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Highlights

- Mnemonic discrimination seems to be influenced by nocturnal sleep
- We tested the effect of daytime sleep mnemonic discrimination
- Performance change was similar after sleep or wakefulness
- A brief daytime sleep episode did not facilitate mnemonic discrimination

Comparing the effect of daytime sleep and wakefulness on mnemonic discrimination

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RUNNING HEAD: *Naps and mnemonic discrimination*

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Abstract

Sleep is considered the optimal state to consolidate hippocampal-dependent memories. A particular memory process is mnemonic discrimination. Mnemonic discrimination refers to the ability to differentiate between novel and previously encountered information. Previous studies have found that mnemonic discrimination is impaired by sleep deprivation, whereas nocturnal sleep seems to protect memory representations when compared to a similar period of wakefulness. In this study we tested whether a daytime nap can facilitate mnemonic discrimination as assessed by the Mnemonic Similarity Task. Thirty-eight participants performed incidental learning of 256 images of unique everyday items at about 12:00 PM. Fifteen minutes later, in a recognition test, they were presented with 192 images: 64 *targets* (Old), 64 *foils* (New) and 64 *lures* (Similar to targets). For each image they had to decide whether it was already presented, never presented, or similar to an image presented during the encoding session. Then participants were split into a Nap group (N=19), who had a 90-min nap opportunity in the lab, and a Wake group (N=19), who stayed in the lab playing a low-arousing game. At 3:00 PM all participants performed a delayed recognition test, similar to the immediate test but with different images. Similar memory discrimination was observed in both the Nap and Wake group. The lack of a beneficial effect of sleep could be due to the differences between diurnal and nocturnal sleep and/or the potential role of videogames in facilitating memory discrimination during wakefulness.

Keywords: hippocampus; memory consolidation; mnemonic discrimination; pattern separation; rest; sleep

1. Introduction

Sleep is considered the optimal state to consolidate memory traces due to the reduced sensory input coming from the environment and the specific neurophysiological activity of each sleep stage (Rasch & Born, 2013). According to the active system consolidation model (Diekelmann & Born, 2010), information, which is transiently encoded in the hippocampus during wakefulness, is reactivated and redistributed all over the cortex during sleep, to form what is known as long-term memory. This sleep-related process appears to occur during non-rapid eye movement sleep (NREM, composed by N1, N2, and N3 stages; see Antony, Schönauer, Staresina, & Cairney, 2018; Klinzing et al., 2016; Staresina et al., 2015). A specific step in the encoding of declarative memories is pattern separation, defined as the process of creating non-overlapping orthogonal neural representations from similar stimuli inputs (McClelland, McNaughton, & O'Reilly, 1995). This process allows the discrimination between similar input targets (e.g., two or more similar events that share some overlapping features), promoting a rapid encoding of this information into non-overlapping, distinct, representations (Yassa & Stark, 2011). Pattern separation, together with pattern completion (i.e., the ability to recover memories when these representations are noisy, partial, or degraded), can be defined as computational processes thought to underlie the storage and retrieval of information by the hippocampus (Liu, Gould, Coulson, Ward, & Howard, 2016).

In humans, pattern separation can be indirectly measured at the behavioral level using tasks such as the Mnemonic Similarity Task (MST), previously known as the Behavioral Pattern Separation Task (BPS-O; Stark, Yassa, Lacy, & Stark, 2013). This task assesses the individual's mnemonic discrimination ability. The MST is a useful tool for testing the ability of the participants to correctly discriminate "lure" items from similar items (in terms of contents, colors, orientation) studied before. To successfully discriminate "lure" (i.e., similar) items,

participants need to create a detailed representation of these items. Using the MST, it has been shown that mnemonic discrimination is impaired in patients with hippocampal damage and clinical conditions such as mild cognitive impairment (Kirwan et al., 2012; Stark, et al., 2013). Sleep deprivation seems to negatively affect subsequent memory discrimination in the MST (Saletin et al., 2016). Participants in this study performed the encoding and memory test after a regular night of sleep, a sleep-deprived night, and a recovery (post-sleep deprivation) 90-min daytime nap. The authors showed an impaired encoding after the sleep-deprived night compared to the regular night of sleep, but a restored encoding ability after the recovery nap. Moreover, the same study showed that post-nap performance correlated with slow oscillatory activity (0.5-4 Hz) during the recovery night, suggesting a role of this specific sleep feature in the offline (i.e., during sleep) processing of mnemonic discrimination. Interestingly, a recent study has attempted to replicate Saletin et al.'s (2020) results, but using only a daytime nap without any previous sleep deprivation (Davidson, Jönsson, & Johansson, 2020). The authors found that about 90 min of sleep did not increase either mnemonic discrimination or general recognition performance at an immediate recognition test compared to a similar period of wakefulness.

Recently, two studies have investigated the role of a night of sleep on memory consolidation of items encoded using the MST (Doxey, Hodges, Bodily, Muncy, & Kirwan, 2018; Hanert, Weber, Pedersen, Born, & Bartsch, 2017). In these studies, the encoding phase and immediate memory test of the MST were followed by a 12-hr interval consisting of either wakefulness or nighttime sleep and then by a delayed memory test. Both studies demonstrated, after the delay, a preserved mnemonic discrimination ability in participants who slept, and a decreased discrimination ability in participants who stayed awake, suggesting that sleep may

play a role in stabilizing (i.e., protecting from interference) mnemonic discrimination (Doxey, et al., 2018; Hanert, et al., 2017).

A key question when investigating the role of sleep in memory is related to the amount of sleep required to promote these memory-related processes. Indeed, since the seminal paper by Mednick and colleagues (2003), several studies have shown that a daytime nap may be enough to improve memory consolidation, mainly by reducing forgetting (see for example Cellini, Torre, Stegagno, & Sarlo, 2016; Diekelmann & Born, 2010; Lau, McAteer, Leung, Tucker, & Li, 2018; Elizabeth A. McDevitt et al., 2018; Scullin, Fairley, Decker, & Bliwise, 2017; Tucker et al., 2006), although more recent studies showed different effects of nighttime and daytime sleep on memory consolidation (Payne et al., 2015; Sugawara et al., 2018).

In the current study we aimed to test whether a daytime sleep episode is able to preserve mnemonic discrimination ability of items encoded before sleep (as assessed by the MST) in the same way as nocturnal sleep. Specifically, based on previous studies, we hypothesized that a daytime nap, compared to a similar amount of wakefulness, would benefit memory consolidation by preserving the level of mnemonic discrimination reached at immediate testing and protecting these encoded memories from forgetting.

2. Material and methods

2.1 Participants

Forty volunteer university students (24 females) participated in this study. All participants underwent an online screening to ensure they had no history of psychiatric, neurological, or sleep disorders. Before the experimental session, participants were assigned to a *Nap* or a *Wake* group based on the order of recruitment. Participants were aware of the study condition (daytime nap or 2 hr of wakefulness). One participant was excluded due to a

recognition memory score (see below) lower than 0.50 (likely reversing the response button) and one participant due to *similar* responses being less than 10%. The final sample consisted of 38 participants, (Nap: N=19, 11 females; 24.89±3.23 years; Wake: N= 20; 11 females; 25.30±2.43 years). The study was approved by the Ethics Committee of the Departments of Psychology, University of Padova. All participants provided written consent before participation in this study. Each participant was paid 13€ for participating.

2.2 Self-reported questionnaires

During the online screening, the participants completed the *Beck Depression Inventory-II* (BDI-II; Beck, Steer, & Brown, 1996) to assess depressive symptomatology and the *State-Trait Anxiety Inventory Y2* (STAI-Y2; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) to assess trait anxiety. For both questionnaires, higher scores indicate higher level of depressive symptomatology and trait anxiety. They also completed the *Pittsburg Sleep Quality Index* (PSQI; Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989; Curcio et al., 2013) to assess subjective sleep quality. For the PSQI, scores higher than 5 indicate the presence of poor sleep quality. We also used the *Morningness–Eveningness Questionnaire* reduced version (rMEQ; Adan & Almirall, 1991; Natale, Esposito, Martoni, & Fabbri, 2006) to assess circadian preferences, with higher scores indicating a tendency to morning preferences. Before the encoding phase and the delayed testing session (see below), participants also completed the *Samn–Perelli Scale* (SAMN; Samn & Perelli, 1982), the *Stanford Sleepiness Scale* (SSS; Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973), and the *STAI-Y1* (Spielberger, et al., 1983) to evaluate fatigue, sleepiness, and state anxiety levels, respectively.

2.3 Experimental Task

To investigate pattern separation, we used the *Mnemonic Similarity Task* (MST) version 0.96 (Bennett & Stark, 2016; Stark, Stevenson, Wu, Rutledge, & Stark, 2015; Stark, et al., 2013). This memory task is designed to measure the ability to discriminate between pictures seen before and new pictures that are similar to those seen before. The task version we used (0.96) contains 6 independent sets of images (C-D, E-F, G-H), each made up of 256 images of everyday objects. In the current study, we used sets C and D, which were matched for difficulty and counterbalanced across participants and conditions in each session (encoding, immediate and delayed testing) using a Latin square design. Each participant performed an encoding session and two testing sessions (immediate and delayed). During the encoding phase, all participants saw 256 images of unique everyday items (128 from each set). Each picture was presented for 2s, preceded by a fixation cross lasting 0.5s. For each image, participants made an indoor or outdoor judgment (i.e., they had to decide if the object is usually found indoors or outdoors) using the keyboard to ensure that they attended to each item during encoding.

In each of the two test phases (immediate and delayed) participants were presented with 192 images: 64 *targets* (Old), 64 *foils* (New), and 64 *lures* (Similar to the targets). Lure items had 5 levels of similarity to targets, ranging from the most (L1) to the least similar lures (L5, see also Stark, et al., 2013). Each picture was presented on the screen for 2s and participants had to indicate whether the image was an "Old" image (already presented during the encoding session), a "New" image (never presented before), or a "Similar" image (similar to one presented at encoding), by pressing "A", "L" or "G" on the keyboard, respectively.

Participants could respond as soon as the image appeared on the screen and with no time constraint (i.e., the test was self-paced). The order of presentation of the sets was counterbalanced between participants in both the encoding and recognition tasks. A schematic representation of the experimental task is depicted in Figure 1b.

For each participant, and each testing session, we computed the probability to respond "Old", "New", and "Similar" to target, foils, and lure stimuli.

From these measures, we derived the *Lure Discrimination Index*, which measures the hippocampal-dependent ability to create a different representation of similar presented items, which is calculated as *p*(Similar responses to lure items)- *p*(Similar responses to foil items). Since lure items are categorized into five levels of similarity (from the most similar to the least similar to target items, see Stark et al., 2013), we computed the *Lure Discrimination Index* separately for each similarity level by subtracting the similar responses to lure items from the average probability (at the individual level) to respond "Similar" to the foil items (see Davidson, et al., 2020).

For each participant we also computed the *Recognition Memory* score (also known as General Recognition), calculated as p(Old responses to target items) - p(Old responses to foil items), to assess the ability to recognize target items.

2.4 Actigraphic recording

Participants' sleep patterns during the 3 days before the experimental session were assessed using the Actiwatch-64 (AW-64; Phillips Respironics, Portland, OR, US), a reliable actigraph to objectively measure sleep parameters based on the level of physical activity (Cellini, Buman, McDevitt, Ricker, & Mednick, 2013) in 1-min epochs. For each participant

and every night, we calculated total sleep time (TST, min), defined as the number of minutes scored as sleep between lights off and lights on; sleep onset latency (SOL, min), the number of minutes between lights off and the first epoch scored as sleep; wake after sleep onset (WASO, min), the number of minutes scored as wake after sleep onset; and sleep efficiency (SE, %), the ratio between TST and total time spent in bed (TIB, min).

2.5 Polysomnographic (PSG) recordings

Polysomnographic (PSG) recordings were conducted according to the American Academy of Sleep Medicine (AASM) guidelines (Iber, Ancoli-Israel, Chesson, & Quan, 2007) by using LiveAmp (Brain Products, GmbH, Munich, Germany) and active electrodes, with 24 electroencephalographic (EEG) channels referred to the FCz and placed following the International 10-20 system (Jasper, 1958). For the electrooculogram, one electrode was placed 1 cm above the corner of the right eye and the second electrode was placed 1 cm below the corner of the left eye following recommended criteria for sleep recording (Iber, et al., 2007). For the electromyogram, we placed 2 electrodes on the chin. All signals were recorded using Brain Recorder (Brain Products, GmbH, Munich, Germany) with a sampling rate of 500 Hz and electrode impedance kept below 10 kΩ.

Before the sleep scoring analysis, the EEG and EOG signals were band-pass filtered to 0.5-35 Hz, while EMG was band-pass filtered to 10-100 Hz. Moreover, we applied a notch filter (50 Hz). Sleep scoring (WAKE, N1, N2, SWS, and REM) was visually performed on 30-sec EEG epochs from central and occipital derivations (C3, C4, O1, and O2) re-referenced to contralateral mastoids in line with AASM criteria (2007).

2.6 Experimental procedure

Before the experimental session, all participants completed an online screening, including the BDI-II, the PSQI, the STAI-Y2, and the rMEQ questionnaires. Moreover, for at least three days before the experimental session, participants were asked to wear an actigraph and to complete a sleep diary to assess their circadian rhythm and sleep patterns, to control for possible between-groups differences in sleep characteristics. The entire experimental procedure (see Figure 1a) took place in the Psychophysiology lab of the Department of General Psychology at the University of Padova. All participants arrived at about 11.30 AM. After reading and signing the informed consent, all participants completed three state questionnaires: the STAI-Y1, the Samn-Perelli Scale, and the SSS. At about 12.00 PM, all participants performed the MST encoding task; then, they spent 15 minutes playing a freely available version of the game "Tetris" to avoid active rehearsal of the pictures. After that, they performed the first MST recognition task (immediate recognition session). At about 1:00 PM, participants assigned to the WAKE condition spent 90 minutes playing a low-arousing version of the game "The Sims 3" (i.e., they only had to build a house), while participants assigned to the NAP condition were prepared for the PSG recording and then spent 90 minutes in bed. Afterward, participants of both groups completed the three state questionnaires again and then performed the second MST recognition task (delayed recognition session).

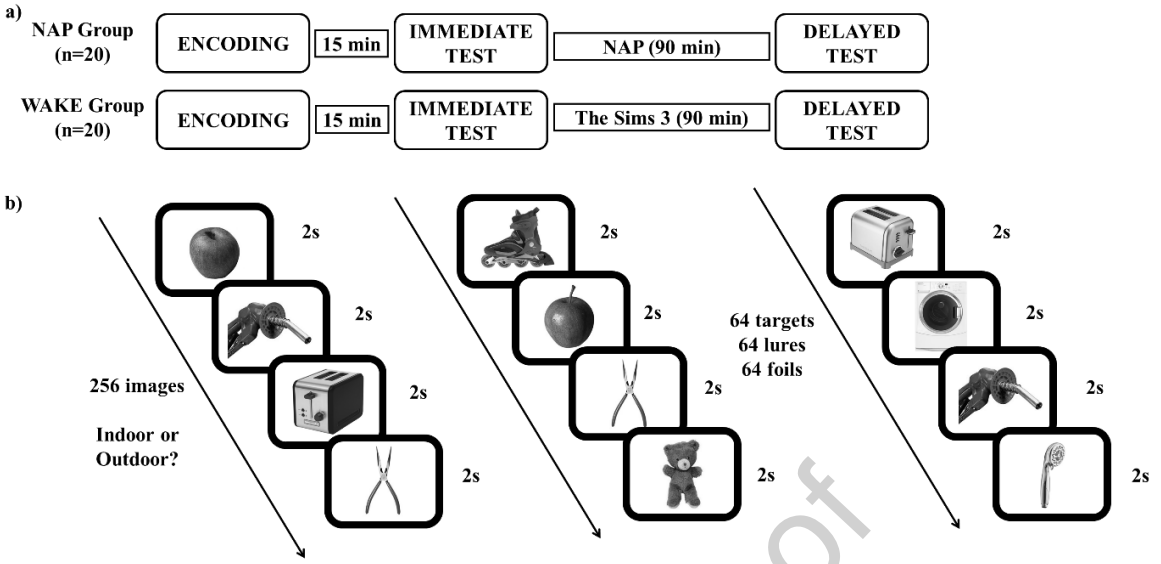

Figure 1. a) Schematic representation of the experimental procedure. Participants encoded a series of images followed by 15 minutes playing the game "Tetris" before the immediate recognition task. After that, they spent 90 minutes sleeping or playing the game "The Sims 3", followed by the delayed recognition task. **b)** Experimental task. During the encoding, 256 everyday objects images were presented; participants were asked to decide if those were objects usually found indoors or outdoors. In both immediate and delayed recognition tests, 192 images were shown: participants had to discriminate between 64 *targets* (Old, already presented in the encoding), 64 *foils* (New, never seen before) and 64 *lures* (Similar to the targets, with 5 degrees of similarity).

2.7 Statistical Analyses

Demographics and actigraphic sleep variables were compared between the two groups using independent t-tests and χ^2 for continuous and categorical data, respectively.

To assess the performance changes across testing sessions in the two groups, we employed linear mixed models (LMM), which take into account factors whose levels are randomly extracted from a population (i.e., participants), yielding to more generalizable results (Baayen, Davidson, & Bates, 2008). For the Lure Discrimination Index, we built a model using *Participant* as crossed random effects and *Group* (Wake, Nap), and *Session* (Immediate,

Delayed), and *Similarity level* (lure bins 1-5) as fixed effects. For the Recognition Memory we built a model using Participant as crossed random effects and Group (Wake, Nap) and Session (Immediate, Delayed) as fixed effects. Bonferroni's test was used for post-hoc comparisons.

In case of a lack of differences between groups, we employed Bayesian statistics to estimate the probability of the null hypothesis being true given the data. Specifically, we reported the Bayes Factor (BF_{01}), with values larger than 3 indicating moderate evidence for the null hypothesis (H0), and BF_{01} values lower than 0.3 moderately supporting the alternative hypothesis (H1; Jarosz & Wiley, 2014). For each Bayesian test, we also reported in the supplemental material the standard robustness check on the prior to show the changes of BFs as a function of a wide range of priors (which accounts for a range of expected effect size, from very large to very small).

Lastly, we explored potential associations (using Spearman' Rho) between individuals' trait characteristics and sleep parameters, and performance changes across the two sessions.

All analyses were run in JASP 0.12.2 (JASP Team, 2020) and JAMOVI 1.2 (The jamovi project, 2020), with the level of significance set at $p < 0.05$.

3. Results

3.1 Demographics

Descriptive statistics of the sample are presented in Table 1.

Table 1. Demographics, psychological measures, and sleep parameters of the sample.

	Wake	Nap	t_{36}	*p*	Cohen's d
Age (years)	25.30±2.43	24.90±3.23	0.43	.670	0.139
Gender (F/M)	11/8	11/8	0.00*	1.00	-
PSQI	6.05±3.22	6.26±3.84	-0.18	.856	-0.059
rMEQ	14.31±3.42	11.74±3.57	2.27	.029	0.738
BDI-II	7.79±6.55	9.68±8.63	-0.76	.451	-0.247
STAI-Y2	40.53±9.75	41.90±12.96	0.37	.715	-0.119
Actigraphic parameters[§]					
Total Bed Time (min)	459.31±62.28	441.63±97.90	0.65	.521	0.220
Total Sleep Time (min)	402.42±67.62	388.04±95.63	0.52	.607	0.176
Sleep Latency (min)	7.38±10.06	7.18±9.71	0.17	.869	0.057
WASO (min)	49.16±29.56	44.50±17.84	0.55	.585	0.187
Sleep Efficiency (%)	87.40±6.62	87.48±5.04	-0.38	.970	-0.013
Polysomnographic parameters					
Total Sleep Time (min)	-	58.53±17.51	-	-	-
Sleep Latency (min)	-	8.45±10.13	-	-	-
WASO (min)	-	21.37±15.04	-	-	-
Sleep Efficiency (%)	-	66.73±20.20	-	-	-
N1 (%)	-	18.86±10.99	-	-	-
N2 (%)	-	61.80±14.01	-	-	-
N3 (%)	-	17.74±13.88	-	-	-
REM (%)	-	19.14±13.17	-	-	-

Notes. Data are presented as mean±standard deviations. BDI-II: Beck Depression Inventory-II; STAI-Y2: State-Trait Anxiety Inventory Y2; PSQI: Pittsburg Sleep Quality Index; rMEQ: Morningness-Eveningness Questionnaire reduced version; WASO: Wake After Sleep Onset. *: χ^2 value. [§] Data are referred to the night before the experimental session. Note that we lost actigraphic data of 3 Nap subjects due to actigraphy malfunctions. Therefore, the data are referred to 19 Wake and 16 Nap, and the degrees of freedom of the t-tests are 33.

Age, gender distribution, anxiety, and depressive trait levels were comparable between the groups. Although the rMEQ score suggested that the NAP participants were more evening-type than the WAKE group, the two samples were comparable for number of evening-type (Wake = 4, Nap = 5), intermediate (Wake = 14, Nap = 13), and morning-type (Wake = 1, Nap =

1) participants (χ^2 = 0.148, p = .929). Nevertheless, the rMEQ score was included in all the subsequent analyses as a covariate. No differences were observed in the sleep pattern the night before the experimental session.

3.2 State variables

The analysis on the state anxiety and sleepiness levels showed no significant effects (all *ps'* > .102). The analysis on the fatigue levels revealed a significant interaction between Session and Group ($F_{1,36}$ = 4.67, p = .037, *coeff* = 1.00, *SE* = 0.46, t =-1.58), with a nominal increase in the fatigue level in the delayed session in the Wake group (p = .427) and a nominal reduction in the fatigue levels in the Nap group (p = .826). Since we observed this interaction on the fatigue level, the SAMN score was included in the subsequent analyses as a covariate.

3.3 Memory performance

Figure 2 depicts the pattern of responses to each type of stimulus in the two sessions (mean and SD can be found in supplemental Table S1).

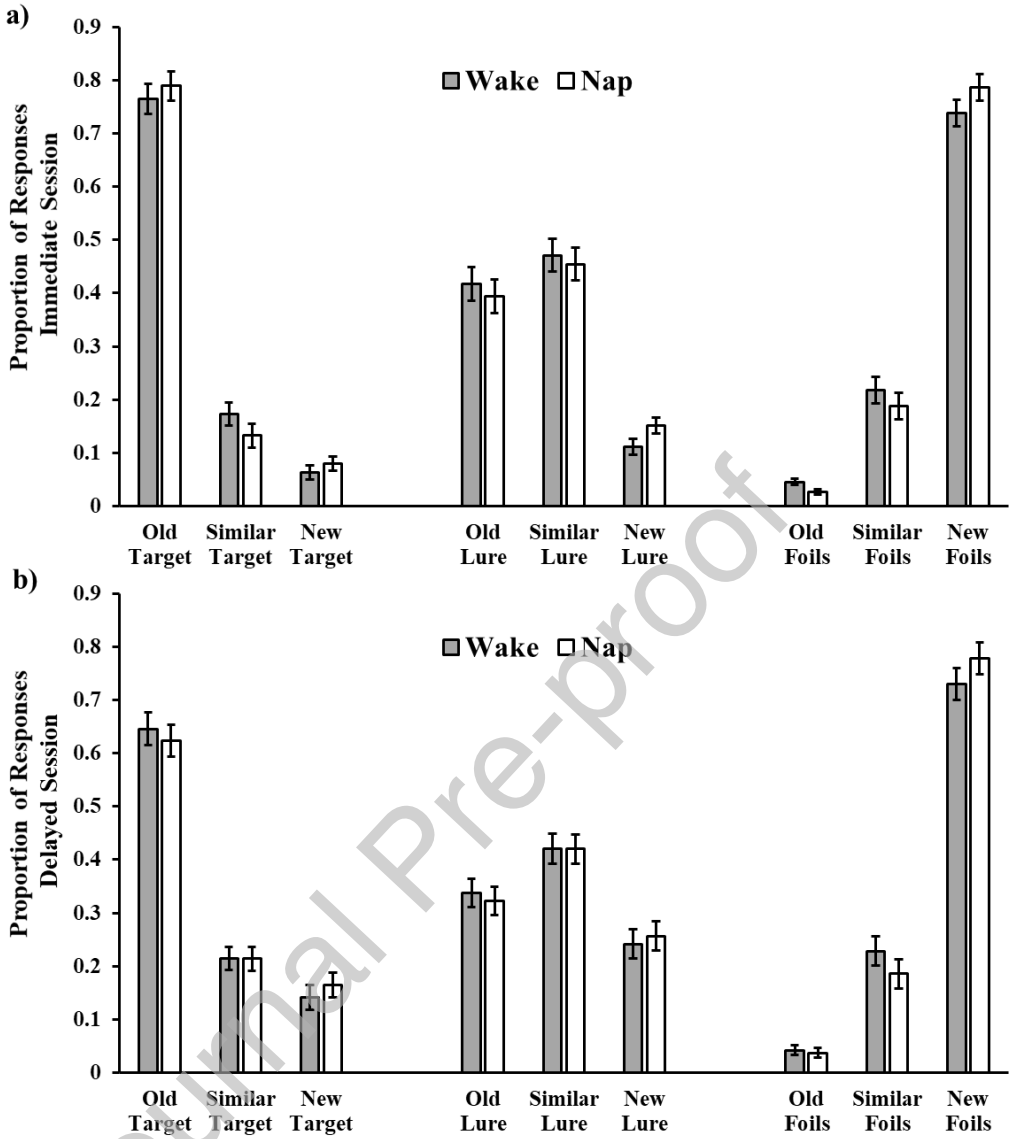

Figure 2. The proportion of responses to targets, lures, and foils in the two groups (Wake and Nap) at the **a)** immediate and **b)** delayed recognition sessions. Error bars represent standard errors of the means.

As for the Lure Discrimination Index, the LMM analysis, with rMEQ and SAMN scores included as covariates, showed a main effect of Similarity Level ($F_{4,323.2}$ = 58.83, p < .001, Figure 3), with a linear increase in memory discrimination as the stimuli became less similar (all p's < .001 except for bin 1 vs bin 2, and bin 3 vs bin 4, with p = .629 and p = .786, respectively),

a significant main effect of Session ($F_{1,323.5}$= 11.78, p = .001), with a decrease in mnemonic discrimination in the second session. The main effect of Group ($F_{1,35.3}$ = 0.639, p = .678, *coff*= -0.04, *SE* = 0.05, t = -0.80) and the interaction between Group and Session were not statistically significant ($F_{1,331.5}$ = 2.01, p = .157, *coff* =-0.04, *SE* =0.03, t = 1.42; see Figure 4a).

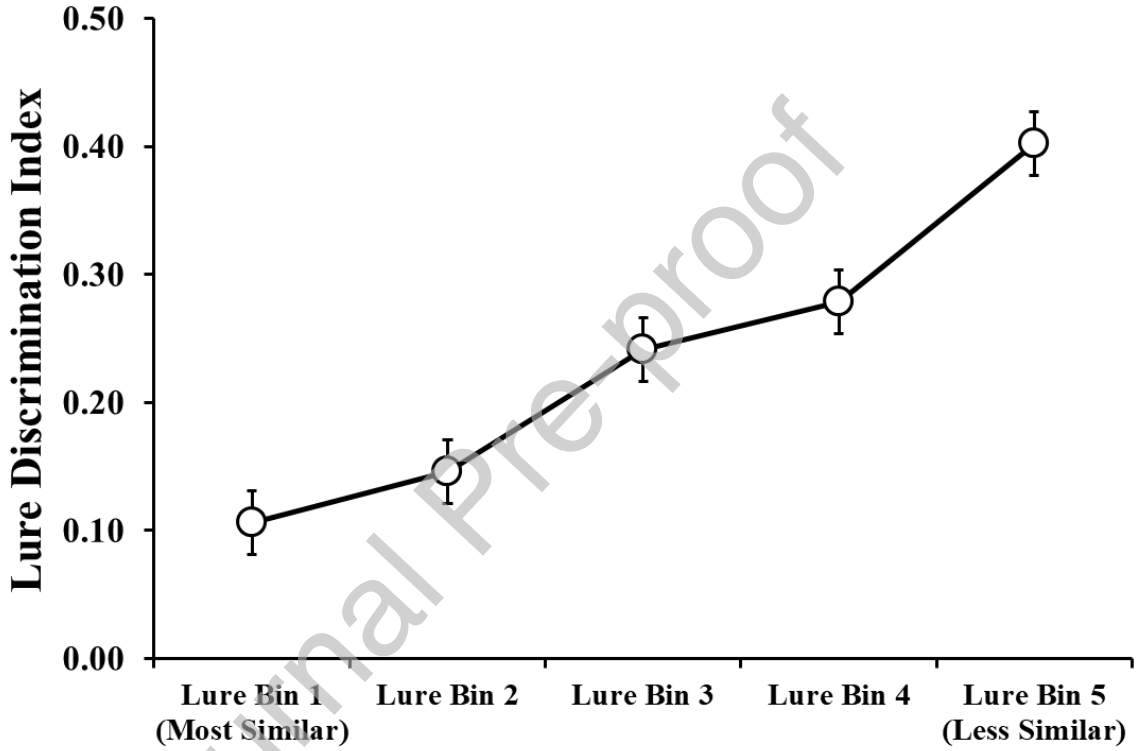

Figure 3. Lure discrimination as a function of the similarity level. Error bars represent standard error of the mean.

This lack of difference was confirmed by analyzing the differential scores of the mean Lure Discrimination Index across the five similarity bins between Delayed and Immediate test (t_{36} = 0.77, p = .449, *Cohen's d* = 0.25, Figure 4b) with a Bayesian Independent t-test (BF_{01} ≈ 2.52, effect size 95% CI:-0.36, 0.78), indicating anecdotal support for the null hypothesis (see

Figure S1 in the supplemental material for Prior and Posterior and Bayes Factor Robustness Check of this test).

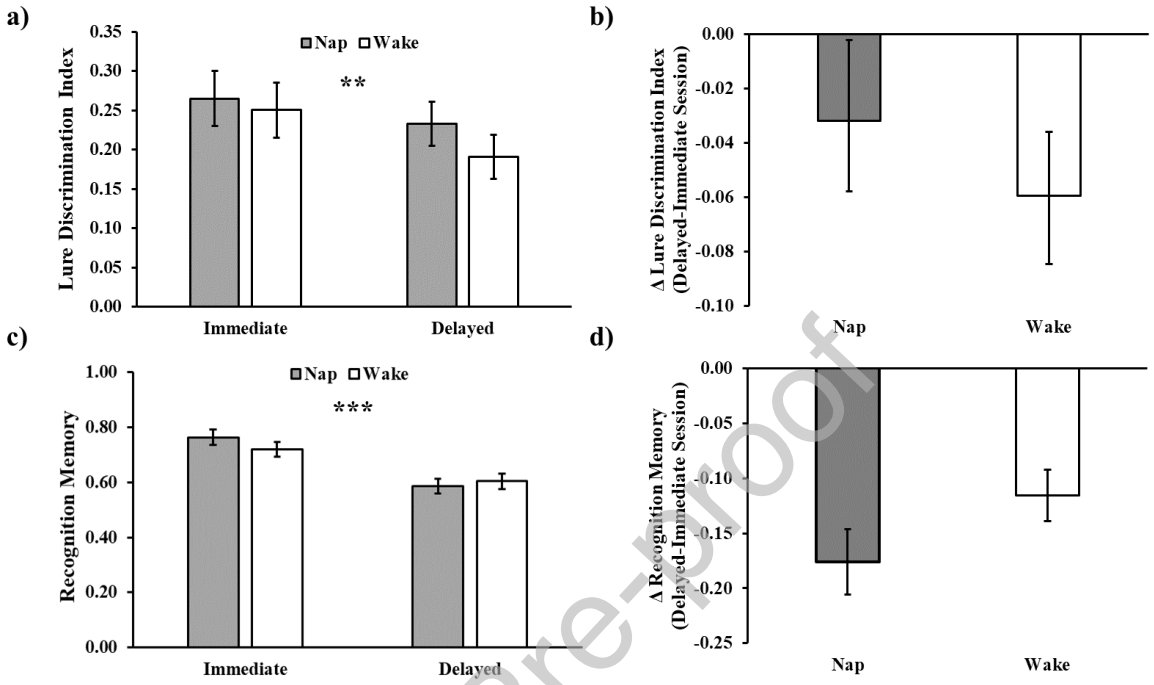

Figure 4. a) Lure Discrimination Index (mean value across the five similarity levels) as a function of the testing session (immediate and delayed recognition sessions) and group (Wake and Nap). **b)** Performance changes (computed as the Lure Discrimination Index at the delayed test minus Lure Discrimination Index at the immediate) as a function of the group. Error bars represent standard error of the mean. **c)** Recognition Memory score as a function of the testing session (immediate and delayed recognition sessions) and group (Wake and Nap). **d)** Performance changes (computed as the recognition memory score at the delayed test minus the recognition memory score at the immediate test) as a function of the group. Error bars represent standard error of the mean. *** = p<. 001.

The LMM analysis on Recognition Memory showed a significant main effect of Session ($F_{1,35.6}$ = 58.44, p< .001, *coff*= -0.15, *SE* = 0.02, t = -7.65), with a recognition memory reduction in the Delayed compared to the Immediate recognition session. Interestingly, there was a significant effect of the rMEQ score ($F_{1,35.9}$ = 11.13, p = .002, *coff* = 0.02, *SE* = 0.01, t = 3.34), suggesting that participants with higher rMEQ scores (tendency to morningness) showed a better recognition memory performance. To further understand this covariation result, we conducted a

series of a-posteriori correlations. Although we found no association between rMEQ and change scores in any of the memory measures (all r's < |.16 |, all p's > .34), we observed a general positive association between rMEQ and recognition memory performance both at the Immediate test (r = .33, p = .044, Figure S3a) and Delayed Test (r = .45, p =.004, Figure S3b), suggesting that participants with a morning tendency (higher rMEQ score) performed better in both testing sessions. This effect was present in both the Nap (r = .46, p =.049, r = .46, p =.045 for Immediate and Delayed test, respectively) and Wake group (r = .39, p = .096, r = .45, p =.051 for Immediate and Delayed test, respectively). The main effect of Group ($F_{1,35.4}$ = 2.46, p = .125, *coff*= -0.05, *SE* = 0.03, t = -1.57) and the interaction between Group and Session were not statistically significant ($F_{1,37.6}$ = 2.71, p = .108, *coff*= 0.07, *SE* = 0.04, t = 1.65; see Figure 4c). This lack of differences was confirmed by analyzing the differential scores between Delayed and Immediate test (t_{36} = -1.59, p = .120, *Cohen's d* = -0.52, Figure 4d) although the Bayesian Independent t-test ($BF_{01} \approx 1.187$, effect size 95% CI: -1.03, 0.16) resulted only in an anecdotal support to the null hypothesis (see Figure S2 in the supplemental material for Prior and Posterior and Bayes Factor Robustness Check of this test). A summary of the performance across the two sessions in the two groups can be found in Table 2.

Table 2. Performance scores across the two sessions in the two groups.

Measure	Session	Wake	Nap
Lure Discrimination Index	Immediate Test	0.25±0.1	0.27±0.15
	Delayed Test	0.19±0.11	0.23±0.13
	Difference	-0.06±0.11	-0.03±0.11
Recognition Memory Score	Immediate Test	0.72±0.10	0.76±0.14
	Delayed Test	0.60±0.10	0.59±0.14
	Difference	-0.12±0.10	-0.18±0.13

Notes. Data are presented as Mean±Standard Deviations. The difference is computed as Delayed test score minus immediate test score for each participant.

3.4 Exploratory correlations

Exploring potential associations between trait variables (BDI-II, STAI-Y2, and PSQI) and performance change showed no significant association (N= 36, all *r's* < .29). Lastly, no significant associations were observed between sleep parameters during the Nap and the changes in memory performance (N=19, all *r's* < .37). Similarly, no significant correlation emerged between trait variables, actigraphic sleep data from the night preceding the experiment, and performance at the immediate test (which represents some form of baseline mnemonic discrimination ability) (see supplemental material for all the correlation values).

4. Discussion

In the current study, we aimed to determine whether a daytime nap facilitates the long-term discrimination of declarative information. Based on previous studies showing a general beneficial role of sleep in memory consolidation (i.e., the process of transforming labile information into memories resistant to interference; see Rasch & Born, 2013), and two recent studies showing a protective role of nocturnal sleep on mnemonic discrimination ability (Doxey, et al., 2018; Hanert, et al., 2017), we expected to observe a greater mnemonic discrimination and recognition memory 2 hr after the encoding phase in participants who slept compared to those who remained awake. Contrary to our hypothesis, we observed a similar decrease in mnemonic discrimination and memory recognition performance in participants who had had a 90 min nap opportunity and those who had stayed awake. The two groups showed a similar performance also when taking into account the level of item similarity (from the most to the least similar to the targets).

This result is in contrast with the two previous studies showing a protective role of nocturnal sleep on mnemonic discrimination. Hanert et al. (2017) showed that, 12 hr after an immediate test, mnemonic discrimination remained stable across a sleep-filled delay, especially for the items less similar to the target, but deteriorated after a similar period of wakefulness. Moreover, they showed a decrease in recognition memory in both groups, but with a more pronounced reduction in the wake group. The authors proposed that sleep improves pattern separation in the hippocampus, and suggested that this improvement may be related to neural replay during sleep. This explanation was questioned by Poh & Cousins (2018). They proposed that the observed effects were due to greater interference during the wake period compared to sleep, which induced a stronger degree of forgetting. This latter explanation was also proposed by Doxey et al. (2018), who also showed that mnemonic discrimination remained unchanged after a 12-hr delay in participants who slept, whereas it decreased in participants who stayed awake. Interestingly, they showed an analogous decrease of recognition memory performance after 12 hr of wake or sleep. The authors suggested that sleep may enhance memory specificity by protecting learned items from interference. At variance with Hanert et al. (2017), they proposed that this beneficial effect of sleep was not due to a modulation of pattern separation at the hippocampal level, but seems to arise from stronger cortical representations of the items to be remembered.

Based on the latter result, the lack of differences between sleep and wake observed here may be the result of a short delay interval. Specifically, 2 hr of delay may not be enough to observe a marked decrease in mnemonic discrimination in the wake group, due to a reduced amount of interference. Indeed, the Wake group displayed a greater, though non-significant, performance decrease, as measured through the Lure Discrimination Index. A longer delay

between immediate and delayed testing (e.g., 4 hr of wakefulness) could induce a greater deterioration of performance linked to a greater amount of wake-based interference (i.e., more sensory information to process). Moreover, the participants in our wake condition played a low-arousing video game for 90 minutes (i.e., building a house in a modified version of the Sims3). Since recent studies have shown that playing complex videogames (e.g., Super Mario, Angry Birds, Minecraft) may improve lure discrimination performance (Clemenson, Henningfield, & Stark, 2019; Clemenson & Stark, 2015), our control condition may have provided an enriching experience (i.e., moving an avatar on a pseudo-3d environment) which, in turn, may have facilitated hippocampal neurogenesis (see Clemenson & Stark, 2015). We cannot exclude that the expected decrease in memory performance in the Wake group was balanced by an increase in hippocampal function induced by either the videogame per se or the low arousal, resting situation (Schapiro, McDevitt, Rogers, Mednick, & Norman, 2018). Future studies may consider both a longer retention period and a different wake control condition to avoid this confounding factor.

Another possibility is that a 60 min daytime sleep episode (here the average sleep duration was 58 min) may not be enough to efficiently consolidate memories whose representations were noisy, partial, or degraded (i.e., it may be insufficient for an efficient pattern completion). Indeed, daytime naps are often characterized by a single sleep cycle, with only a portion of subjects obtaining any amount of REM sleep. A specific process like pattern separation or pattern completion may require several sleep cycles, including both NREM and REM sleep, which seem to cooperate in the consolidation and integration of encoded information (Conte & Ficca, 2013; Giuditta, 2014). In particular, as proposed by McDevitt and colleagues (2015), REM sleep seems to be the optional state to rescuing noisy memories and separating

overlapping information. In the current study, only 9 participants obtained REM sleep during their nap, and the lack of REM (or enough NREM-REM cycles) may have limited the consolidation of the more weakly encoded items. It is also worth noting that in the current study participants had to encode a large number of items (i.e., 256), which may have interfered with the ability to rapidly create a stable mnemonic representation of these items. Indeed, the Lure Discrimination Index in the current study (~0.25) is lower than what has typically been observed in this age group (usually 0.35-0.40; see Stark, et al., 2015 among others), although it is more similar to what reported by Doxey et al. (2018). These explanations may suggest that, despite evidence supporting the notion that even a nap has an impact on specific declarative memory, sequence learning, and perceptual learning tasks (Cellini & McDevitt, 2015; Diekelmann & Born, 2010; Elizabeth A. McDevitt, et al., 2018; Mednick, et al., 2003; Whitehurst, Cellini, McDevitt, Duggan, & Mednick, 2016), the beneficial effect of daytime sleep may differ from nighttime sleep in terms of magnitude and specificity of the consolidation process (Payne et al., 2015; Schapiro et al., 2017; Sugawara et al., 2018).

It is also possible that circadian factors, which have been suggested to influence both encoding and recognition of declarative memories (Tilley & Warren, 1983), and to modulate plasticity-related gene expression (Martin-Fairey & Nunez, 2014), play a key role in the pattern separation process. Nevertheless, Saletin and colleagues (2016), using a within-subjects design, showed that lure discrimination performance was similar after a full night of sleep and a daytime nap, but impaired after a period of sleep deprivation. The latter result, as also discussed by Poh & Cousins (2018), clearly indicates that sleep before learning may be essential for the pattern separation process, due to its role in minimizing representation overlaps during encoding. However, the role of sleep in the mnemonic discrimination *after* learning, as in the current study,

may be different, and it is possible that a subsequent offline reorganization of this information may not require sleep, at least not in the short-term.

Related to circadian factors, we observed an interesting association between rMEQ scores and recognition memory both at the immediate and delayed test (but not with the change in this memory index), with participants with a morningness tendency (higher rMEQ scores) performing better in both testing sessions. This association was similar in the two groups, and may partially explain the lack of interaction between the sleep/wake condition and the testing session. Indeed, we expected an effect of sleep on recognition memory (i.e., a forgetting over time, but with a lower magnitude than the wake condition), but we failed to find any difference. Considering that the encoding session occurred for all participants at about 12:00 PM, an optimal time for cognitive functioning in individuals with a morning preference, this time-of-the-day effect may have facilitated the initial encoding of participants in both groups and reduced the effect of the sleep/wake manipulation (Schmidt, Collette, Cajochen, & Peigneux, 2007). Future studies on memory need to take into account not only the timing of testing sessions, but also participants' circadian preferences, which may indeed influence their ability to encode, store, and retrieve information.

Nevertheless, it should be noted that also Doxey et al. (2018) reported a worsening of recognition memory performance across 12 hr of daytime wakefulness or nocturnal sleep. Therefore, another explanation may be that the number of items to be remembered may have activated forgetting rather than consolidating processes. This idea is supported by the findings of Feld and colleagues (2016). They showed that post-learning nocturnal sleep reduced forgetting, compared to a wake condition, when participants had to remember up to 160 items (word-pairs), but this effect disappeared when the items to be remembered were 320. The latter number is

closer to the number of items used in the current study. The authors suggested not only a limited capacity of the memory-related sleep processes but also that sleep may activate processes that facilitate forgetting whenever the system reaches its capacity limit.

We must also acknowledge that the lack of significant differences between sleep and wake observed here may be a consequence of the low sample size (38 participants). Indeed, with 19 participants per group, our current study is powered at >=0.8 to detect effect sizes of Cohen's d >= 0.85 (one tail). However, the results from Hanert et al. (2017), who tested 13 participants in a within-subjects design, seemed to suggest that the effect size of sleep for both the pattern separation and recognition memory performance was Cohen's d > 1. Moreover, Doxey et al (2017), who tested 48 participants (24 per group), showed no effect of sleep on recognition memory, but a large effect of sleep (Cohen's d >= 0.8) on mnemonic discrimination. Therefore, whether there is any effect of daytime sleep on the memory processes assessed by the MST, they are likely in the medium-low range (e.g., Cohen's d < 0.5). Nevertheless, the Bayesian analysis seems to suggest that these small differences between groups are more likely due to a general response variability in the current sample rather than to an overly underpowered study. Moreover, our results are partially consistent with Doxey et al (2017), who tested 48 participants (24 per group). However, future studies with a larger sample size are needed to clarify the effect of daytime sleep on the mnemonic discrimination process.

Interestingly, our data appear consistent with a very recent study with a large sample investigating the effect of daytime sleep on mnemonic discrimination (Davidson, et al., 2020). Compared to our study, Davidson and colleagues (2000) used two different versions of the MST (one in the morning and one in the afternoon), investigating the effect of sleep on the *encoding* rather than *consolidation*. Nevertheless, they reported that either mnemonic discrimination or

general recognition performance did not improve after a daytime nap compared to a similar period of wakefulness.

In conclusion, here we showed that a brief daytime sleep episode did not facilitate mnemonic discrimination compared to a similar period of wakefulness. Whether this lack of sleep benefit was due to the duration of the sleep episode per se (~ 60 min, with a limited amount of REM sleep), to the reduced delay period (i.e., ~ 2 hr), or to possible benefits of playing low-arousal games on the wake group, remains unclear. Future studies may aim to examine mnemonic discrimination at different times of day, its trajectory over time (e.g., hours, days, weeks), and to disentangle whether and how diurnal and nocturnal sleep (or other resting conditions) impact this particular memory process.

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