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Sleep Does not Help Relearning Declarative Memories in Older Adults

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Abstract

How sleep affects memory in older adults is a critical topic, since age significantly impacts both sleep and memory. For declarative memory, previous research reports contradictory results, with some studies showing sleep-dependent memory consolidation and some other not. We hypothesize that this discrepancy may be due to the use of recall as the memory measure, a demanding task for older adults. The present paper focuses on the effect of sleep on relearning, a measure that proved useful to reveal subtle, implicit memory effects. Previous research in young adults showed that sleeping after learning was more beneficial to relearning the same Swahili-French word pairs 12 hours later, compared with the same interval spent awake. In particular, those words that could not be recalled were relearned faster when participants previously slept. The effect of sleep was also beneficial for retention after a one-week and a 6-month delay. The present study used the same experimental design in older adults aged 71 on average but showed no significant effect of sleep on consolidation, on relearning, or on long-term retention. Thus, even when using relearning speed as the memory measure, the consolidating effect of sleep in older adults was not demonstrated, in alignment with some previous findings.

Keywords: sleep-dependent memory consolidation; ageing; learning; relearning; repeated practice

Sleep, Memory, and Age

The importance of sleep in cognitive functioning is now well established. For instance, sleep has been shown to benefit the consolidation of declarative memories acquired during the day. It is usually observed that sleeping after a learning episode improves recall performance during a test compared to the same delay without sleep (see Rasch & Born, 2013, for a comprehensive review). Such memory consolidation is thought to originate from two

complementary processes. First, the reactivation or “replay” of recent memory traces during slow-wave sleep (SWS) causes declarative memories that are initially hippocampal-dependent to become increasingly dependent on the prefrontal cortex (Takashima et al., 2009). In parallel, a downscaling process during sleep leads to the recalibration of synaptic connections that were modified during learning (Tononi & Cirelli, 2014). The overnight memory improvement has been clearly demonstrated in young adults but is more controversial in older adults (Harand et al., 2012).

Sleep undergoes both quantitative and qualitative changes over the course of ageing. The most obvious change in sleep in healthy older adults is a decrease in total sleep time (TST) induced by an increase in the time spent awake both after bedtime (i.e., sleep latency) and during the night (Carrier et al., 1997). As a result, sleep efficiency (i.e., ratio TST / time in bed) declines and reaches 79% or less at age 70 (Bliwise, et al., 2005) compared to about 90% in healthy adults. Sleep architecture is also modified, with a reduction in SWS (Lombardo et al., 1998), whereas time in lighter stages (non-Rapid Eye Movement nREM1 and nREM2) increases (Ohayon et al., 2004). However, the time spent in REM sleep remains relatively unchanged. Modifications in sleep microstructure are also observed. A reduced spectral EEG power is observed, in particular for slow-wave activity (SWA) during SWS, especially over the prefrontal cortex (Dubé et al., 2015). Spindle density, frequency, and duration are also diminished (Crowley et al., 2002; Guazzelli et al., 1986), as well as the density of phasic REM phases (Darchia, Campbell, & Feinberg, 2003). Thus, many sleep components underpinning sleep-related memory consolidation in young adults, such as SWA and spindle activity, are reduced with increasing age (Carrier et al., 2011; Martin et al., 2013).

Aging is also associated with declarative memory changes. Overall, older adults exhibit poorer memory recall while their recognition performance remains relatively spared (e.g. Danckert & Craik, 2013; see Grady & Craik, 2000 for review). They also exhibit an increasing difficulty to learn new material compared to the younger adults, because of poor encoding strategies (see Craik & Rose, 2012, for review). These effects might be mainly explained by an impairment in forming associations (Old & Naveh-Benjamin, 2008).

It has been proposed that changes in sleep may contribute to age-related memory impairments (Buckley & Schatzberg, 2005; Hornung, Danker-Hopfe, & Heuser, 2005; Mander et al., 2014; see Scullin & Bliwise, 2015). A proposed mechanism (Mander et al., 2013) is that reduction of gray matter volume associated with aging impedes the generation of SWA and spindles during sleep, thereby impairing memory consolidation.

Despite these age-related changes in sleep, some research reported the persistence of sleep-dependent memory consolidation in the older adult (Aly & Moscovitch, 2010; Sonni & Spencer, 2015; Wilson et al., 2012), whereas others failed to demonstrate it or demonstrated a lesser consolidation compared to young adults (Baran, Mantua, & Spencer, 2016; Cherdieu et al., 2014; Mander et al., 2013, 2014; Mary, Schreiner, & Peigneux, 2013; Scullin, 2013; Scullin et al., 2017). Other research described a more complex picture (Jones et al., 2016).

Most of these studies used free- or cued-recall performance as a measure of consolidation. Such measures may be suboptimal to reveal consolidation and may thus contribute to the contradictory findings, especially since recall is a demanding task specifically impaired in the older adult (e.g. Troyer, Graves, & Cullum, 1994; Danckert & Craik, 2013). In addition, these measures are binary (i.e., correct/incorrect) and are poorly informative as to the strength of a memory trace. It seems possible to assess memory retention in an alternative, more implicit manner by measuring how fast participants relearn the information (i.e., savings in relearning). In a recent study, Mazza et al. (2016) found that young adults significantly benefitted from sleep to improve their memory performance in both relearning and retention of word pairs. The Sleep group, who slept during the 12-hour interval between the learning and the relearning sessions, displayed a faster rate of relearning compared to the Wake group that did not sleep. This was true even after controlling the recall performance just before relearning. In other words, those words that could not be recalled before the relearning session were relearned faster. The present study consists of a close replication of the study by Mazza et al. (see Figure 1) with older adults and using the same type of material. We tested the hypothesis that sleep does still favor consolidation in older adults, as evidenced when relearning speed is measured instead of recall.

Method

Participants

Forty French healthy participants completed the study. They were aged between 65 and 80 and had normal sleep and cognitive abilities. Participants with sleep problems, as assessed by a score of 8 or above on the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989), or presenting altered cognition, as assessed by a score below 27 in the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), were excluded. Health information was gathered from all participants during an interview about their medical history and medication. Participants with a medical history and/or taking medications with known sensory or neurological effects were also excluded. All participants in the study were native French-speaking and present normal or corrected-to-normal vision. The present study was in accordance with the ethical standards of the responsible committee on human experimentation of the Helsinki Declaration of 1975, as revised in 2000. Informed written consent was obtained from each participant.

Furthermore, all participants underwent a neuropsychological and sleep assessment with sleep quality (PSQI), circadian topology (the Horne and Ostberg morning/evening questionnaire; Horne & Ostberg, 1976), level of sleepiness (Epworth Sleepiness Scale; Johns, 1991), basic long-term and short-term memory capacity (subtests from the Wechsler Adult Intelligence Scale IV, Wechsler, 2008, and from the Wechsler Memory Scale III; Wechsler, 1997), global cognitive ability (MMSE), and anxiety and depression levels (The Hospital Anxiety and Depression Scale; Zigmond & Snaith, 1983).

The participants were randomly assigned to the Sleep or the Wake group. Three participants did not pursue the experiment after having spent too much time completing the learning session. Eventually, the data from 19 participants in the Sleep and 18 in the Wake group were included for analysis. Their age ranged from 65 to 80 (mean age 71.6 +/- SE) with 20 women in total. The Sleep and Wake groups did not significantly differ on any of the following variables: gender, age, number of attended school years, sleep quality, circadian topology, level of sleepiness, basic long-term and short-term memory capacity, global cognitive ability, and anxiety and depression levels. An additional 6 participants started but did not complete the study for various reasons (e.g., not available for the upcoming session).

Material and Procedure

During the first session, participants were trained to learn the French translation of 12 Swahili words (e.g., nyanya-tomate), using repeated tests with feedback. The number of pairs was decreased from 16 in Mazza et al. (2016) to 12 here to adjust to the memory difficulties encountered by the older adult. A perfect learning criterion was adopted in which pairs were tested until they received a correct answer (Figure 1A). Twelve hours later, in the second (relearning) session, they

had to relearn the pairs to the criterion of correctly answering the 12 items in a row (Figure 1B). This equated the participants' performance at the end of the relearning session. Initial performance on the first trial for the 12 items and the number of trials necessary to attain the relearning criterion were measured.

The Wake group performed the learning session at 9:00 a.m. and the relearning session at 9:00 p.m. the same day (Figure 2). They did not sleep between the two sessions, as was instructed. The Sleep group performed the learning session at 9:00 p.m. and the relearning session at 9:00 a.m. the following day. They experienced a night of sleep between the two sessions, during which actimetry (Actiwatch system, CamNtech, Cambridge, UK) was used to quantify TST. One week and six months after the relearning session, the retention of the material was further assessed for each group using a cued-recall task without feedback.

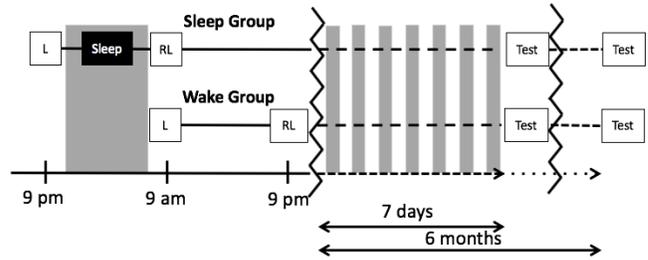


Figure 2. Temporal description of the experimental design. L = Learning session. RL= Relearning session. Nights are represented by grey areas.

Results

Based on the results obtained in the young adults in Mazza et al. (2016), it was expected that the Sleep group would start the relearning session with an advantage over the Wake group, would relearn faster, and would perform better after one week and six months. The overall results are presented in Figure 3.

Along with inferential frequentist statistics (two-tailed Student's *t*-tests) using a critical *p*-value of .05 and effect sizes reported using Cohen's *d*, dependent variables were also submitted to two-tailed Bayesian *t*-tests (Rouder, et al., 2009) comparing the Wake and the Sleep groups. Because we observed weak effects, we will present the BF_{01} , that is, the odds ratios in favor of the null hypothesis H_0 (i.e., no difference between the means) against the alternative hypothesis (i.e., a difference between the means). They were computed using JASP (JASP software, 2016) and will be considered according to the following scale: values inferior to 3 as anecdotal evidence, values ranging from 3 to 10 as substantial evidence, and values above 10 as strong evidence in favor of H_0 , with higher values indicating gradually increasing confidence (Jarosz & Wiley, 2014; Jeffreys, 1961).

The learning session was performed similarly by the two groups with respect to the proportion of correct answers provided at the first trial ($M = 0.21$, $SE = 0.04$ in both groups). The estimated Bayes factor ($BF_{01} = 3.14$) suggested that the data were 3.14 times more likely in favor of H_0 than of the alternative hypothesis, i.e., indicative of anecdotal to substantial evidence in favor of the absence of a difference. The number of trials necessary to achieve the learning criterion was not significantly different (Sleep: $M = 5.79$, $SE = 0.41$; Wake: $M = 6.00$, $SE = 0.45$; $t(35) = 0.35$, $p = .73$), with an anecdotal evidence in favor of H_0 ($BF_{01} = 3$).

During the relearning session, the proportion of correct answers on the first trial did not differ in the Sleep ($M = 0.46$, $SE = 0.04$) and in the Wake group ($M = 0.40$, $SE = 0.05$; $t(35) = 0.93$, $p = .36$, Cohen's $d = 0.31$, $BF_{01} = 2.23$, anecdotal evidence in favor of H_0). Both groups needed an equivalent number of trials to achieve the relearning criterion (Sleep: $M = 7.63$, $SE = 0.76$; Wake: $M = 8.00$, $SE = 1.16$; $t(35) = 0.27$, $p = 0.79$; $d = 0.09$; $BF_{01} = 3$, anecdotal evidence in favor of H_0). The *relearning speed* was computed by dividing the number of unrecalled items at the first trial by the number of

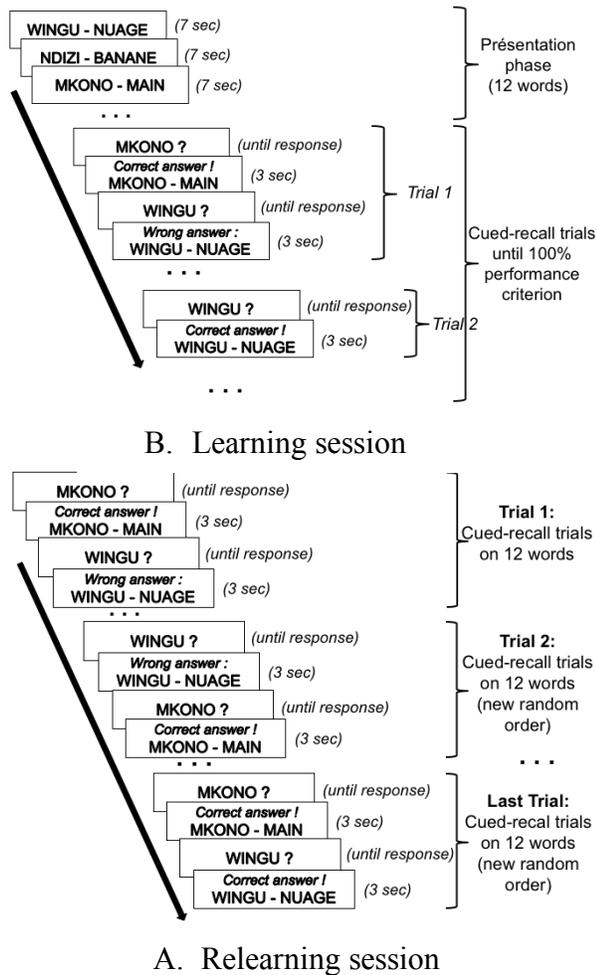


Figure 1. Procedure for the Learning (A) and Relearning (B) sessions.

trials necessary to complete the session. This was a way to control for the influence of initial performance on relearning speed. Indeed, the more the participants initially recalled, the fewer items remained to be relearned. The relearning speed did not differ between the Sleep ($M = 0.96$, $SE = 0.09$) and the Wake group ($M = 1.06$, $SE = 0.08$, $t(35) = 0.78$, $p = .44$; $d = 0.26$; $BF_{01} = 2.5$, anecdotal evidence in favor of H_0). Thus, contrary to our expectation, there was no clear-cut indication of a consolidating effect of sleep, since neither the initial retrieval performance nor the relearning speed varied between the two groups.

After one week, there was no significant difference between the performance in the Sleep ($M = .75$, $SE = .04$) and the Wake group ($M = .64$, $SE = .06$; $t(35) = 1.59$, $p = .12$; $d = .52$; $BF_{01} = 1.19$, anecdotal evidence in favor of H_0). In addition, these scores were overall relatively high, indicating that the specific relearning method used was quite efficient at inducing long-term retention. For the six-month delay, the data from 4 participants in the Sleep group and from 2 participants in the Wake group could not be obtained. There was no significant difference between the groups (Sleep: $M = .42$, $SE = .08$; Wake: $M = .30$, $SE = .06$; $t(29) = 1.22$, $p = .23$; $d = .44$; $BF_{01} = 2.35$, anecdotal evidence in favor of H_0).

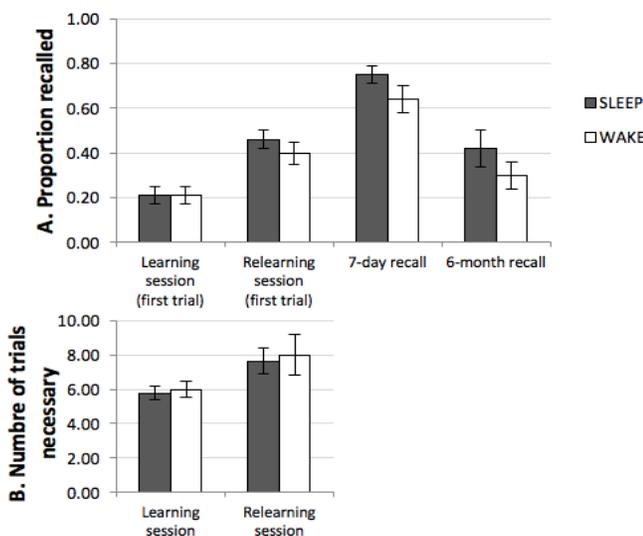


Figure 3: Upper part: Mean proportion correct in the first trial of the learning and relearning sessions, and in the 7-day and 6-month recall sessions.

Lower part: Number of trials necessary to achieve the criterion in the learning and the relearning session. The error bars represent standard errors of the mean.

The actimetric data was lost for 4 participants in the Sleep group. The Sleep group ($N = 15$) exhibited a mean TST of 402 min (6 hours and 42 minutes; 308 - 469 min; $SE = 12.1$). The correlation between TST and initial performance on the relearning session was not significant ($r = .40$; $df = 13$; $p = .14$). The correlation between TST and the number of trials needed at the relearning session was surprisingly positive but

not significant either ($r = .45$, $p = .09$). In addition, the correlation between TST and the relearning speed was significant and negative ($r = -.74$, $p = .0015$), indicating that the more the participants slept, the slower they were to relearn. Finally, there was no correlation between TST and the performance after one week ($r = -.03$, $p = .92$).

Discussion

The present results display major differences from those of the Mazza et al. study that used similar methods and sample sizes ($n=20$ in each group) with younger adults. In the present study with older adults, an episode of sleep did not significantly boost subsequent recall 12 hours after learning, compared to wakefulness. Thus, contrary to our hypotheses, even with more fine-grained and implicit measures of declarative memory, we did not show significant benefits of sleep on relearning in this population. The effect on the long term, however, is more ambiguous, with a potential weak benefit of interpolated sleep after 7 days and 6 months, which is not significant in the present study, most likely due to lack of power. In any case, the size of this benefit is far weaker in the older than in the younger adults.

Our hypothesis that the sleep-dependent processes that consolidate memories are subtle in the older population and therefore require more implicit measures to be shown was not validated. These results are however consistent with other studies that did not show any sleep-dependent benefit for declarative memory in the older adult (see Gui et al., 2017 for a review). Contrary to younger adults, recommendations such as “you should sleep between learning and relearning” does not seem as relevant for the aging population, although it does not seem detrimental either (especially for long-term retention).

One surprising finding is the negative correlation between TST and the relearning speed, indicating that the more the participants slept, the more trials they needed in order to reach the relearning criterion. This is in contradiction with results from Aly & Moscovitch (2010) but is consistent with that of Scullin (2013) and Tsapanou et al. (2017). A possibility is that people with poorly efficient sleep with respect to consolidation and maybe other functions tend to sleep more to compensate.

How to reconcile these results with those indicating clear sleep-dependent consolidating effects of sleep in the older adult (e.g., Aly & Moscovitch, 2010; Sonni & Spencer, 2015; Wilson et al., 2012)? A first limit might be that the task was too difficult and not well calibrated for the participants, therefore impeding the emergence of potential effects of sleep. However, the relatively high scores observed after one week go against this limitation. Another limit could be that the criteria of perfect-performance during learning and relearning did not leave enough possibility for sleep-dependent improvement. However, the relatively low performance at the beginning of relearning and the fact that the paradigm was identical to that in Mazza et al.’s study go against this limitation. Finally, the discrepancies could be linked to the material used. Our study consisted of learning

pseudowords which are verbal representations that do not yet exist in the mental lexicon and need to be integrated into it. This integration has been shown to require time (e.g., Dumay & Gaskell, 2007). Moreover, in the present study, in addition to creating such a novel verbal representation, participants needed to associate it to a known French word in order to succeed at the cued-recall task. Such associative learning is impaired in aging (e.g., Service & Craik, 1993). Therefore, it would be interesting to examine in future research whether the absence of sleep-induced benefits would also be observed when older adults learn and relearn word pairs instead of pseudoword-word pairs (see Kurdziel, Mantua, & Spencer, 2017 for an overall review of the effect of sleep on word learning in the older adult).

Quality of sleep and memory performance are critical issues in modern societies, especially for older people. Their functional relationship needs to be investigated further (Scullin & Bliwise, 2015). In particular, an intriguing issue is whether improving sleep quality could efficiently improve memory functioning. Such possibility could lead to potential practical applications for improving the aging population's quality of life.

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