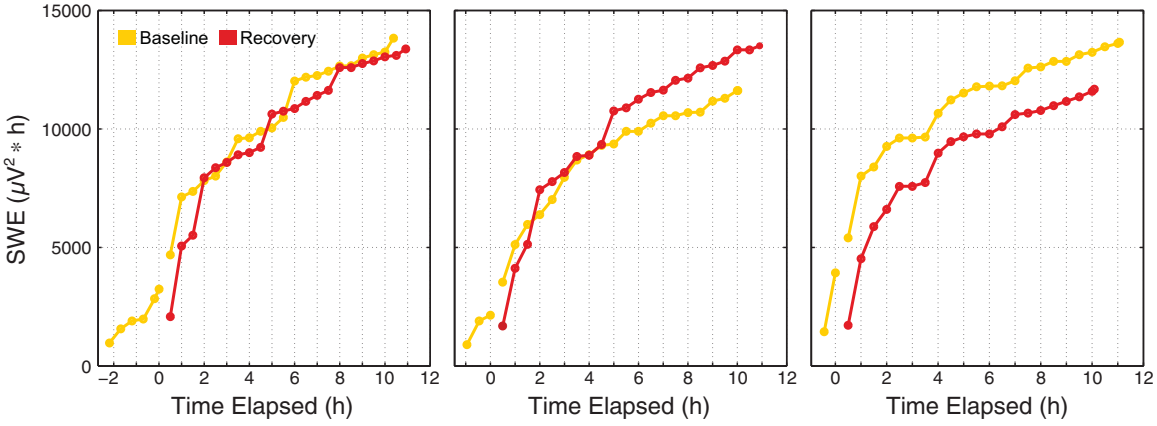

Fig. 4. Plots of slow-wave energy (SWE) from three individual participants. Time is presented as h elapsed relative to sleep onset (time 0) in the all-night recordings. Points depict SWE accumulated every 30 min. Baseline Nap SWE is plotted prior to time 0, and Baseline Night SWE is added to the total SWE value of the nap after time 0. The left panel shows a child who achieved greater SWE in the Recovery Night compared to the combined Baseline Nap and Night; the middle panel shows a child who achieved similar SWE in the two conditions; the right panel shows a child who achieved greater SWE in the combined Baseline Nap and Night than the Recovery Night.

to 124% of Baseline. This finding is consistent with Campbell and colleagues (Campbell et al., 2005), who also showed large inter-individual variability in a sample of adults when examining the effects of a nap on subsequent night SWE, reporting a range of 74–145% of baseline. Thus, napping has a highly variable effect on 24 h capacity for deep sleep. In the present study, 60% of children failed to achieve the same or higher SWE level in the Recovery condition compared to Baseline, suggesting some toddlers may be more vulnerable than others to the effects of a missed nap. This assumes, however, that within-subject recovery processes are stable across multiple trials of sleep loss, a concept that has yet to be examined in young children. Therefore, a one-size-fits-all model may not be adequate to meet the sleep demands of many toddlers, especially when they experience sleep loss as a consequence of a missed nap. Whether toddlers who produce more SWE in Recovery than Baseline sleep may be protected from adverse behavioral, cognitive, or emotional outcomes that otherwise might result from a missed nap remains an important unanswered research question.

4.3. Limitations and future directions

The present study assessed sleep with the gold-standard of sleep measurement, EEG, and used a well-controlled experimental design; however, some limitations should be mentioned. First, the demanding nature of the experimental protocol restricted our study's sample size. Thus, our findings necessitate replication with a larger sample. The number of assessments we performed was also limited for the same reason. Therefore, future research may investigate whether the degree to which toddlers recover from a missed nap is stable within individuals across repetitions of acute sleep restriction. Such an investigation is important in light of recent data showing that features of the NREM sleep EEG are unique to an individual and stable across both baseline and recovery sleep following sleep deprivation (Tarokh et al., 2015). Second, characterizing the sleep of healthy, good sleepers is a necessary first step in the examination of recovery sleep physiology in toddlers; however, future experiments should also focus on ethnically diverse children and those with sleep and/or behavioral

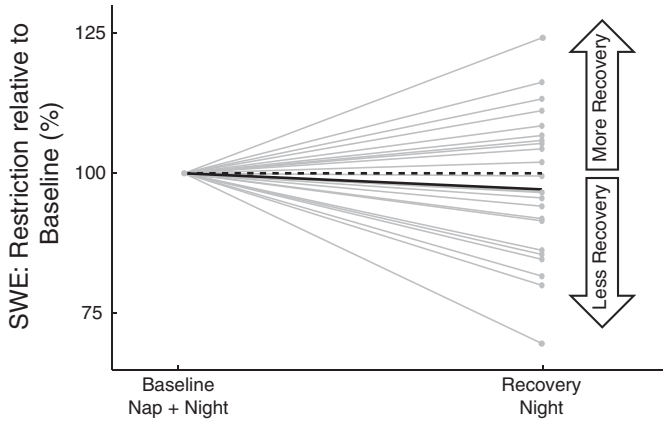

Fig. 5. Recovery Night slow-wave energy (SWE) levels relative to the combined Baseline Nap and Night for each individual, expressed as percentages. As a reference, the dashed line represents equal levels of SWE in the two conditions (100%). Grey lines above the dashed line characterize individuals who achieved more SWE in the Recovery Night relative to the combined Baseline Nap and Night, and grey lines below the dotted line characterize individuals who achieved the inverse. The solid black line represents average data of all participants.

problems to increase generalizability (Crosby et al., 2005). Third, we recognize that the timing of the nap in this study does not map onto that of our children's habitual naps, a byproduct of analyzing data from a larger study protocol. Further research is needed to determine whether our results would be replicated with naps scheduled at different times of the day (i.e., morning, afternoon, evening). Fourth, although findings from multiple studies in adults suggest that one night of recovery sleep does not return performance to baseline levels following chronic sleep restriction (Van Dongen et al., 2003; Belenky et al., 2003; Banks et al., 2010), the effects of repeated nap deprivation in early childhood are unknown. Furthermore, in this study, we focused on NREM sleep homeostasis. Although we found no differences in REM sleep % between Baseline and Recovery conditions, changes in REM sleep homeostasis as result of acute sleep restriction in early childhood is an important area of study. Lastly, future research should assess the relationship between recovery sleep physiology and functional outcomes on the day of a missed nap, the subsequent days, and longitudinally in order to determine the short- and long-term effects of sleep loss during early childhood.

4.4. Summary

Based on parent reports, ~30% of young children sleep less than recommended (National Sleep Foundation, 2004) and/or have behavioral sleep problems associated with insufficient sleep (Owens et al., 2000). Yet to date, little is known about the neurophysiological response to acute or chronic sleep loss in young children. Our study addresses this gap in the literature by simulating sleep restriction in the context of a missed nap and examining its effects on the nighttime sleep EEG. Findings suggest that a missed nap elicits changes to sleep architecture and quantitative measures of brain activity indicative of a substantial homeostatic response. Insufficient sleep in children is linked to a variety of behavioral (Minde et al., 1994; Lavigne et al., 1999; Hiscock et al., 2007; Simola et al., 2014; Wake et al., 2006), attentional (Hiscock et al., 2007; Simola et al., 2014), and cognitive problems (Gottlieb et al., 2004; Friedman et al., 2009; Sadeh et al., 2003; Urschitz et al., 2003); however, not all children show such deficits as a result of experimental sleep loss or in association with shorter sleep (Berger et al., 2012; Kurdziel et al., 2013; Miller et al., 2014). Our data demonstrate large inter-individual variability in the brain physiology of recovery from missed sleep and may provide important insights into the neurophysiological basis of vulnerability to sleep loss in early childhood.

Conflicts of interest

The authors have none to declare.

Contributions

MKL and PA designed the study; JML, MKL, and AMS collected the data; JML, PA, TR, and AMS analyzed the data; JML, MKL, PA, AMS, and SK wrote the paper; all authors approved the final manuscript.

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