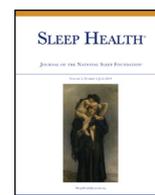




Contents lists available at ScienceDirect

Sleep Health

Journal of the National Sleep Foundation

journal homepage: sleephealthjournal.org

Variations in habitual sleep and relational memory in 6-month-olds

Elaine K.H. Tham, PhD^a, Jenny Richmond, PhD^b, Joshua J. Gooley, PhD^c, Nur K. Jafar, BSc^a, Yap-Seng Chong, MRCP, MMed, MD, FAMS^{a,d}, Fabian Yap, MBBS, MRCP, MMed, GDipHLM, FAMS, FRCPH^d, Oon-Hoe Teoh, MBBS, MMed, MRCPCH^e, Daniel Y.T Goh, MBBS, MMed, FRCPC, FCCP, FAMS^f, Birit F.P. Broekman, MD, PhD^{a,g}, Anne Rifkin-Graboi, PhD^{a,*,1}

^a Singapore Institute for Clinical Sciences, Agency for Science and Technology Research (A*STAR), Singapore

^b School of Psychology, University of New South Wales, Sydney, Australia

^c Program in Neuroscience and Behavioral Disorders, Duke-NUS Medical School, Singapore

^d Department of Obstetrics & Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

^e KK Women's and Children's Hospital, Singapore

^f Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

^g Department of Psychological Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

ARTICLE INFO

Article history:

Received 5 March 2018

Received in revised form 10 December 2018

Accepted 11 December 2018

Keywords:

Infant

Sleep duration

Sleep recommendations

Latency

Relational memory

ABSTRACT

Objectives: Adequate sleep duration and good sleep quality are considered essential for development, especially during periods of major neurodevelopmental change. Still, relations between parent-reported habitual sleep and emerging cognitive abilities within the first year of life are not well studied. Here, we examined relations between habitual sleep measures and an aspect of cognitive functioning, relational memory, which emerges as early as 6 months of age, as compared to other abilities (ie, recognition memory and attentional orienting), both of which are considered to emerge earlier in development.

Participants: Participants were a subset of 267 healthy typically developing 6-month-olds taking part in the Growing Up in Singapore towards Healthy Outcomes cohort study.

Measurements: Sleep duration, sleep latency, and number and duration of night awakenings were derived from the Brief Infant Sleep Questionnaire (BISQ). *Short sleep* was defined as <10 hours per day, categorized as "not recommended" based on the National Sleep Foundation recommendations. Associations between sleep variables and infants' performance on 2 relational memory tests (deferred imitation and relational binding) were examined independently using hierarchical (blockwise entry) linear regression. Associations between sleep and recognition memory and attentional orienting were also explored.

Results: Habitual short sleepers had poorer relational memory recall in the deferred imitation task compared with 'typical' sleepers (10–18 hours per day). Shorter sleep latency was related to a greater proportion of correct responses for certain aspects of relational binding. There were no associations between sleep and recognition memory or attention.

Conclusions: Our findings suggest that habitual sleep duration and short sleep latency associate with 6-month-olds' relational memory, suggesting a preferential association with memory tasks that are sensitive to development during the second half of the first year.

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Recent studies have shown that sleep following exposure to new knowledge is beneficial for memory consolidation in early infancy.^{1–4} For example, 3-month-old infants who napped after learning

demonstrated enhanced memory for cartoon faces than their counterparts who remained awake for an equivalent duration⁴; and in 6- and 12-month-old infants, only those who had napped after learning object-action associations were able to demonstrate the target actions after a 4-hour and 24-hour delay (compared to age-matched controls).¹

However, to the best of our knowledge, only 1 study has investigated the relationship between habitual sleep (*prior* to knowledge exposure) and memory in infants. Ten-month-old children (N =

* Corresponding author at: Centre for Research in Child Development, National Institute of Education, National Institute of Education, Nanyang Technological University, Block 5, Level B3, 1 Nanyang Walk, Singapore 637616. Tel.: +65 6219 6253.

E-mail address: anne.rifkin@nie.edu.sg (A. Rifkin-Graboi).

¹ Anne Rifkin-Graboi is now at the Centre for Research in Child Development, National Institute of Education, Nanyang Technological University, Singapore.

25) were tested using an elicited imitation task⁵ in which the infants were visually presented with six 2-step event sequences accompanied with narration. Recall memory was elicited through a verbal prompt by the experimenters, immediately after experimenters demonstrated target actions (as a measure of encoding), and after a 2-hour delay. The 2-hour delay test also included a generalization test using comparable versions of the learnt stimuli. The researchers found that daytime sleep duration was positively related to memory encoding and memory generalization. Percentage of nighttime sleep and frequency of night awakenings were negatively related to memory encoding and memory generalization, respectively. In contrast, sleep was not significantly related to delayed memory. However, it is unclear whether these findings suggest a specific relation between sleep and memory encoding and memory generalization per se or, rather, suggest that the relation between sleep and cognition must be viewed in a developmental context, with the most prominent associations expectable on emerging functions.

In contrast to the limited work regarding habitual sleep and cognitive functioning in infancy, there is more work concerning habitual sleep in older toddlers/children and adults. Such research demonstrates that sleep duration and individual differences in sleep architecture are important for learning and memory. In such studies of habitual sleep behavior, variations in sleep duration,^{6–9} sleep latency, sleep efficiency,⁹ and night awakenings¹⁰ were found to associate with memory for newly learnt items. Moreover, recent studies have shown that deviations from average/recommended sleep duration have a negative impact on memory and cognition.^{6,8,11} For example, children who were habitual short sleepers in earlier childhood had lower vocabulary knowledge when tested later at 5 years of age,¹² suggesting that persistent habitual short sleep was prospectively associated with poorer memory formation of newly learnt words.

Infancy represents a period of major neurodevelopmental change, especially within the domain of memory. Infants display *recognition memory* (defined in infancy as a preference or response to a novel stimulus)¹³ shortly after birth. As such, recognition memory may be dependent on brain regions that are largely mature at birth.¹⁴ In contrast, other forms of memory, such as relational memory, emerge later and show a protracted developmental pattern.¹⁴ For example, the ability to learn relations between an object and a place (referred to here as *relational binding*) begins to emerge around 6 to 9 months of age,^{15,16} and the ability to learn the association between an object and an action (here referred to as *deferred imitation*) emerges around 6 to 12 months of age.¹⁷ Relational memory is key developmental milestone in preverbal infants and an important aspect of cognitive development—where the demonstration of relational binding suggests that preverbal infants are able to form associations between unrelated visual stimuli,^{15,16} and deferred imitation provides evidence that preverbal infants have the ability to form an internal memory (of an association/binding between an object and a target action) and that the memory can be stored for subsequent recall.^{17,18} Both relational memory and deferred imitation are important, as memory binding is a potential precursor of event/episodic memory¹⁹ and deferred imitation is a strong predictor of subsequent language development.^{20–22} Interestingly, the protracted development in relational memory may reflect changes in brain development,¹⁴ which may be influenced by sleep.^{23–25} Indeed, data from mammalian models suggest that sleep plays a role in brain maturation.^{26–28}

Here, we investigated associations between habitual sleep among a cohort of typically developing 6-month-old Singaporean infants with performance on tasks considered to assess individual differences especially during the onset of relational memory processes (emerging as early as 6 months of age).^{1,15,29} We were particularly interested in the onset of development for the relational memory tasks, as individual differences associated with sleep may be most prominent during periods of developmental change. The study also explored whether

sleep behavior is related to domains of memory or aspects of general cognition, such as recognition memory (ie, preference or response to a novel stimulus)¹³ and attentional orienting (ie, the ability to shift attention toward a particular stimulus),³⁰ respectively, unlikely to be undergoing equivalent developmental change. We hypothesized that short sleep duration (<10 hours per day, based on National Sleep Foundation's [NSF's] recommendations),³¹ longer sleep latency, and greater frequency and duration of night awakenings would be independently associated with poorer relational memory performance (ie, deferred imitation and relational binding tasks) but not with performance on tasks that assess recognition memory or attentional orienting, which develop earlier in infancy.

Methods

Participants

The infants in the study were enrolled in the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) study, which recruited 1247 pregnant women from 2 major birthing hospitals in Singapore. When infants were 6 months old (± 2 weeks, $M = 183.43$ days, $SD = 4.94$), caregivers were asked to complete the Brief Infant Sleep Questionnaire (BISQ),³² which was used to assess infants' habitual sleep behavior. A subsample of infants with normal perinatal outcomes and born of normal pregnancies took part in a cognitive testing battery at the Singapore Institute of Clinical Sciences Neurocognitive Development Centre. The current work focuses upon 267 infants (male = 56.2%) with completed BISQ data and who took part in the test battery. Detailed descriptions of the cohort and recruitment for cognitive testing have been reported in previous publications.^{33,34} The GUSTO study was approved by the National Health Care Group Domain Specific Review Board and the SingHealth Centralized Institutional Review Board. Written informed consent was obtained from each child's caregiver. Please see Appendix A for further information about the exclusion criteria and sample characteristics.

Brief Infant Sleep Questionnaire

The BISQ is a caregiver-reported questionnaire about infant sleep patterns over the last 2 weeks. Total sleep duration was assessed by summing night and day sleep duration. *Short sleep duration* was defined as <10 hours per day, which is an amount categorized as “not recommended” by the NSF (United States) for children 4 to 11 months old. *Typical sleep duration* was defined as the range from 10 to 18 hours, which includes sleep durations categorized as either “recommended” (12–15 hours) or “may be appropriate” (10–11 hours or 16–18 hours) in the 2015 NSF recommendations for sleep durations in infants 4 to 11 months of age.³¹ In addition to sleep duration, we examined questions on the BISQ that relate to sleep latency (“How long does it take to put your baby to sleep in the evening?”) and sleep (dis)continuity (“How much time does your baby spend in wakefulness from the time he/she falls asleep in the evening to waking up the following morning?” and “What is the average number of times that your child wakes up per night?”).^{35,36} Data points were considered outliers and removed where total sleep duration was <4 hours or >22 hours, sleep latency >2 hours, duration of night awakenings >4 hours, or number of awakenings >5, as described in previous studies.³⁷

Cognitive measures

Memory tasks were administered as part of a 2- to 3-hour laboratory assessment. With the exception of the deferred imitation task (where the baseline and learning phase occurred at the start of the

visit and the test phase occurred at the end of the visit), the order of tasks was counterbalanced across infants. To minimize effects of fatigue on performance, the visits were scheduled at times of the day when parents felt their infants would be most alert, and breaks were given between tasks. Each cognitive task will be described briefly below. A more detailed account of each task has been described in a previous publication.³³ Unless otherwise stated, computerized stimuli were presented using Eprime software (Psychology Software Tools), eye movements were recorded using a TOBII eye tracker (TOBII Technology) with a sampling rate of 60 Hz, and video recordings were taped using Canon Legria camcorders.

Relational memory

Deferred imitation

Infants were seated on their caregiver's lap and held firmly at the hips. Throughout the task, the puppet was held in the experimenter's right hand, with the experimenter kneeling in front of the infant such that the puppet was positioned at the infant's eye level and was within reach (approximately 30 cm from the infant's chest). The entire procedure was video recorded. The task (modeled after the task of Barr et al¹⁷) began with a baseline phase to assess spontaneous production of any of the target actions. During baseline, the infant was given 90 seconds to interact with a puppet rabbit that had a removable mitten on its right paw. After the baseline phase, the experimenter demonstrated 3 target actions (how the mitten could be [1] removed, [2] shaken to make the bell inside ring, and [3] replaced) a total of 6 times over 60 seconds. Similar to Barr et al, the demonstration occurred without narration or practice opportunities. The test phase occurred after a 2- to 3-hour ($M = 2.27$, $SD = .06$) delay, in the same context, where the infant had 90 seconds to display imitation of the trained actions without receiving any memory prompts. Researchers followed the 3-point coding system of Barr et al, identifying instances of removing, shaking, and trying to replace the mitten. Infants who did not pull off the mitten during the testing phase and who were not able to demonstrate the ability to pull off the mitten in a separate subsequent test were excluded from the analysis so as to ensure that differences in motor abilities did not confound the memory assessment.

Relational binding

The relational binding (eye-tracking) paradigm tested infants' ability to learn relations between arbitrary object-background pairs.^{15,16} Infants viewed a block of 3 study trials, each with a toy superimposed on an audiovisual scene comprised of a scenic background and a folksong to facilitate attention. Following the 3 study trials, 1 of the audiovisual scenes was again displayed, and all 3 of the now familiar toys were superimposed upon the top left, top right, and bottom of the background (position counterbalanced). The proportion of time that infants spent fixating on the toy that matched the background was used as an index of relational memory. There were 12 blocks of trials. Similar to Richmond and Nelson's procedure,¹⁶ half of the test trials were in the immediate condition (ie, the scene/toy match appeared on the previous study trial), whereas half were in the delayed/interference condition (ie, the scene/toy match appeared 2 trials back). Looking behavior was analyzed during the first 1000 milliseconds, as this is a time frame within which 6- to 9-month-old infants have been found to display preferential looking in previous work using this task.^{15,16,38}

Recognition memory

Recognition/novelty preference

This paradigm used "Habit" software³⁹ to test the speed with which infants habituated to a repeatedly presented stimulus and

the extent to which they recognized that stimulus compared with a novel stimulus. Each trial began when the infant looked at the stimulus (toy bear or wolf) and ended when the infant looked away. At the end of each trial, an attention grabber was presented on the screen to get the infant to look back at the screen. The infant met habituation criterion when the sum of the infant's look time in 3 consecutive trials was less than half the sum of the 3 consecutive longest trial durations. After habituation occurred, two 10-second paired comparison trials were used to test recognition. Novel and familiar stimuli were presented on the left and right of the screen (counterbalanced). The current study focused on 2 variables, namely, the number of trials to habituation and recognition/novelty preference (operationalized as the average proportion of time spent looking at the novel vs learnt/habituated stimulus).

Attentional orienting

Visual expectation

The paradigm tested components of attentional processing. Specifically, the task examined orienting speed to eighteen 700-millisecond "baseline" movie clips that were presented randomly on the left or right of the eye tracker screen. Attentional orientation was measured via the timing of reactive saccades—the time taken for infants to shift their eyes towards each randomly presented stimulus. Trials where fixation occurred within 133 milliseconds of stimulus onset were excluded; given constraints in infant eye movement, such looks would have had to originate prior to the onset of the stimuli.⁴⁰ The analysis included only data from trials where stimuli appeared on the screen in the opposite location of the prior trial to limit any effects of perseveration.

Covariate measures

Breastfeeding exposure

Interviewer-administered questionnaires about feeding practices were administered to mothers when the infants were 3 weeks, 3 months, and 6 months. For this analysis, breastfeeding exposure was categorized into high, intermediate, and low. Infants in the high-breastfeeding exposure group were predominantly breastfed (only breastmilk and water) until 4 months and at least partially breastfed (mixture of breastmilk and formula milk) until 6 months. Infants in the low-breastfeeding exposure group were exclusively formula fed before 3 months. Infants who were partially or predominantly breastfed beyond 3 months but did not meet the criteria for the high-exposure group were categorized as intermediate exposure. Detailed information about breastfeeding practices in the GUSTO sample has been reported in previously.³³

Napping

Although the visits were scheduled at times of the day when parents felt their infants would be most alert and breaks were given between tasks, 57.7% of the infants napped during the visit. One possible reason may be that infants of this age have multiple naps across the day³⁷ which unfortunately overlapped with the duration of the visit. Still, it should be noted that with the exception of the deferred imitation task, all tasks mentioned in the paper used eye-tracking methods, which required infants to have their eyes open to provide useable data. Therefore, nap/nap duration was not adjusted as a covariate for these tasks, as infants who had fallen asleep within the administration of these tasks would not have provided useable data for analyses. For the deferred imitation task, the baseline and learning phase occurred at the start of the visit, and the test phase occurred at the end of the visit. As the task spanned the whole duration of the visit, all the naps mentioned took place between learning and testing phase and were adjusted as covariates in the analyses for

deferred imitation (see “Statistical analyses” section). In addition, after the infants had woken up from their naps, research coordinators always checked to ensure that the infants were alert and responsive (before beginning the next task).

Maternal anxiety

Maternal (postnatal) anxiety was measured via the State-Trait Anxiety Inventory⁴¹ at the 3-month postnatal time point. The State-Trait Anxiety Inventory measures symptom severity for both “state” and “trait” anxiety, referring, respectively, to levels of current anxiety symptoms and anxious personality traits.⁴¹ As previous work on the GUSTO cohort found that maternal (postnatal) trait anxiety was related to relational binding performance, we only included trait anxiety in our current analysis.²⁹

Maternal sensitivity

As part of the 6-month laboratory assessment, mother-infant interactions were also recorded in a 15-minute observational session. Maternal sensitivity was assessed via the Revised Mini-A short form of the Maternal Behavioral Q Sort V (Mini-MBQS-V).⁴² Detailed descriptions of the procedure of the observational session and scoring of the Mini-MBQS-V can be found in previous publications,^{29,43} as can its association with relational memory within this cohort.²⁹

Statistical analyses

Statistical analyses were carried out on IBM SPSS version 23 using hierarchical (blockwise entry) linear regression, where block 1 adjusted for socioeconomic status (maternal education); step 2 adjusted for other known task-related confounders (if any); step 3 adjusted for baseline performance (if any); and in the final block, the key sleep measure was entered.

For the deferred imitation task, block 2 adjusted for the duration of the delay between training and test ($M = 2.27$ hours, $SD = .06$) and the total duration of naps ($M = 28.24$ minutes, $SD = 22.08$) that occurred during that delay, as most infants napped during the 2- to 3-hour visit and napping has previously been found to improve performance on this task in 6- and 12-month-old infants.¹ Block 2 also adjusted for breastfeeding exposure, as this has been found to predict task performance.³³ Next, block 3 adjusted for the number of types of spontaneous “target” actions (out of the 3 possible actions) that the infant produced during the baseline phase.³³

For the relational binding task, block 2 adjusted for breastfeeding exposure,³³ maternal sensitivity, and postnatal anxiety, as these factors have been found to be associated with relational binding task performance in our sample of infants.²⁹

For the recognition memory/ novelty preference test, block 2 adjusted for the stimulus type (whether the infants habituated to a wolf or a bear stimulus), as data from the larger GUSTO sample with similar exclusion and inclusion criteria showed that novelty preferences were higher when the wolf ($M = .58$, $SD = .13$) was the novel stimulus as compared to when the bear ($M = .49$, $SD = .12$) was the novel stimulus ($P < .001$).

Results

The infants had an average (SD) of 8.46 hours (1.97) of night sleep, 3.29 hours (1.85) of day sleep, 0.56 hour (0.40) of sleep latency, and 1.04 hours (1.18) of night awakenings and woke up an average of 1.73 (1.11) times each night. A total of 77.2% had a total sleep duration within the range of 10 to 18 hours (classified as typical sleepers). Of the 61 infants (22.8%) whose sleep duration fell outside of this range, 59 infants were classified as short sleepers (<10 hours) and 2 infants were extreme long sleepers (> 18 hours). Because of the small sample size of infants classified as extreme long sleepers, they

were excluded from the current analyses. As expected, a 1-way analysis of variance (ANOVA) revealed that infants classified as typical sleepers ($M = 12.79$ hours, $SD = 1.86$) had significantly longer total sleep durations than short sleepers ($M = 7.79$ hours, $SD = 1.65$); $F_{1,263} = 346.63$, $P < .001$.

Relational memory

Deferred imitation

The infants demonstrated an average (SD) of 0.44 (0.67) spontaneous (target) action during baseline and 0.99 (0.90) target action during the test phase. A repeated-measures ANOVA revealed also that infants demonstrated significantly more target actions during the test phase compared to the baseline phase ($F_{1,161} = 30.07$, $P < .001$).

The adjusted regression model (Table 1) indicated that infants who slept 10 to 18 hours per day (typical sleepers) demonstrated more target actions on the deferred imitation task during the test phase compared with children with <10 hours of sleep per day (short sleepers) ($B = .42$, $SE = .19$, $P = .031$). In contrast, there was no significant difference in the number of spontaneous target actions demonstrated by typical and short sleepers during the baseline phase ($B = .03$, $SE = .15$, $P = .86$; see Appendix B for regression table). As performance between short and typical sleepers differed for the test phase but not baseline phase, we ran separate repeated-measures ANOVAs to further explore the baseline vs test phase within the sleep duration groups. Interestingly, there was no difference in number of target actions demonstrated in the baseline ($M = .33$, $SD = .55$) and test ($M = .63$, $SD = .62$) phase for the short sleepers ($F_{1,29} = 2.77$, $P = .11$; Fig. 1). In contrast, the typical sleepers demonstrated more target actions during the test ($M = .99$, $SD = .85$) phase compared to the baseline ($M = .43$, $SD = .65$) phase ($F_{1,118} = .3443$, $P < .001$; Fig. 1).

There was no association between sleep latency ($B = -.19$, $SE = .19$, $P = .33$) and the duration ($B = -.12$, $SE = .08$, $P = .11$) or frequency ($B = .02$, $SE = .07$, $P = .72$) of nighttime awakenings with deferred imitation performance during the test phase.

Relational binding

The infants spent an average (SD) of 0.34 (0.01) proportion of time looking at the correct toy stimulus in the immediate condition and 0.39 (0.23) proportion of time looking at the correct toy stimulus in the delayed/interference condition.

Longer sleep latency was negatively associated with performance on the immediate condition ($B = -.11$, $SE = .04$, $P = .014$; Table 2), with children who took longer to fall asleep spending a smaller proportion of time looking to the correct toy stimulus (Fig. 2). In contrast, there was no association between sleep latency and performance on the delayed/interference condition ($B = .04$, $SE = .05$, $P = .47$; see Appendix B for regression table).

There were no associations between sleep duration (immediate: $B = .009$, $SE = .06$, $P = .88$; delayed: $B = -.03$, $SE = .06$, $P = .67$) and duration (immediate: $B = -.03$, $SE = .02$, $P = .15$; delayed: $B = .003$, $SE = .02$, $P = .90$) or frequency (Immediate: $B = -.02$, $SE = .02$, $P = .25$; delayed: $B = .01$, $SE = .02$, $P = .48$) of night awakenings with relational binding performance.

Recognition memory

Recognition/novelty preference

There was no association between sleep duration ($B = .50$, $SE = .96$, $P = .60$), sleep latency ($B = -.11$, $SE = .97$, $P = .91$), and duration ($B = -.03$, $SE = .38$, $P = .93$) or frequency ($B = -.27$, $SE = .36$, $P = .45$) of night awakenings with the number of trials to reach habituation. Similarly, there was no association between sleep duration ($B = -.04$,

Table 1
Sleep duration (short vs typical sleepers) and deferred imitation performance (test phase)

	Block 1 (maternal education)			Block 2 (task-related confounders)			Block 3 (baseline performance)			Block 4 (sleep duration)		
	B	SE	P value	B	SE	P value	B	SE	P value	B	SE	P value
Maternal education	-.02	.08	.80	-.03	.09	.74	-.03	.09	.74	-.04	.09	.64
Delay duration				.001	.003	.66	.001	.003	.66	.001	.003	.79
Nap duration				-.003	.005	.49	-.003	.005	.49	-.004	.005	.39
Breastfeeding exposure				.01	.11	.92	.01	.11	.93	-.03	.11	.81
Baseline performance							.006	.12	.96	.002	.12	.98
Sleep duration										.42	.19	.031
R ² (model)	Model 1 R ² < .001			Model 2 R ² = .005			Model 3 R ² = .005			Model 4 R ² = .041		

SE = .02, P = .07), sleep latency (B = -.03, SE = .02, P = .23), and duration (B = .009, SE = .009, P = .23) or frequency (B = .01, SE = .02, P = .48) of night awakenings with novelty preference.

Attentional orienting

Visual expectation

No associations were observed between sleep duration (B = 9.53, SE = 10.36 P = .36), sleep latency (B = 1.92, SE = 10.27, P = .85), and duration (B = .65, SE = 3.84, P = .87) or frequency (B = .10, SE = 3.56, P = .98) of night awakenings and speed of attentional orienting.

Discussion

Although work with children, adults, and the elderly finds that habitual sleep relates to cognitive functioning and despite work demonstrating the importance of sleep for general aspects of infant development, few studies have examined the association between habitual sleep and performance on developmentally relevant cognitive abilities during infancy. Here, in our examination of 6-month-old infants, we report an association between habitual sleep and cognitive processes thought to emerge at this stage of infancy (ie, relational binding and deferred imitation) but not performance on tasks likely to emerge earlier in development (ie, recognition memory and attentional orientation). Infants who were short sleepers (<10 hours per day) recalled significantly fewer target actions in the deferred imitation task (test phase) than infants with longer sleep durations (10–18 hours per day). In addition, only infants who slept between 10 to 18 hours demonstrated significantly more target actions during

the test phased compared to spontaneous baseline actions. There was no difference in spontaneous baseline actions and test target actions for the short sleepers. These findings support previous work demonstrating that deviations from average/recommended sleep durations associate with poorer memory as well as cognitive outcomes.^{6,8,12} For example, habitual short sleep durations throughout early childhood increased the risk of poor verbal and nonverbal cognition, and in adulthood, habitual short sleepers had poorer verbal fluency and memory recall performances than typical sleepers. Moreover, taking less time to fall asleep (ie, shorter sleep latency) was associated with a greater proportion of correct looking time in the immediate condition of the relational binding task.

The association between habitual sleep and relational memory in infancy is also important, as relational memory performance is a strong predictor of subsequent cognitive outcomes, such as language development. As compared with other developmental milestones such as recognition memory and turn taking ability, deferred imitation performance in preverbal infants was the strongest predictor of subsequent gestural communicative development at 14 months.²⁰ A recent study also showed that infant deferred imitation ability predicted productive language at 16 months.²¹ The relation between infant deferred imitation performance and subsequent cognitive performance was even present in early childhood, where infants with low deferred imitation (and joint attention) scores had significantly lower cognitive ability scores (McCarthy Scales) at 50 months.²² In contrast to deferred imitation, there have been fewer studies looking at the relational binding task in infants. Still, it is widely accepted that memory binding is a key precursor of subsequent episodic memory (that develops in mid childhood)⁴⁴ As our current findings suggest that poor habitual sleep is associated to poorer deferred imitation

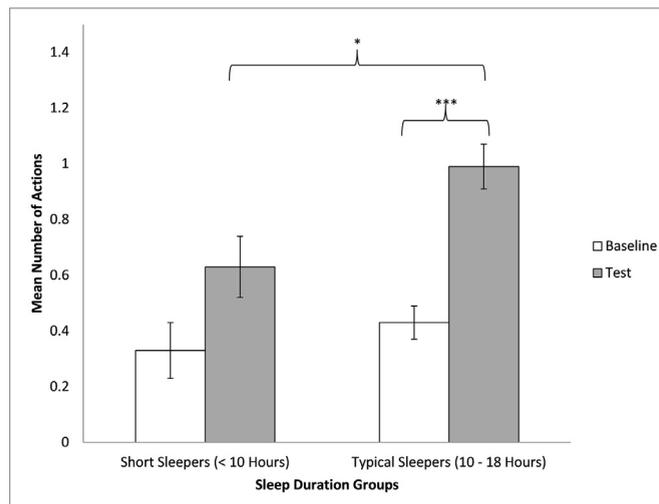


Fig. 1. Mean number of target actions produced during baseline (spontaneous) and test phase. Error bars represent standard errors of the means.

Table 2
Sleep latency and relational binding proportion of correct looks (immediate condition)

	Block 1 (maternal education)			Block 2 (task-related confounders)			Block 3 (sleep latency)		
	B	SE	P value	B	SE	P value	B	SE	P value
Maternal education	-.001	.02	.95	.001	.02	.95	-.008	.02	.74
Maternal sensitivity				-.02	.05	.67	-.05	.05	.34
Breastfeeding exposure				-.008	.03	.77	-.02	.03	.55
Maternal anxiety				-.001	.002	.67	<.001	.002	.85
Sleep latency							-.11	.04	.014
R ² (model)	Model 1 R ² = .001			Model 2 R ² = .005			Model 3 R ² = .057		

and relation binding performance, it would be useful to consider promoting better habitual sleep even in early infancy, such as emphasizing the importance of a consistent bedtime routine,⁴⁵ because individual differences in infant habitual sleep may indirectly affect later cognitive and memory development.

In Lukowski and Milojevic's (2013) study on 10-month-old infants, the researchers did not observe a significant relation between total sleep duration and delayed recall. This is in contrast to the current 6-month-old sample, where an association between sleep duration and delayed recall was observed. The reason for differences may be multifold and likely include variation in both procedures and developmental stage. Unlike Lukowski and Milojevic's elicited imitation task, the deferred imitation task used in the current study did not include narration or prompts. Previous work has shown that performance is improved by cues and narrations⁴⁶ and also suggested that the deferred imitation task is a more challenging memory task than elicited imitation.⁴⁷ As our participants were younger than those in Lukowski and Milojevic's study, it is possible that 6-month-old GUSTO infants may have found the delayed recall task to be more challenging (as it occurred without any cues) than the 10-month-old infants in Lukowski and Milojevic's study where delayed recall was accompanied by a verbal prompt to encourage the production of the target actions. Although it is not possible within the scope of this study to investigate the precise brain regions underlying elicited imitation compared to deferred imitation or the rate of their development, it is interesting to consider one implication of these findings: namely, that sleep may affect different aspects of relational memory in a developmentally dependent manner.

Results also revealed that sleep latency was associated with immediate performance on the relational binding task. Past work in the larger GUSTO cohort and within the current subsample suggests

that 6-month-old infants found the delayed/interference condition most cognitively challenging¹⁵ and perhaps more likely to be affected by concurrent sleep-related changes. Unexpectedly, there was no association between sleep measures and delayed/interference performance. Still, in Richmond and Power's (2014) study which used a similar eye-tracking paradigm on 6-month-old infants, infants only displayed significant above-chance proportion of looks towards the matching (correct) stimulus in the immediate but not delayed/interference condition,³⁸ which is similar to our current results where we find sleep-related associations in terms of greater proportions of correct looks in the immediate condition but not in the delayed/interference condition. Future work should explore the link between sleep and delayed/interference performance, taking into account influences from processes like working memory, which may have obscured any relations between sleep and delayed/interference performance.

Interestingly, sleep did not relate to infants' performance in the recognition/novelty preference task. In contrast to relational memory, recognition memory is apparent shortly after birth and may be dependent on brain regions that are largely mature at birth.¹⁴ Therefore, current findings suggest that a preferential association exists between habitual sleep and memory tasks that are sensitive to current development (relational memory) rather than tasks that depend on processes that are relatively mature at the stage of development (recognition memory). One commonly cited limitation in sleep and memory research is that it is difficult to disentangle the relation between attention and learning in memory formation.⁴⁸ Likewise, habitual sleep did not affect attentional orienting. Hence, it is unlikely that current findings between habitual sleep and deferred imitation or relational binding performance are confounded by individual differences in attentional processes during the task administration.

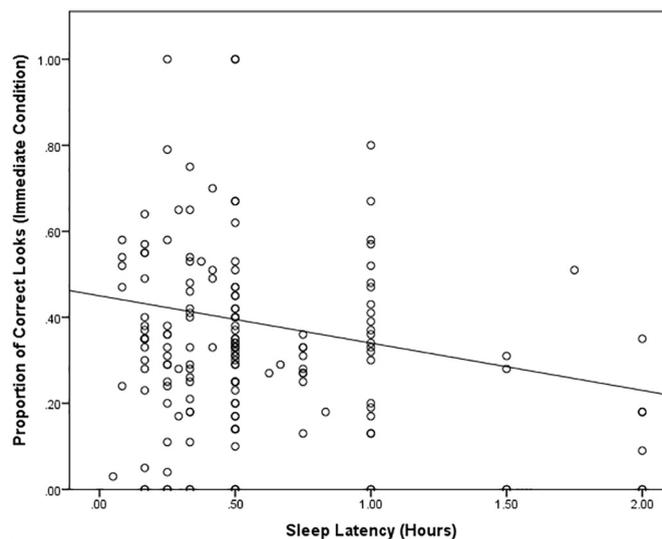


Fig. 2. Relational binding immediate condition: proportion of correct looks as a function of sleep latency.

Consistent with the 2-stage systems consolidation models⁴⁹ involving the hippocampal and neocortical systems, recent work suggests that longer sleep duration between learning and testing allows for more efficient hippocampal-neocortical transfer of memories in infants.¹ It is suggested that this transfer may allow for increased capacity in the hippocampal system to encode and store newly learnt memories during subsequent wakefulness. Our findings for the deferred imitation task could be explained by effects of insufficient habitual sleep on the ability to transfer memory from the hippocampal to neocortical systems.

Still, the system consolidation models typically refer to postlearning sleep rather than habitual sleep, and some researchers have also suggested that performance on deferred imitation and relational binding tasks cannot be fully explained by hippocampal networks until 18–24 months of age, and as such, it is likely that the early ability to perform such tasks is cortically driven.⁵⁰ If this is the case, then sleep-associated effects on early infant memory may be driven by sleep's impact upon cortical consolidation,⁵¹ which may be explained by the synaptic homeostasis hypothesis (SHY).^{52,53} According to the SHY, learning and encoding new memories cause an increase in synaptic strength (synaptic potentiation), and a saturation of synaptic plasticity reduces learning capacity. Slow-wave activity during subsequent sleep then leads to a downscaling of synaptic strength where weak cortical connections are pruned and the remaining stronger cortical connections are consolidated. This pruning process also frees up brain networks for subsequent learning by restoring synaptic plasticity.^{52,53} As sufficient amounts of sleep are needed for the above processes, our findings between insufficient habitual sleep and relational memory performance (deferred imitation task) are also consistent with the SHY.

A limitation of our study is that it is not possible to conclude if sleep latency plays a direct role in influencing relational memory performance. Unlike the relation between habitual short sleep and deferred imitation, the relation between sleep latency and relational binding can be explained neither by the systems consolidation model nor the synaptic homeostasis hypothesis. Existing research has shown that longer sleep onset latency is related to internal⁵⁴ and external (behavioral) dysregulation,^{55,56} which could also have resulted in poorer relational binding performance. Still, even if sleep latency plays an indirect role in relational memory, the association is still important, as steps to promoting shorter sleep latency (eg, informing parents of good sleep health practices) may be easier than treating internal/external dysregulation. In addition, sleep duration and sleep latency associate with different relational memory measures in this study (ie, short sleep was related to deferred imitation but not the relational binding task). Still, past research has also shown that sleep latency and sleep duration associate differently with cognitive performance measures. In school-aged children, longer sleep latency was related to lower accuracy levels across all working memory loads, but shorter sleep duration only related during the highest load condition.⁵⁷ Therefore, it will be interesting to follow this cohort to determine if different associations for sleep duration and latency with memory will emerge later in development.

Another limitation is that the effect sizes of our findings are relatively small. However, as with other exposures demonstrating small effect sizes (eg, breastfeeding^{58,59}), findings may still be of consequence at the population level. Also, we had to exclude infants who did not provide usable data due to fussiness and lack of compliance (Appendix A). Although further analysis did not reveal any relations between current task performance and an earlier (3 months) temperament measure (Appendix C), it would be useful for future studies to include a concurrent measure of infant temperament, as it is possible that individual differences in infant temperament may confound relations between sleep and memory. Furthermore, many infants napped within the visit, and although research coordinators checked

that infants were alert before proceeding to the next task, it is possible that the infants were still experiencing some sleep inertia. However, it should be noted that, with the exception of the deferred imitation task, all the other tasks were eye-tracking tasks, where the useable/analyzable data should not have been affected by sleep inertia, as infants who were not alert enough to focus on the stimuli/screen would not have provided useable data for analyses. In addition, the BISQ relies on subjective caregiver-reported sleep, and the BISQ also explores average/habitual sleep patterns which may not be reflective of the quality of sleep directly preceding the cognitive testing, for example, if the infant takes much longer (than usual) to fall asleep on that particular night. Therefore, it would be useful to replicate the study using more objective measures of sleep, such as actigraphy devices or sleep polysomnography. Future work should also include a measure of sleep patterns directly preceding the cognitive testing to ensure that the relations between infant habitual sleep (BISQ) and relational memory are not confounded by any unforeseen irregularities in sleep patterns prior to testing.

Despite these limitations, this study has several strengths including being the largest study to explore relationships between sleep and memory in infants as young as 6 months, use of multiple types of memory assessments, and an evaluation of attentional performance. This study's findings may also have useful implications for parents and health practitioners. That is, as habitual sleep relates to infant relational memory, which in turn predicts longer term cognitive development, the promotion of good sleep education to parents of young infants may also have long-term benefits for early life cognition.

In summary, this study helps fill a gap in existing research on habitual sleep and emerging memory/cognitive abilities within the first year of life. Our findings indicate that 6-month-old children who slept 10–18 hours per day exhibited better performance on a deferred imitation task compared to habitual short sleepers (<10 hours). Shorter sleep latency was also associated with better immediate performance on a relational binding task. Our results suggest that individual differences in habitual sleep are particularly associated with memory processes undergoing current development as compared to processes that are relatively matured, and that underscores the importance of infant sleep. Future work should examine whether infant sleep behavior impacts memory development.

Disclosure

Dr. Rifkin-Graboi declares that the larger GUSTO project received funding from from Abbott Nutrition and The Singapore National Research Foundation under its Translational 646 and Clinical Research (TCR) Flagship Programme and administered 647 by the Singapore Ministry of Health's National Medical Research Council (NMRC), Singapore-NMRC/TCR/004-NUS/2008; NMRC/TCR/ 649 012-NUHS/2014, during the conduct of the study.

Dr Goh has nothing to disclose.

Dr Gooley has nothing to disclose.

Dr Yap has nothing to disclose.

Dr Tham has nothing to disclose.

Dr Teoh has nothing to disclose.

Dr Broekman has nothing to disclose.

Dr Abdul Jafar has nothing to disclose.

Dr Richmond has nothing to disclose.

Acknowledgments

We would like to thank the GUSTO study group and all the participants.

Funding source

This research is supported by the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship Programme and administered by the Singapore Ministry of Health's National Medical Research Council (NMRC), Singapore NMRC/TCR/004-NUS/2008; NMRC/TCR/012-NUHS/2014. Additional funding is provided by the Singapore Institute for Clinical Sciences; Agency for Science Technology and Research (A*STAR), Singapore; Biomedical Research Council Strategic Positioning Fund (grant ID: SPF2013/002).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sleh.2018.12.007>.

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