The influence of sleep on auditory learning: a behavioral study

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Evidence continues to support a role for sleep in delayed learning without further practice. Here we demonstrate the beneficial influence of sleep on auditory skill learning. Fifty-six subjects were randomly assigned to two groups, trained and tested on a pitch memory task three times across 24 h. The morning group was trained at 09.00 h, retested 12 h later that same day, and again after 12 h sleep. The evening group was trained at 21.00 h, retested 12 h immediately after sleep, and again 12 h later the next day. At retesting, both groups combined showed significant delayed learning only after sleep, but not across equivalent periods of wake, regardless of which came first. These data add to the growing literature describing sleep-dependent learning throughout sensory and motor domains. *NeuroReport* 15:731–734 © 2004 Lippincott Williams & Wilkins.

Key words: Auditory learning; Pitch memory; Sleep

INTRODUCTION

In 1970, Lucero first demonstrated an increase in rapid eye movements (REM) sleep in response to a maze learning experiment in rats [1]. Since then, a large number of studies have shown the influence of sleep on learning, and concomitantly, the influence of learning on subsequent sleep augmentation (for reviews see [2–4]). More specifically, several studies in humans have reported that sleep may be especially important for the consolidation of procedural skill learning in the visual [5–7] and motor [8–11] domains. However, few studies have assessed the direct influence of sleep on auditory learning in humans.

Several studies have investigated the influence of auditory stimulation on sleep architecture. For example, changes in EEG characteristics during human slow-wave sleep are seen after 6 h continuous auditory stimulation during previous wakefulness [12,13]. Synaptic reorganization during sleep after prolonged exposure to a novel sensory experience was hypothesized to underlie this observation. Mandai and colleagues [14] have shown that Morse code learning can lead to an increase of REM sleep and number of REM episodes, with a correlation between performance and rapid eye movement activity. There is also evidence that learning of a complex logic task while hearing a clicking sound in the background during wakefulness can be modified by presenting the same auditory cues during REM sleep periods leading to improved performance when tested 1 week later, compared with a group with no auditory REM sleep stimulation [15]. Despite these findings, few studies have assessed the differential contribution of time periods containing wake or sleep on the consolidation and delayed learning of auditory skills. In the current study, we used a previously developed auditory pitch memory task [16] with the aim to differentiate between the effects of time periods containing either wake or sleep on subsequent delayed learning of this task, following initial training.

MATERIALS AND METHODS

Fifty-six normal right-handed volunteers (age range 18–40 years (mean $\pm$ s.d. 26.5 $\pm$ 4.7); 35 females and 21 males), participated in the study after giving written informed consent. We only included non-musicians in this study, since we observed a musicianship effect in this task in a previous study [17]. One subject had to be excluded from the final analysis because he had only slept for 2 h before the retesting. Subjects may have received some musical theory classes, usually as part of their elementary, high school, or college education, but none were professional musicians and none of our subjects actively played any instruments. No subject had a history of any hearing impairments, psychiatric or neurological disease, nor were they under the influence of any hypnotic, anti-allergic, sedative or antidepressant medications. Subjects were not allowed to consume coffee or tea during the 24 h before the experiment or during the experiment. All subjects were strongly right handed according to a standard handedness questionnaire. Subjects were randomly assigned to either the morning or evening group (28 subjects in the morning group and 28 in the evening group). This study was approved by the institutional review board of the Beth Israel Deaconess Medical Center.

Experimental task: Subjects were instructed to listen to a sequence of individual sine wave tones (either 6 or 7 tones) with a duration of 4.6 s for each sequence. Each tone was 300 ms long with an attack and decay rate of 50 ms and an inter-stimulus interval of 300 ms. Our target tones corresponded to the frequencies of semitones of the Western musical scale (based on A = 440 Hz). Target tones had a frequency range from 330 to 587 Hz. The frequency difference between the first and the last or second to last tone was 41–64 Hz. Tones in between the first and the last or second to last tone were distractor tones. They did not correspond to fundamental frequencies of the Western Musical scale with frequencies that differed only slightly from the target tones. The frequency range from the lowest to the highest tone in all tone sequences was $\leq$ 108 Hz.

Subjects had to compare either the last or the second last tone (depending on the visual prompt second last or very last) with the first tone and we asked subjects to make a decision whether these tones were same or different. We chose to vary the total number of tones (6 or 7 tones per sequence) and the comparison to be made (second last tone with first tone or last tone with first tone) across sequences to reduce the possibility that subjects could choose to be inattentive to interfering tones. The sequence length was kept constant for the 6 and 7 tone sequences by introducing a short pause prior to the first tone for the 6 tone sequences. Subjects were asked to focus on a fixation cross that remained in the center of the screen except when interrupted for the short visual prompt.

Experimental paradigm (Fig. 1): All subjects underwent three sessions (S1–S3). Each session consisted of two testing trials (here referred to as first testing and second testing) and two training trials separated by a short break between the testing trials (Fig. 1). Each testing and training trial lasted 8 min. In the training trials, subjects were provided with a visual feedback indicating a correct or incorrect answer.

Subjects in the morning group (MG) underwent their initial session (S1) at 09.00 h ($\pm$ 1 h) which was followed by two more sessions, the first one 12 h later (period of wakefulness) and the second one 24 h later after a night of sleep.

Subjects in the evening group underwent their initial session at 21.00 h ($\pm$ 1 h) followed by a session 12 h later (after a night of sleep) and a second session 24 h later after a period of wakefulness. All subjects filled out a sleep log to detail the amount of sleep during the night before the initial test and the night within the experimental sessions and to screen for possible sleep disorders and medication use. Furthermore, at each testing point, all subjects completed the Stanford Sleepiness Scale (SSS), a standard measure of subjective alertness [18]. The behavioral performance for each testing and training trial was calculated as correct responses (in %) of all responses. None of the subject missed more than 4 trials per session.

Statistical analysis: Statistical analyses were performed using paired *t*-tests and repeated measurement ANOVAs across groups using SPSS software. Dependent variables were percentage correct responses, change in percentage between sessions, amount of sleep, and Stanford Sleepiness Scale (SSS) scores. We first tested whether or not there is any performance difference between the two groups in their initial session and for each of the groups within subsequent sessions to exclude possible diurnal effects on delayed sleep dependent learning. A repeated measurement ANOVA was performed for the initial session and each of the two subsequent sessions with group as a factor (MG and EG) and four percentage correct responses as dependent variable. All ANOVAs have been tested in regards to the assumption of equal variances. No violation of this assumption could be found. We then tested whether or

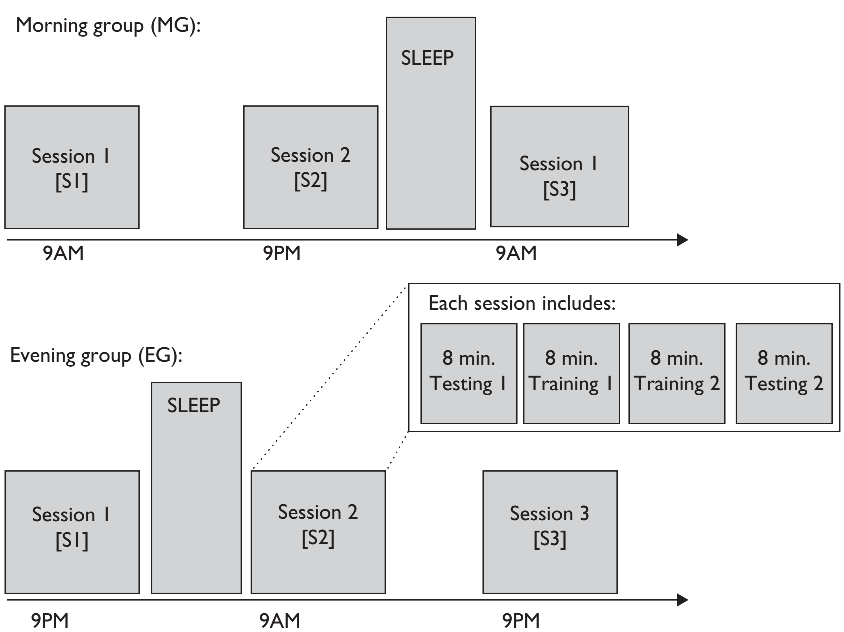

Fig. 1. Experimental paradigm.

not both groups combined showed a significant delayed learning effect only after sleep, but not across equivalent periods of wake, regardless of which came first.

RESULTS

Group effects in initial session (session 1): Across both groups, there was significant performance improvement comparing percentage correct responses in testing 1 with testing 2 of the initial session using a repeated measurement ANOVA ($F=11.683$,. $df=1$, $p=0.001$; $\chi^2=0.178$). Performance (i.e. percentage correct responses) was not different across this initial session (two testing and two training trials) when comparing the two groups ($F=1.399$, $df=3$, $p=0.245$; $\chi^2=0.026$). Subjects achieved almost identical performance levels by the end of this initial session with a mean performance difference of 1.8%. Thus, performance improved significantly within the first (initial) session for morning and evening groups equally, despite the differing circadian time points.

Sleep/wake effects across groups: In order to test for an effect of delayed learning following sleep in comparison to learning following wakefulness we applied a *t*-test with the improvement in percentage correct following sleep and following wakefulness in both groups as variables. This analysis revealed a significant difference for delayed learning following sleep ($t=3.173$; $p<0.005$; see Fig. 2 and Fig. 3 for individual group results).

Learning within retest sessions: Neither the morning nor the evening group showed a significant change in their performance within each of the retest sessions (morning group: session 2, $F=0.708$; $df=3$, $p>0.05$; $\chi^2=0.026$; session 3, $F=0.732$; $df=3$, $p>0.05$; $\chi^2=0.027$; evening group: session 2, $F=0.195$; $df=3$, $p>0.05$; $\chi^2=0.007$; session 3, $F=1.744$; $df=3$, $p>0.05$; $\chi^2=0.063$). Thus, there was no evidence of subsequent within session learning either in the morning or the evening group.

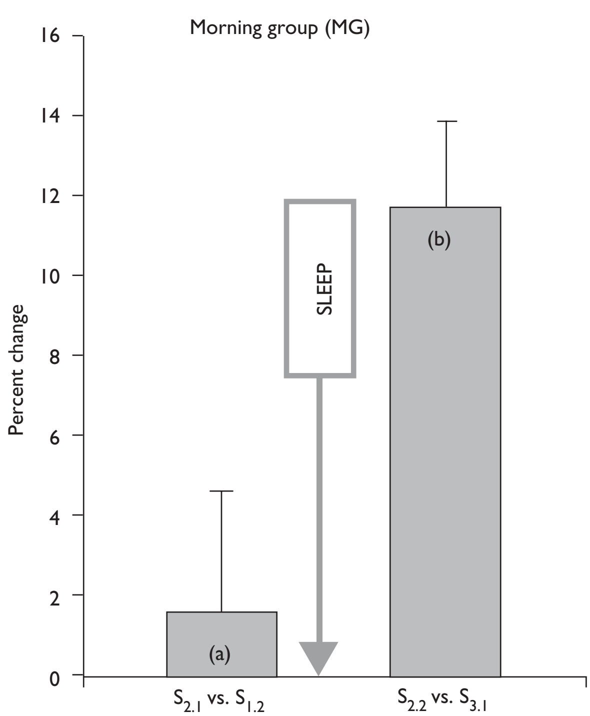

Fig. 2. Percentage change in performance rate for the morning group comparing (**a**) the first testing in Session 2 (S2.1) with the second testing in Session 1 (S1.2) and (**b**) the first testing in Session 3 (S3.1) with the second testing in Session 2 (S2.2).

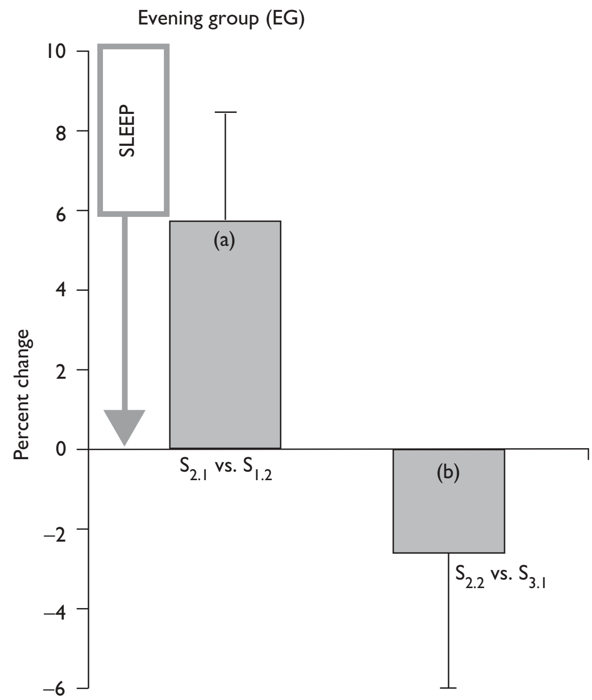

Fig. 3. Percentage change in performance rate for the evening group comparing (**a**) the first testing in Session 2 (S2.1) with the second testing in Session 1 (S1.2) and (**b**) the first testing in Session 3 (S3.1) with the second testing in Session 2 (S2.2).

Sleep quality and alertness: A repeated measurement ANOVA did not reveal any significant difference in the SSS ratings of alertness within any of the groups (morning group: $F=0.857$, $df=2$, $p=0.430$, $\chi^2=0.031$; evening group: $F=1.203$, $df=2$, $p=0.309$, $\chi^2=0.046$) or across groups for the three sessions ($F=0.786$, $df=2$, $p=0.458$, $\chi^2=0.024$). On the 7-point scale (1 being most alert), mean values for all sessions were 2.265 (morning group) and 2.20 (evening group). There were no differences in the SSS ratings between sessions for either group as well as between groups. There was no significant correlation with retest performance scores and alertness ratings either for the morning group ($r=0.089$; $p=0.517$) or the evening group ($r=0.079$; $p=0.567$).

Based on the documented sleep logs, subjects in the two groups did not differ in the amount of sleep across each experimental night ($t=1.691$; $p=0.097$). Group averages were 7.63 ± 0.77 h for the morning group and 8.00 ± 0.86 h for the evening group.

DISCUSSION

Our study investigated the effects of time, time awake and time containing sleep on the consolidation and delayed learning of an auditory pitch memory task. Our results demonstrate that, additional learning takes place in the absence of further practice, following an initial training induced performance improvement. However, the delayed learning occurred exclusively across time periods containing sleep, and not across equivalent time periods of daytime wakefulness, regardless of whether the time awake or time asleep came first.

This study cannot completely rule out circadian factors that may have prevented the expression of learning after 12 h of wakefulness. However, we feel this explanation is unlikely for several reasons. First, learning across the initial training session was similar for both groups of subjects, regardless of whether they were trained at 09.00 h or 21.00 h. Second, there was consistently no further practice-dependent, within session learning, at each subsequent retest session for either group, either in the morning or evening. Third, there were no significant differences between subjective alertness ratings either in the morning or evening, and no correlation was found between these measures and task performance. Thus, we consider sleep itself to be the most reasonable source of the delayed improvement on this task. Our findings support previous studies indicating an interaction between auditory learning and sleep [12–15,19]. While these studies have demonstrated either alterations in sleep architecture following a prior waking experience, or changes in the electrical evoked response after sleep, here we report the description of improved behavioral performance following sleep on an auditory skill task. Our data are consistent with evidence of sleep-dependent learning in studies probing both visual and motor skill domains [5–11]. Several of these studies have specifically highlighted particular types of sleep at certain times of the night as being important for the consolidation process. In the current study, we did not record sleep in the sleep lab using polysomnography, and it therefore remains an open question as to whether this overnight improvement is sleep, sleep stage- or sleep stage window-specific. While our current behavioral study did not assess the specific neural correlates of this sleep-dependent auditory learning, we have previously demonstrated functional imaging changes in secondary auditory-related brain regions within the posterior superior temporal gyrus and the inferior parietal cortex after 7 days of intensive training on this task in subjects who showed a strong learning effect. Those subjects that did demonstrate only a weak learning effect showed functional imaging changes in the lingual, inferior frontal and parahippocampal gyrus [20]. We therefore hypothesize that the sleep-dependent behavioral improvements observed in this study, may in part, be related to an overnight consolidation or reorganization in early cortical processing regions, together with decreasing activity in brain regions associated with attention and working memory leading to improved efficiency of stimulus processing.

CONCLUSION

Supporting previous studies in the visual and motor domain, we now demonstrate that delayed learning of an auditory pitch memory task following initial training is enhanced by sleep. Whether subjects were trained in the morning or evening, delayed improvements occurred only across a night of sleep and not across a time of wakefulness, regardless of which came first. Our results therefore suggest that sleep plays a critical role in the consolidation of an auditory skill task. This adds an important piece to the growing body of literature that shows the influence of sleep on procedural learning, not only in the motor and the visual domain, but also in the auditory domain, and highlights the need to consider the influence of sleep on learning in future studies assessing training induced functional plasticity.

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