Is Statistical Learning Affected by Sleep Apnea?

Joanne Arciuli
Faculty of Health Sciences, The University of Sydney, Australia
Corresponding author: joanne.arciuli@sydney.edu.au

Andrew Vakulin
Adelaide Institute for Sleep Health, Repatriation General Hospital, School of Medicine, Flinders University, Australia
Woolcock Institute of Medical Research, Sleep and Circadian Research Group, Central Clinical School, The University of Sydney

Angela D'Rozario
Woolcock Institute of Medical Research, Sleep and Circadian Research Group, Central Clinical School, The University of Sydney

Hannah Openshaw
Woolcock Institute of Medical Research, Sleep and Circadian Research Group, Central Clinical School, The University of Sydney

David Stevens
Woolcock Institute of Medical Research, Sleep and Circadian Research Group, Central Clinical School, The University of Sydney

Doug McEvoy
Adelaide Institute for Sleep Health, Repatriation General Hospital, School of Medicine, Flinders University, Australia

Keith Wong
Woolcock Institute of Medical Research, Sleep and Circadian Research Group, Central Clinical School, The University of Sydney

Caroline Rae
Neuroscience Research Australia, University of New South Wales, Australia

Ron Grunstein
Woolcock Institute of Medical Research, Sleep and Circadian Research Group, Central Clinical School, The University of Sydney

Abstract

It is thought that sleep is important for learning yet we know strikingly little about the relationship between sleep and a form of implicit learning known as statistical learning (SL). SL can be assessed using a distinct familiarisation phase in which participants are exposed to a stream of stimuli that contains statistical regularities but are not given any instruction to learn or any form of reinforcement. This is followed by a surprise test phase some time later where implicit learning of those statistical regularities is assessed. In the current study we investigated the relationship between sleep and SL across a period that included night time sleep with polysomnography (PSG) monitoring. Participants were 47 adults (mean age = 48.79 years, sd = 8.76 years) known to have impaired sleep due to obstructive sleep apnea. They were exposed to familiarisation in the evening prior to going to sleep and undertook the surprise test phase the following evening, approximately 24 hours later (mean overnight sleep time = 399.60 mins). Results revealed that, as a group, participants showed statistically significant SL despite the substantial delay between familiarisation and test phases. Although we found no relationship between individual differences in SL and clinical measures of sleep apnea severity, our findings revealed that SL is positively correlated with non rapid eye movement sleep (NREM).

Keywords: statistical learning; VSL; sleep; sleep apnea; sleep apnoea; sleep-dependent learning

Introduction

The brain's ability to detect statistical regularities in the environment is known as statistical learning (SL). SL is implicit in that it occurs without any intention to learn, without any form of reinforcement, and without conscious awareness (Perruchet & Pacton, 2006). SL has been shown to operate across a range of modalities and different types of stimuli including speech, musical tones, geometric shapes, scenes, and cartoon figures. With regard to sequentially presented stimuli it has been shown to operate across both adjacent and non-adjacent dependencies. SL is present from infancy. This powerful learning mechanism is thought to underpin a wide variety of critical mental tasks. For a review of SL research in recent decades see Arciuli and von Koss Torkildsen (2012).

Lasting learning is desirable in a mechanism underpinning mental activity. However, there has been relatively little research investigating the lasting effects of SL. In fact there is only a handful of previous studies that have examined SL over time. Some of these previous studies have been conducted with infants, while others have examined adults. Here we restrict our discussion to previous studies of adults. Before discussing these previous studies we review the embedded triplet paradigm which is often used to assess SL.

Although SL can be assessed using a number of different methods, the embedded triplet task is frequently used to test sensitivity to adjacent dependencies in sequentially presented stimuli (e.g. Arciuli & Simpson, 2011, 2012; Aslin et al., 1991; Brady & Oliva, 2008; Evans et al., 2009). This task includes a familiarisation phase where participants are exposed to a stream of individually presented stimuli containing statistical regularities (in this case, embedded triplets). After this initial phase has been completed participants undertake a forced-choice test phase where they are asked to identify regularities that occurred in the familiarisation phase across a number of trials: on each trial they make a decision between an embedded triplet versus a foil triplet and the number of correct responses is tallied as a percentage of the total number of trials. Although participants usually report no conscious sense of familiarity during the test phase, average group performance demonstrates that healthy participants identify embedded triplets at a rate greater than chance (using a one-sample t-test to compare the group average against the chance level of 50%).

A study by Kim et al. (2009) investigated SL in healthy adults using an embedded triplet task with visual stimuli. When the test phase was administered 24 hours after the familiarisation phase participants showed significant levels of SL.[1] In their study of healthy adults using an embedded triplet task, with different visual stimuli, Arciuli and Simpson (2012) manipulated the time between familiarisation and a surprise test phase. Specifically, they incorporated 5 time intervals: 30 mins, 1 hour, 2 hours, and 24 hours. Their between-participants design revealed statistically significant SL at each time interval and no difference in the magnitude of learning at each interval. Like Kim et al. (2009), Arciuli and Simpson (2012) found that SL can be observed 24 hours after exposure to statistical regularities. However, Arciuli and Simpson's (2012) finding regarding equivalent levels of SL at each of five different time intervals raises questions about whether sleep plays a role in consolidating SL.

If sleep plays an important role in consolidating SL we might have expected to see more learning in the participants who were in the 24 hour delay group in the study reported by Arciuli and Simpson (2012). In previous research on sleep and learning (not specifically SL), it has been hypothesised that sleep may play an active role in consolidating learning (especially during NREM sleep: e.g., Diekelmann & Born, 2010). By contrast, some have suggested that sleep may play a more passive role by offering an absence of stimulation (e.g., Ellenbogen, Payne & Stickgold, 2006). Also, it is noteworthy that neither Kim et al. (2009) nor Arciuli and Simpson (2012) collected data on participants' sleep activity. Direct measurement of sleep activity is required for a better understanding of the link between sleep and SL.

A previous study of healthy adults examined the relationship between sleep and SL using polysomnography (PSG). Durrant et al. (2011) examined SL using sequentially presented auditory stimuli. Their SL task, which was not based on the embedded triplet paradigm, was comprised of a distinct familiarisation phase containing statistical regularities, followed by an immediate test phase and, later, a delayed test phase. Experiment 2 included a wake group and a day time sleep group. The sleep group underwent PSG monitoring in a lab – with approximately 4 hours delay (mean sleep time = 83.08 mins) between immediate and delayed testing. The data revealed some marginal results which made it difficult to draw firm conclusions from group comparisons in Experiment 2. However, there was a significant correlation between the duration of slow wave sleep (a type of non rapid eye movement sleep, NREM, known as stage 3) and improvement between immediate and delayed testing within the sleep group. Durrant et al. (2011) interpreted their findings in terms an active role for sleep in the consolidation of learning.

A recent study by Nemeth et al. (2012) examined implicit sequence learning using the alternating serial reaction time task (ASRT) with visual stimuli in 20 adults with obstructive sleep apnea and 20 controls. They found intact and equivalent learning in both groups. However, that study did not examine learning over time. Csabi et al. (2014) used the same ASRT task to assess learning over 10–12 hours (including overnight sleep) in 17 adults with sleep apnea and 17 controls. Group comparisons indicated that sleep disturbance did not affect learning. It is important to note that neither of these previous studies explored the relationship between individual differences in learning and individual differences in sleep apnea severity.

In summary, previous research examining the link between sleep and SL has been limited. A study of healthy adults used PSG but the sleep period was a four hour day time nap. Two other studies have looked at learning in adults with sleep apnea. One of these examined immediate learning while the other investigated learning over 10–12 hours of night time sleep. In the current study we sought to investigate the link between sleep and SL over a 24 hour period in sleep apnea – with participants undergoing PSG for a full period of night time sleep. In view of previous research, we expected that we would likely see intact SL based on group performance, as well as a link between SL and NREM sleep. We were unsure as to whether we would see a link between SL and clinical measures of sleep apnea severity because, as far as we are aware, our study is the first to look at these kinds of individual differences in this population.

[1] Kim et al. used a rapid serial visual presentation (RSVP) reaction time test during their test phase rather than a forced-choice test of familiarity.

Method

Participants

Participants were 47 adults (3 females) who had previously received a clinical diagnosis of sleep apnea (mean age = 48.79 years, sd = 8.76 years).

Study Protocol

Participants arrived for a two night weekend stay at the sleep laboratory at the Woolcock Institute for Medical Research at 7.00 pm. Following brief patient interview participants underwent the familiarisation phase of the SL task. Following polysomnography (PSG) set up patients went to bed at an average time of 9:52 pm and were awakened at an average time of 5:58 am. The surprise test phase of the SL task took place approximately 24 hours after familiarisation.

Overnight Polysomnography (PSG). Participants had overnight PSG with the following recordings: Electroencephalography (EEG: F3, C3, O1, Fz, Cz, Pz, Oz, F4, C4, O2 lead placements), left and right electro-oculograms, submental electromyogram, nasal cannula to measure nasal pressure, leg movement sensors, chest and abdominal motion bands, lead II electrocardiography and arterial oxygen saturation (finger pulse oximetry). Signals were digitized and stored using Embla Titanium hardware and REMLogic software sleep system. Sleep and EEG arousals were scored using standardized criteria (Iber et al., 2007). Apneas were defined as cessations of nasal flow lasting ≥10 s and hypopneas as a >50% decrease in nasal flow (or in both thoracic and abdominal excursions) and associated ≥3% oxygen desaturation or an EEG arousal. Two clinical indexes of severity were obtained: an apnea hypopnea index (AHI); ≥30/hour is considered to be severe (Ruehland et al., 2009, based on AASM criteria), and an oxygen desaturation index (ODI). REM and NREM sleep (including a breakdown across stage 1, stage 2, and stage 3) was calculated as a percentage of total sleep time.

Statistical Learning Task. We used the same visual SL task originally reported by Arciuli and Simpson (2011), presented on a laptop via E-Prime software (Schneider, Eschman & Zuccolotto, 2002). Stimuli were eighteen cartoon-like characters that could not be easily verbalized (i.e. did not resemble known animals, people, or popular cartoon characters). Of these, six were used during instruction and practice leaving 12 for exclusive use during the familiarisation phase and subsequent surprise test phase (see Appendix of Arciuli & Simpson, 2011, for stimuli). These 12 characters were divided into four groups of three (i.e. four triplets).

The familiarisation phase consisted of a continuous stream of individually presented characters which appeared on the screen for 400 ms each. The characters were divided into four groups of three (four embedded triplets): *ABC*, *DEF*, *GHI* and *JKL* Each triplet appeared in the familiarisation stream 24 times (i.e., a total of 96 triplets). In 6/24 instances, one character was presented twice in a row (i.e., repeated) in order to provide a cover task: participants were required to press the space bar of the computer every time they saw the same alien appear twice in a row. These repetitions were counterbalanced among the three characters within each triplet to ensure that repetitions did not draw participants' attention to the existence of triplet boundaries. The order of triplets presented during the familiarisation phase was randomised although it was ensured that the same triplet would never appear twice in a row.

The surprise test phase included 64 trials. For each forced-choice trial participants were presented with two triplets, one following the other: an embedded triplet which had occurred during familiarisation and a foil triplet. Each of the four foil triplets contained one character from three different embedded triplets. These foil triplets never occurred in the familiarisation phase (*AEI, DHL, GKC,* and *JBF)*. Thus, there was a statistical contrast between embedded versus foil triplets: embedded triplets had high internal transitional probabilities (i.e., *B* followed *A* and *C* followed *B* with almost perfect certainty), whereas the internal transitional probabilities of the foil triplets were 0.[2] The presentation order of the embedded versus foil triplets was counterbalanced. During test trials each embedded triplet and each foil triplet was seen an equal number of times (16 times), and each individual character was seen 32 times. Order of test trials was randomised for each participant.

For each participant the number of correct responses was divided by the total number of test trials and reported as a percentage.

Results

Clinical Measures of Sleep Apnea (AHI and ODI)

On average, the sample had moderate to severe sleep apnea (AHI: 35.35 events/hour, *SD* = 22.61) with frequent dips in oxygen saturation (ODI: 26.88 events/hour, *SD* = 21.84). Participants slept for an average of 399.60 mins (*SD* = 45.13) and the average amount of total sleep time spent in NREM sleep was 80.68% (remainder was REM sleep).

Descriptive Statistics from PSG

Descriptive statistics for the entire sample of 47 participants relating to total sleep time (TST: in mins), percentage of total sleep time spent in REM, percentage of total sleep time spent in NREM and percentage of total sleep time spent in stages 1/2/3 are presented in Table 1.

[2] Each character in each embedded triplet was occasionally repeated in the familiarisation phrase, in order to provide a cover task. Thus, internal TPs of the embedded triplets was 0.92.

Table 1: Descriptive statistics.

	Mean	SD
TST (mins)	399.60	45.13
% REM	19.32	6.13
% NREM	80.68	6.13
% stage 1	4.26	2.29
% stage 2	60.94	10.10
% stage 3	15.48	8.32

Statistical Learning

The average SL of the group was significantly greater than chance (mean = 55.39, sd = 15.07, $t(46) = 2.45$, $p = 0.018$, Cohen's $d = 0.722$). There was variability in performance across participants and no evidence of a floor effect.

Relationship between SL and Sleep Variables

Bivariate correlational analyses using Pearsons r were conducted in order to examine the relationship between SL and AHI and ODI, as well as total sleep time (TST: in mins), percentage of total sleep time spent in REM, percentage of total sleep time spent in NREM, and percentage of time spent in stages 1/2/3.

There was no significant relationship between SL and either of our two measures of sleep apnea severity. For SL and AHI we observed $r = -0.064$, $p = 0.668$. For SL and ODI we observed $r = -0.066$, $p = 0.659$.

There was a positive correlation between SL and NREM, $r = 0.297$, $p = 0.042$ (and, due to dependency in the data, an equivalent negative correlation between SL and REM). There was no correlation between SL and total sleep time ($r = -0.019$, $p = 0.897$). There was no significant correlation between SL and stage 1 ($r = 0.033$, $p = 0.827$), stage 2 ($p = 0.103$, $p = 0.491$), or stage 3 ($r = 0.085$, $p = 0.569$).

Discussion

Our participants undertook an SL task which used sequentially presented visual stimuli. They were exposed to a familiarisation phase containing statistical regularities before undergoing a full night of sleep monitoring via polysomnography (PSG). Approximately 24 hours later they were given a surprise test phase to assess implicit learning of embedded regularities in the familiarisation stream.

Our results revealed that statistical learning is remarkably long lasting, even in participants with sleep apnea. Previous studies of healthy adults by Kim et al. (2009) and by Arciuli and Simpson (2012) observed significant SL some 24 hours after participants had been exposed to a familiarisation phase containing embedded statistical regularities. Likewise, based on a group average, the participants with sleep apnea that were assessed in the current study showed statistically significant SL approximately 24 hours after exposure to regularities (a period which included a mean overnight sleep duration of 399.60 mins). This finding is in line with recent studies using the ASRT task that found intact implicit sequence learning in participants with sleep apnea (Nemeth et al., 2012, who looked at immediate learning; Csabi et al., 2014, who looked at learning over 10–12 hours of night time sleep).

Our results revealed no relationship between SL and two commonly used clinical measures of sleep apnea severity (AHI and ODI). Furthermore, there was no relationship between SL and total sleep time. However, as we had hypothesized, we did discover a significant relationship between SL and percentage of total sleep time spent in NREM sleep. Our data revealed that greater SL was associated with a larger percentage of NREM sleep. There were no significant relationships between SL and any of the stages within NREM sleep.

More research is needed to investigate why NREM sleep is associated with SL in both healthy and sleep impaired adult populations. In line with Durrant et al. (2011) we expect that this relationship may point to an active role for sleep in the consolidation/facilitation of learning (e.g. Diekelmann & Born, 2010). However, we note that while Durrant et al. (2011) observed a relationship between SL and stage 3 (slow wave) sleep in their study of healthy adults (which included brief day time sleep), we did not observe a relationship between SL and stage 3 sleep in the current study of overnight sleep in participants with sleep apnea.

One possible link between SL and NREM sleep is via the production of sleep spindles. Sleep spindles (waxing and waning oscillations of 0.5–3 seconds, usually ranging 11–16 Hz) are thought to play an important role in the maintenance of NREM sleep continuity (McGinty & Szymusiak, 2011). Another potential importance of sleep spindles is for new learning and memory consolidation (Fogel & Smith, 2011). Slowing of spindles in sleep apnea patients compared with healthy controls, predominantly in frontal brain regions, has been observed in two studies (Himanen et al., 2003, Schonwald et al., 2012). However, sleep spindles are generally associated with a particular type of NREM sleep (stage 2 sleep) – our analyses did not reveal a significant correlation between SL and stage 2 sleep.

In conclusion, our results suggest that, on average, participants with sleep apnea demonstrate intact SL after 24 hours and that current clinical measures of sleep apnea severity are not related to individual differences in SL. Individual differences in SL are linked with NREM sleep and it would be worthwhile exploring this relationship further using additional techniques such as direct investigation of production of sleep spindles.

Acknowledgments

This research was conceptualised by Arciuli (who presented her idea for collaborative research at an invited presentation at the Woolcock Institute for Medical Research in 2012). Arciuli undertook primary responsibility for the data analysis and writing. Vakulin and D'Rozario supervised data collection and contributed to some sections of the writing (listed in order of their contributions). Openshaw and Stevens were research assistants who collected data (listed in alphabetical order). The project was supported by a National Health and Medical Research Council (NHMRC) grant awarded to the final four authors (CIA: Grunstein, CIB: Rae, CIC: Wong, CID: McEvoy). Arciuli was supported by a mid-career fellowship granted by the Australian Research Council (ARC).

References

Arciuli, J., & Simpson, I. (2011). Statistical learning in typically developing children: the role of age and speed of stimulus presentation. *Developmental Science, 14,* 464–473.

Arciuli, J., & Simpson, I. (2012). Statistical learning is lasting and consistent over time. *Neuroscience Letters, 517,* 113–135.

Arciuli, J., & Von Koss Torkildsen, J. (2012). Advancing our understanding of the link between statistical learning and language acquisition: the need for longitudinal data. *Frontiers in Psychology – Language Sciences, 3,* Article 324.

Aslin, R., Saffran, J., & Newport, E. (1998). Computation of conditional probability statistics by 8-month old infants. *Psychological Science, 9*, 321–324.

Brady, T., & Oliva, A. (2008). Statistical learning using real-world scenes. *Psychological Science, 19,* 678–685.

Csabi, E., Varszegi-Schulz, M., Janacsek, K., Malecek, N., & Nemeth, D. (2014). The consolidation of implicit sequence memory in obstructive sleep apnea. *PLOS One, 9,* e109010.

Diekelmann, S., & Born, J. (2010). The memory function of sleep. *Nature Reviews: Neuroscience, 11*, 114–126.

Durrant, S., Taylor, C., Cairney, S., & Lewis, P. (2011). Sleep-dependent consolidation of statistical learning. *Neuropsychologia, 49*, 1322–1331.

Ellenbogen, J. M., Payne, J. D., & Stickgold, R. (2006). The role of sleep in declarative memory consolidation: Passive, permissive, active or none? *Current Opinion in Neurobiology, 16*, 716–722.

Evans, J., Saffran, J., & Robe-Torres, K. (2009). Statistical learning in children with Specific Language Impairment. *Journal of Speech Language and Hearing Research, 52*, 321–335.

Fogel, S. M., & Smith, C. T. (2011). The function of the sleep spindle: a physiological index of intelligence and a mechanism for sleep-dependent memory consolidation. *Neuroscience & Biobehavioral Reviews, 35*, 1154–1165.

Himanen, S., Virkkala, J., Huupponen, E., & Hasan, J. (2003). Spindle frequency remains slow in sleep apnea patients throughout the night. *Sleep Medicine, 4,* 361–366.

Iber C, Ancoli-Israel S, Chesson A, & Quan S. (2007) for the American Academy of Sleep Medicine. 1st ed. *The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specification* Westchester: IL: American Academy of Sleep Medicine.

Kim, R., Seitz, A., Feenstra, H., & Shams, L. (2009). Testing assumptions of statistical learning: is it long-term and implicit? *Neuroscience Letters, 461*, 145–149.

McGinty, D., & Szymusiak, R. (2011). Neural Control of Sleep in Mammals. In *Principles and Practice of Sleep Medicine*. M. H. Kryger, Roth, T. and Dement, W. C. (Eds) Missouri: Elsevier. 76–91.

Nemeth, D., Csabi, E., Janacsek, K., Varszegi, M., & Mari, Z. (2012). Intact implicit probabilistic sequence learning in obstructive sleep apnea. *Journal of Sleep Research, 21,* 396–401.

Perruchet, P., & Pacton, S. (2006). Implicit learning and statistical learning: one phenomenon two approaches. *Trends in Cognitive Sciences, 10,* 233–238.

Ruehland, W., Rochford, P., O'Donoghue, F., Pierce, R., Singh, P., & Thornton, A. T. (2009). The new AASM criteria for scoring hypopneas: impact on the apnea hypopnea index. *Sleep*, *32*(2), 150–7.

Schneider, W., Eschman, A., & Zuccolotto, A. (2002). *E-Prime Reference Guide*. Pittsburgh: Psychology Software Tools Inc.

Schonwald, S., Carvalho, D., de Santa-Helena, E., Lemke, N., & Gerhardt, G. (2012). Topography-specific spindle frequency changes in obstructive sleep apnea. *BMC Neuroscience, 13*, 89.