A visual paired associate learning (vPAL) paradigm to study memory consolidation during sleep

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Abstract

Sleep improves memory consolidation, including hippocampus-dependent declarative memory. It is thought that by associating multiple aspects of an experience, the hippocampus enables its transformation into an enduring memory. Most research on human sleep and declarative memory uses exhaustive learning of word-pair associations. Here we present the visual paired association learning (vPAL) paradigm, in which participants learn new associations between images of celebrities and animals. vPAL associations are based on a one-shot exposure that resembles learning in natural conditions. Furthermore, vPAL is an engaging short paradigm that does not require rehearsal or reading, making it valuable for clinical settings. We tested if vPAL can reveal a role for sleep in memory consolidation by assessing the specificity of memory recognition, and the cued recall performance, before and after sleep. We found that a daytime nap improved the stability of recognition memory (decay was minimized) compared to identical intervals of wakefulness. By contrast, cued recall of associations did not exhibit significant sleep-dependent effects. Investigating memory consolidation during sleep with the vPAL paradigm opens up new avenues for future research across ages and heterogeneous populations in health and disease.

Keywords

recognition, association, memory, consolidation, sleep, nap

Introduction

New memories are initially weak, but such labile memories are further strengthened and integrated into pre-existing long-term memory through consolidation. Accumulating evidence established that sleep is critical for memory consolidation (Datta & MacLean, 2007; Diekelmann & Born, 2010; Dudai et al., 2015; Maquet, 2001; Tononi & Cirelli, 2014; Walker & Stickgold, 2004). The first demonstration that sleep benefits memory was obtained in 1924 using the paired associate learning (PAL) paradigm in humans (Jenkins & Dallenbach, 1924). Over time, it has been repeatedly confirmed that sleep supports memory consolidation (Diekelmann & Born, 2010) and that sleep-related benefits in learning are not simply due to lower fatigue, circadian time, or reduced interference. Numerous studies confirmed the beneficial effect of sleep memory in various tasks including motor, procedural, perceptual, and emotional memories (Fischer et al., 2002; Karni et al., 1994; Mednick et al., 2003; Payne et al., 2008; Robertson et al., 2004; Wagner et al., 2001; Walker et al., 2005). Significant benefits of sleep on memory are observed after an 8-hour night of sleep, but also after shorter naps of 1–2 hours (Korman et al., 2007; Mednick et al., 2003; Nishida et al., 2009; Tucker et al., 2006).

Consolidation of hippocampal-dependent declarative memory benefits from sleep. Several studies have shown that sleep reduces forgetting of facts and events compared to an interval of wakefulness (Barrett & Ekstrand, 1972; Gais et al., 2006; Lahl et al., 2008; Lau et al., 2010; Plihal & Born, 1997; Rasch et al., 2007; Ruch et al., 2012; Studte et al., 2015; Tucker et al., 2006; Werchan & Gómez, 2013). Apart from improving retrieval performance, sleep may also alter new memories to render them less prone to interference (Ellenbogen et al., 2006, 2009). The beneficial role of sleep in the consolidation of declarative memory is believed to be mediated by interactions between hippocampal and neocortical networks (Buzsáki, 1989). While new memories are initially encoded by the hippocampus, they are gradually integrated into long-term memory without compromising pre-existing memories (Frankland & Bontempi, 2005; Káli & Dayan, 2004; McClelland et al., 1995), a process that occurs preferentially during sleep and rest. During NREM sleep, driven by the slow oscillations that originate in the neocortex (Steriade & Timofeev, 2003), newly encoded information in the hippocampus is repeatedly reactivated (in conjunction with sharp wave–ripple activity and thalamocortical spindle activity, (Buzsáki, 1989; Nádasdy et al., 1999; Peyrache et al., 2009; Rudoy et al., 2009). Such reactivations likely facilitate the transformation of the newly encoded information from hippocampal to neocortical dependence.

Nearly all previous studies on human sleep and declarative memory used a word-pair learning task where two nouns (e.g. flowerpot and airplane) are paired, and memory retrieval is tested after sleep either by

recognition and/or by free/cued recall. This approach follows a tradition of verbal learning and memory (Hall, 1971) but despite its wide utility, relying solely on this specific semantic-oriented task also has disadvantages. First, it has been argued that the failure to replicate some key findings on sleep and memory may stem from the fact that effects depend on the specific task used (Bailes et al., 2020; Cordi & Rasch, 2021; Pöhlchen et al., 2021). Furthermore, it has been shown that laboratory-based and more natural autobiographical retrieval substantially differ in their neural substrates (McDermott et al., 2009). Thus, expanding experiments to use other closer-to-real-life tasks would potentially improve robustness in this research domain. Second, word-lists are often difficult to memorize, thereby evoking weaker memory performance. Accordingly, learning such lists typically requires repeated encoding and extensive rehearsal before reaching an adequate performance level. Such rehearsal inevitably involves factors such as motivation that go beyond memory per-se. Third, using word pairs to study the relation between sleep and memory consolidation may be suboptimal for research in elderly and clinical populations (e.g. dementia), where such research is important. However, learning word-pair lists depends on reading speed and attention span that are often impaired in such individuals.

To go beyond some of these limitations, it would be beneficial to expand the toolset for research on sleep and declarative memory consolidation beyond the classical word pair task. Hence, we developed the visual paired associate learning (vPAL) paradigm: a short (~15 minute), image-based memory paradigm with high ecological validity. Our objective was to design a paradigm that encompasses more aspects of natural memory formation relative to the frequently used word lists. To this end, new associations are formed between image pairs of celebrity faces and animals. These associations enable an everyday-like experience, due to its natural sense of familiarity and its engaging one-shot learning. Moreover, by presenting familiar and engaging images, the vPAL paradigm is well suited for clinical populations because it is time-efficient (no rehearsal), less reliant on reading, and easy to comprehend. We set out to test how sleep affects memory consolidation in this novel vPAL paradigm by employing a within-subject design in young healthy volunteers. Each participant learned and retrieved associations before and after an interval of either wake or sleep (in two separate sessions), to investigate the effects of sleep beyond those of time elapsed or circadian factors.

Results

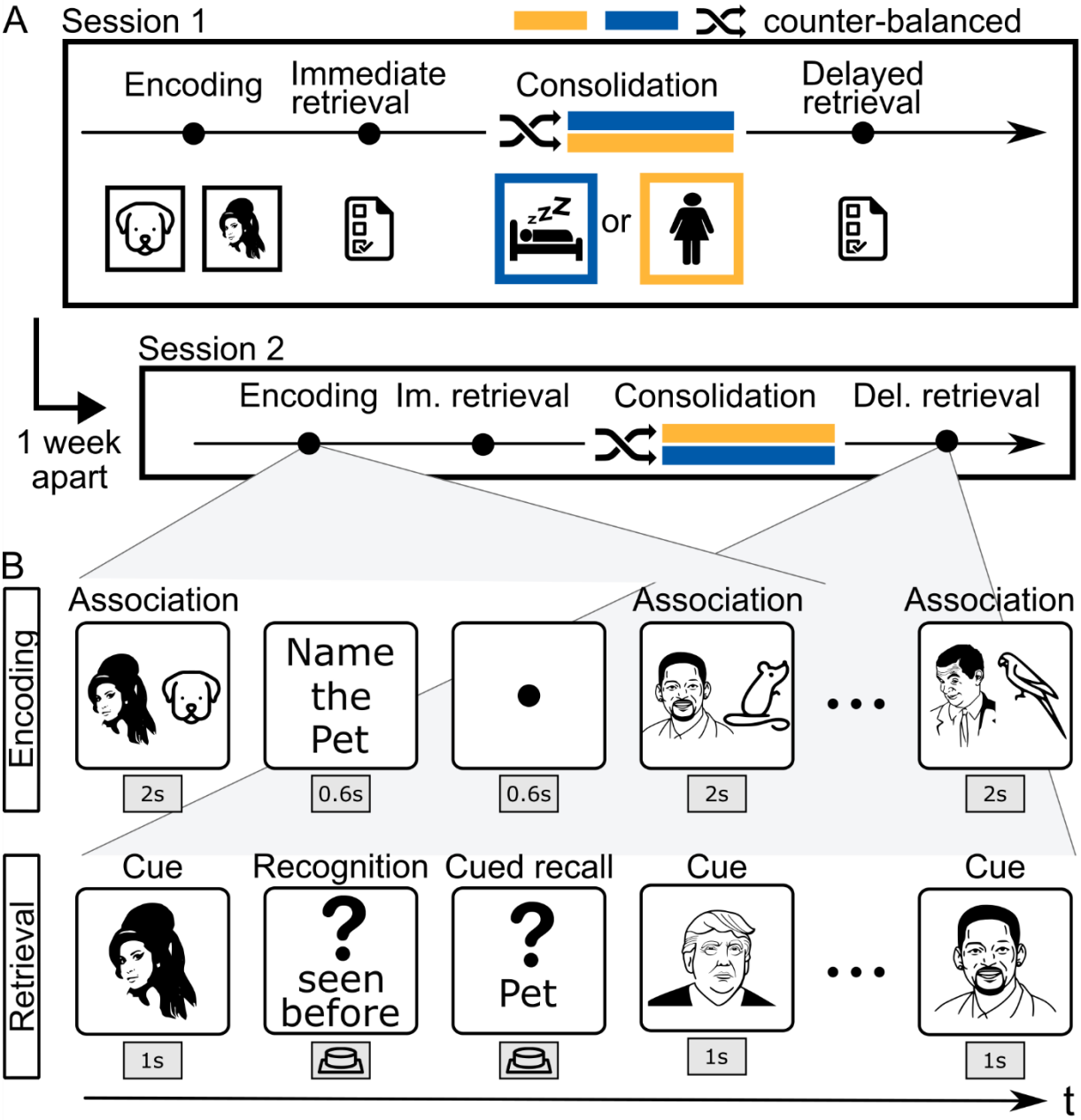

Figure 1. Study design: (A) Session design: participants completed two sessions, each including an encoding phase, a consolidation period, and two retrieval tasks (immediate and delayed). The two sessions took place one week apart. We varied the consolidation-period between the sessions, i.e. participants either stayed awake (yellow) or slept (blue) during the consolidation period (2.5 hours; order was counterbalanced). **(B)** Task description: encoding and retrieval consisted of the following parts. Encoding phase: associative pairing of celebrity and pet was followed by naming the animal type. Retrieval tasks (immediate and delayed): participants were presented a celebrity image (cue); then were asked to identify whether the celebrity was earlier paired with a pet or not (recognition) and finally asked to name the specific pet that was paired with the presented celebrity (cued recall).

103 To investigate the possible effects of sleep on memory consolidation with a visual paired associate
104 learning (vPAL) paradigm, healthy young volunteers (n = 23, average age = 27.7 years, range: 22 to 37
105 years, 33% female) participated in two sessions taking place one week apart (**Figure 1A**, Methods). Each
106 session started with a short (~15 min) encoding session around noon, where participants learned 25
107 pairings between photographic images of famous people and animals (contextualized as "pet owners"
108 and their pets). Learning was followed by an 'immediate retrieval' test, and an identical 'delayed retrieval'
109 test, separated by 2.5 hours during which participants were either asked to nap while monitored with
110 polysomnography and high-density EEG or stayed awake. The order of sleep/wake sessions was
111 counterbalanced, and a different image set was used in each session.
112
113 To verify that participants had adequate sleep, we first performed sleep scoring according to established
114 criteria (AASM, Iber et al., 2007) using a combination of electroencephalography (EEG), electromyography
115 (EMG), electrooculography (EOG) and video (see methods). **Figure 2A** shows a representative hypnogram
116 (time-course of sleep stages) throughout the 150 min (2.5h) period when sleep was allowed. On average,
117 subjects had a total sleep time (TST) of 114.8 ± 27.8 minutes (mean ± SD), representing sleep efficiency
118 (SE, sleep time per time in bed) of 75.8 ± 17.8 % with a sleep latency of 9.5 ± 9.6 minutes. Average NREM
119 sleep, REM sleep, and wake after sleep onset (WASO) constituted 96.6 ± 24.6, 18.2 ± 13.3, and 19.5 ± 31.4
120 minutes of sleep time, respectively. Within NREM sleep, N1, N2, and N3 constituted 10.5 ± 7.9 %, 39.9 ±
121 16.7 %, and 22.1 ± 13.7 % of sleep time, respectively (**Figure 2B**). These features represent a typical profile
122 for a daytime nap in healthy young volunteers (Mednick et al., 2003).
123
124 Next, three aspects of memory performance were assessed in each retrieval session. First, the specificity
125 of recognition memory ('was this celebrity seen before?') was evaluated via (yes/no) responses to
126 previously learned images and a set of lures (same set of lures was used in immediate and delayed
127 retrieval). We assessed recognition memory with two different measures, each of which is likely
128 differentially optimal for either clinical contexts or for healthy volunteers (see also Discussion). We
129 quantified ***recognition discrimination*** as the difference between hit-rate and false-detection rate (see
130 methods). This approach provided due representation for false detections and is likely optimal for
131 contexts with poor memory performance and high error rates, despite their relatively rare occurrence in
132 healthy participants. Second, recognition memory was also evaluated by quantifying ***retention accuracy***,
133 the overall percent of correct answers irrespective of whether images were previously presented or lures,
134 a measure that may be more optimal for healthy participants as described here. Third, we evaluated the

successful association of each person to their associated animal ('what was the pet of this celebrity?') in terms of percent of correct pairings. Performance on each of these three measures was assessed four times for each participant (2 time points * 2 sessions), without any feedback on responses: in the late morning and the afternoon, separately in sessions with a nap opportunity or in sessions with wakeful rest.

Memory performance declines over time

Participants successfully learned the celebrity-pet associations, recognizing 84.8 ± 13.5% (mean ± SD) of previously presented celebrities in the immediate retrieval session (significantly more than chance, $p < 0.0001$), and correctly associating some of their pets (35.3 ± 19.8%, $p < 0.0001$ against chance). Such performance represents successful learning that is not at ceiling, which is useful for comparing different individuals and conditions. We compared memory performance in the immediate and delayed retrieval tasks and found that, as would be expected, multiple aspects of memory performance declined over time in all experimental conditions. Recognition discrimination declined between the first and second retrieval tests conducted 2.5 hours part. In the wake sessions, recognition discrimination declined on average by 14.1 ± 20.0% over time (**Figure 2C**, Wilcoxon signed-rank test $V = 271$, $p < 0.0001$, Cohen's $d = 0.85$, recognition memory: $M_{morning} = 0.87$ (0.12), $M_{afternoon} = 0.73$ (0.18)). In the sleep sessions, recognition discrimination declined on average by 7.7 ± 10.8% (Wilcoxon signed-rank test $V = 125$, $p = 0.003$, Cohen's $d = 0.638$, recognition memory: $M_{morning} = 0.83$ (0.15), $M_{afternoon} = 0.75$ (0.22)). Similar results were observed for retention accuracy (**Figure 2D**), where performance declined on average by 5.2 ± 5.3%. In wake sessions, performance declined by 7.0 ± 5.1% over time (**Figure 2D**, $t(22) = 6.60$, $p < 0.0001$, Cohen's $d = 1.4$, retention accuracy: $M_{morning} = 0.92$ (0.07), $M_{afternoon} = 0.85$ (0.09)). Retention accuracy declined also after sleep by 3.4 ± 5.0% ($t(22) = 3.21$, $p < 0.005$, Cohen's $d = 0.67$, retention accuracy: $M_{morning} = 0.90$ (0.09), $M_{afternoon} = 0.87$ (0.11)). Finally, successful association performance also declined over time. Participants remembered significantly more celebrity-associated pets in the immediate retrieval session compared with the delayed retrieval session after wakefulness (**Figure 2E**, $t(17) = 2.15$, $p = 0.045$, Cohen's $d = 0.51$, percentage correct association : $M_{morning} = 0.35$ (0.21)%, $M_{afternoon} = 0.29$ (0.22)), and a trend for lower performance over time was observed in sleep sessions ($t(17) = 2.03$, p-value = 0.058, Cohen's $d = 0.48$, cued recall: $M_{morning} = 0.35$ (0.19), $M_{afternoon} = 0.32$ (0.22)). These results demonstrate that memory performance declined over time.

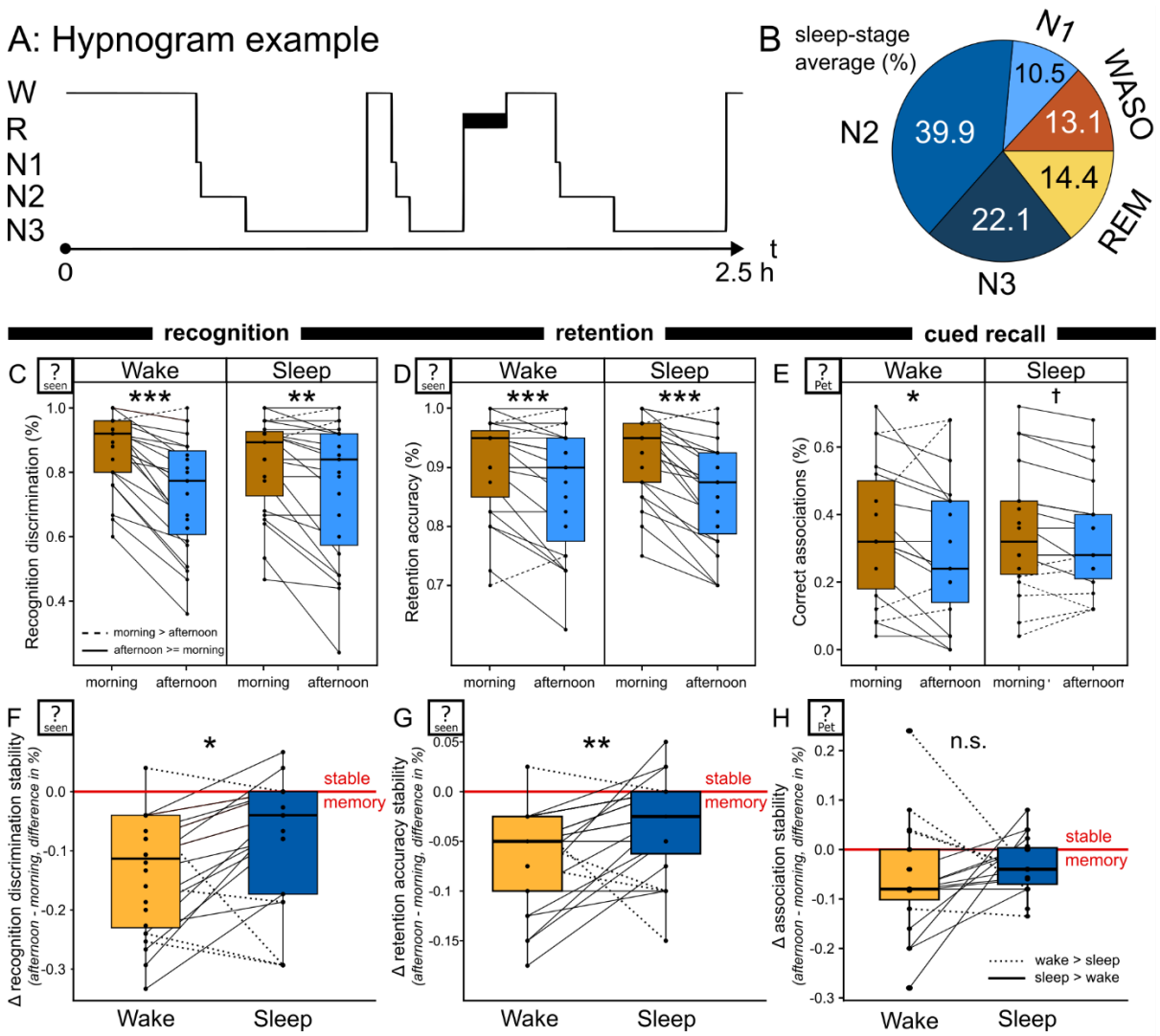

Figure 2. Memory performance: (A) Representative example of a hypnogram (progression of sleep stages on y-axis as a function of time on x-axis) in one participant. W = wake, R = REM sleep, N1-N3 = NREM sleep stages 1-3. **(B)** Pie chart showing average sleep stage distribution across all participants (N=18). WASO = wake after sleep onset. Difference in memory retrieval compared between morning and afternoon (top), as well as between consolidation periods (wake vs sleep, bottom). **(C)** Recognition discrimination before (orange) and after (blue) wake sessions (left) or sleep sessions (right). Boxplots depict memory performance (y-axis) and retrieval session (morning or afternoon, x-axis). The horizontal black line marks the median. The box contains the 25th to 75th percentile the vertical black line marks the 5th and 95th percentile limits. Dots depict individual subjects (n = 23) and their performance in the two separate sessions. Full (and dotted) lines compare data of the same participant in both sessions when memory was higher (or lower) in the immediate retrieval session in the morning, respectively. **(D)** Same as **C** for retention accuracy (n = 23). **(E)** Same as **C** for successful association in cued recall (n = 18). **(F)** Recognition discrimination stability (afternoon-morning difference in performance, y-axis) in wake (orange) or sleep (blue) sessions. Here full (and dotted) lines compare data of the same participant in both sessions when memory was more (or less) stable after sleep (compared to wake). Red line indicates stable memory (no memory decline between immediate and delayed recall). **(G)** Same as **F** for retention accuracy **(H)** Same as **F** for association stability. * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$, † = $p < 0.1$, n.s. = not significant.

Memory recognition is better conserved after sleep than after wakefulness

To assess whether sleep benefited memory consolidation, we compared whether memory performance was better maintained after sleep than after an equally long interval of wakefulness. We found that recognition discrimination was better conserved after sleep (**Figure 2F**, Wilcoxon signed-rank test V = 236, p = 0.003, Cohen's D = 0.61, Δ recognition discrimination stability: M_{sleep} = -0.08 (0.11), $M_{wake\ rest}$ = -0.14 (0.10)). The second measure of recognition memory, retention accuracy, showed a similar profile with better conserved performance after sleep compared with wakefulness (**Figure 2G**, t(22) = 2.83, p < 0.01, Cohen's D = 0.59, Δ retention accuracy stability: M_{sleep} = -0.03 (0.05), $M_{wake\ rest}$ = -0.07 (0.05)). Notably, these effect sizes (~0.6) are considered medium to large, and higher than the recommended effect size for sleep and memory studies (Cordi & Rasch, 2021). By contrast to recognition memory that was more stable after sleep, the cued recall of the celebrity-pet associations only showed a weak trend for better stability of successful associations after sleep, which was not statistically significant (**Figure 2H**, Δ association stability: t(17) = 1.03, p = 0.317, Cohen's D = 0.24, M_{sleep} = -0.026 (0.054), $M_{wake\ rest}$ = -0.06 (0.119)). Thus, measures of recognition memory are better conserved after sleep, while cued associations did not exhibit a significant sleep-associated improvements.

Discussion

We tested if and how sleep affects memory consolidation in a novel visual paired associate learning (vPAL) paradigm. We found that memory decay was less pronounced after sleep, compared to identical intervals of wakefulness, reflecting better memory consolidation. Improved performance after sleep was observed for both measures of recognition memory (recognition discrimination and retention accuracy), whereas cued recall of associations did not show a significant sleep-dependent modification.

The vPAL holds promise as a new tool that can enrich the experimental toolset for investigation of sleep and memory consolidation, above and beyond widely used PAL tasks using word pairs (Barrett & Ekstrand, 1972; Ellenbogen et al., 2006; Gais et al., 2006; Lau et al., 2010; Plihal & Born, 1997; Tucker et al., 2006; Werchan & Gómez, 2013). Given that sleep's effects on memory may depend on specific conditions (Cordi & Rasch, 2021), vPAL could help shed light on how general sleep-mediated memory benefits are - beyond those observed with one specific but widely used task. In this context, our results replicate that sleep benefits memory consolidation in healthy subjects and those benefits are observed using an image-based PAL task. The vPAL task does not include rehearsal or feedback, to resemble a natural encoding process. Despite the absence of any rehearsal and its short duration, vPAL exhibits an effect size that is higher than most effects reported in studies of human sleep and declarative memory (Cordi & Rasch, 2021). In addition to its effectiveness, the intuitive and engaging nature of vPAL makes it particularly suitable for clinical applications where learning, reading, attention, and rehearsal abilities may be limited. Some limitations of the study should also be acknowledged. The sample size (24 tested subjects) is relatively small, which limits statistical power and is suboptimal for correlation analysis. Similarly, the ecological design leads to a low number of stimuli (25) and we cannot exclude biases due to varying levels of prior celebrity-knowledge among the participants. Finally, we focused on a daytime nap which may not fully represent the effects of overnight sleep.

The main result observed here is a reliable beneficial effect of sleep on memory consolidation in the recognition task. Consolidation during sleep, when compared to wakefulness, improved recognition discrimination (the ability to differentiate previously presented celebrities versus lure images), an aspect that is often associated with hippocampal function (Quiroga et al., 2005; Suthana et al., 2015). Since we tested celebrities, participants were familiar with the faces to be recognized items prior to the study. By cueing pre-existing, conceptual information, we opted to investigate hippocampus-dependent memory specificity that goes beyond extra-hippocampal familiarity processes (Bird, 2017; Smith et al., 2014). We measured recognition memory via two parallel approaches – by either quantifying the recognition

discrimination or simply by a retention score (number of correct responses), where each approach could be optimal for different memory load situations. In clinical settings, individuals are more prone to make errors due to multiple factors such as impaired cognition, hospital environment, and medication. For example, false alarms (FA) - falsely identifying lure items as being previously seen – are frequent in mild cognitive impairment (MCI) or Alzheimer's patients (Anderson et al., 2008; Gallo, 2004). Along this line, Geva-Sagiv and colleagues (Geva-Sagiv et al., 2023) applied vPAL in epilepsy patients and focused on how sleep affects their recognition discrimination score. By contrast, when applying vPAL in young and healthy participants as in the present study, retention accuracy is likely the best measure of recognition memory performance, because false alarms are rare and detection discrimination may over-represent very few false alarms. We believe that different measures of recognition performance may be optimal for different difficulty and memory load situations, as is often the case in clinical settings or in healthy volunteers.

One intriguing aspect of the results is that sleep benefited memory recognition but was not associated with a significant improvement in cued recall (associations), a result also observed in a separate cohort of epilepsy patients performing this task before and after overnight sleep (Geva-Sagiv et al., 2023). However, we cannot exclude the possibility that sleep also affects recalling celebrity–pet associations. It could be that, with our specific experimental design, the cued recall task was not sufficiently sensitive to detect differences evoked by sleep, but that such differences do exist. Along this line, the initial retrieval rate immediately (minutes) after learning was around one-third of the associations. With this low success rate, sporadic lapses of attention or other noise sources could mask the potential influence of sleep on memory consolidation. Indeed, although not significant, cued recall did show a trend toward better performance after sleep (Figure 2F).

An alternative possibility is that the results represent a genuine difference in how sleep affects consolidation of recognition memory vs. associations. In this case, the results may be at odds with previous PAL studies reporting greater benefits of sleep for recall than for recognition (Newbury & Monaghan, 2019). If true, such a discrepancy would pose an open question and, at this point, we can only speculate about how and why these two aspects of memory may differ in their sleep-dependent consolidation. Three options come to mind. First, initial differences in memory strength could drive subsequent differences in sleep-related consolidation. In our paradigm, initial learning favored a 'one-shot' approach to model a natural memory acquisition process, without extensive rehearsal. With this approach, after learning, the initial memory strength of recognition memory (~85%) was higher than that of cued association (~35%). Since a new memory must pass a certain minimal level of performance to be

able to further benefit from sleep (Drosopoulos et al., 2007; Schoch et al., 2017), these initial differences in memory strength could have driven subsequent the sleep-dependent consolidation difference. This aspect might have been magnified by the task design. Participant had to repeat the pet name during encoding and thus focused on the pet rather than on the association itself. In addition, our paradigm included an immediate retrieval task (not always employed in sleep and memory studies), which constitutes a re-consolidation step involving intentional re-activations ('testing effect', (Rowland, 2014; Sutterer & Awh, 2016). Intentional rehearsal would likely mostly affect recognition because of the high retention rate at the immediate retrieval. A second option is that a short nap is not sufficient to significantly strengthen the relational aspect of memory association, which may require longer consolidation than that needed for recognition memory. However, sleep effects in the cued associate retrieval were also not detectable in the vPAL paradigm after longer sleep periods in epilepsy patients (Geva-Sagiv et al., 2023). Third, sleep may preferentially stabilize aspects of memory connected to prior knowledge. Evidence from rodents (Tse et al., 2007) and humans (Hennies et al., 2016; Kesteren et al., 2013) suggest that prior knowledge to which learning items can be connected facilitates memory consolidation. This has even been demonstrated for targeted memory reactivation (Groch et al., 2017). In the vPAL task, we used pictures of easily recognizable celebrities that could have biased the consolidation towards these images, relative to the newly learned association between celebrities and pets. Contrary, we admit that competing models for memory stabilization, such as contextual binding theory, could explain these results. Thus it is a possibility that sleep reduced contextual interference (and thus improving recognition), rather than strengthening the associations (Yonelinas et al., 2019). Additional studies are needed to determine whether and how memory accuracy and association differ in their sleep-dependent consolidation profiles.

Future studies with vPAL could expand this investigation along several avenues. Adding another memory task may help clarify further what aspects of declarative memory benefits from sleep. For example, a relational memory task could help focus on the associative aspects of the memory which may particularly depend on hippocampal activity (Bunsey & Eichenbaum, 1996). In addition, this task could be further combined with neuroimaging or intracranial monitoring of brain activity to further determine the neural processes mediating sleep-dependent memory consolidation. Finally, future research will determine the utility of vPAL in other populations such as elderly and patients with amnesia, epilepsy, or cognitive impairment due to neurodegeneration and, with time, may be used to investigate methods for boosting memory, particularly in people with learning and memory impairments.

Methods

Participants

Overall, 24 participants (average age = 27.7 years, range: 22 to 37 years, 33.3% female) were each tested on two separate experimental days. All participants were between 18 and 30 years old, without history or present of neuropsychiatric or sleep disorders. One participant was excluded because he could not sleep at all in the 'sleep' session, resulting in 23 participants available for recognition memory measures. Data of 5 participants were not available for the cued recall of associations due to technical issues, resulting in 18 participants available for association memory measures. One participant was excluded from EEG analysis of sleep architecture (Figure 3) due to insufficient quality of the electrophysiology recording.

Experimental procedure

Each participant participated in two visual paired associative learning (vPAL) experimental sessions, conducted one week apart at the same time of day (around noon), each consisting of an encoding (learning) phase and two retrieval tests (**Figure 1**). We ran a 2x2 within-subject design (2 time points x 2 session types) such that memory performance was assessed 4 times in each participant (without any feedback). The two retrieval tests were separated by 2.5 hours when subjects were either given an opportunity to sleep (daytime nap with EEG, details below) or rest awake in the lab, thereby forming either a learning-test-wake-test or a learning-test-sleep-test schedule. The order of sleep and wakefulness sessions was counterbalanced across participants (either wake first or sleep first), and different image sets were used for each session (their assignment to either first or second sessions also counterbalanced). Participants were instructed to avoid drinking coffee and sleep in the 6h before each session. Each session consisted of the following steps: (a) learning: encoding of image-pair associations, (b) immediate retrieval: recognition and cued recall of learned associations, (c) a consolidation period of 2.5h between the two retrieval task when participants either stayed awake or were given an opportunity to sleep, and (d) delayed retrieval: identical to the immediate retrieval step testing recognition and association recall. The constant schedule in each session helps focus on the comparison between sleep and wake conditions and go beyond effects of learning or circadian effects of time of day, which are similarly present in both sleep and wake sessions.

vPAL encoding phase. Participants were asked to memorize a series of 25 image pairs. Each pair consisted of a celebrity (e.g. Amy Winehouse) and their pet (e.g. dog) and participants were asked to learn which pet belongs to which celebrity ("Try to memorize the pet for each celebrity"). Each image pair was presented for 2s. To ensure that subjects are attentive, that the association is encoded, and to ensure that the pets are recognized correctly, participants repeated the pet's name out loud. The learning phase enabled encoding of 25 associations within 15min. Images of celebrities were used for quick, one-trial learning, because they are easy to remember (memorability of emotional vs neutral memory, LaBar & Cabeza, 2006; Wagner et al., 2001). The downfall of having a quick encoding of only 25 associations is a high subject-variability, which we addressed by a within-subject design (two sessions per subject).

vPAL retrieval phase. Participants underwent two identical retrieval tests, before ('immediate retrieval') and after ('delayed retrieval') the consolidation period. During the retrieval task, single images of celebrities were presented for two seconds and subsequently queried (40 images in total). Of these images, 25 celebrities were images that were originally presented and paired with a pet during the learning phase and thus represent pet-owners. 15 additional images of celebrities were new ('lures'). The same set of lures was used in the immediate and the delayed retrieval. We separately probed two different aspects of memory retrieval: (i) the accuracy of memory recognition where participants were asked to identify pet-owners and reject lures ("Is this a pet owner?", Yes/No) and, only if a celebrity was identified as a pet-owner, (ii) participants then concluded a cued recall by naming the associated pet ("name the pet") while their verbal response was registered. The cued recall (ii-retrieval) was skipped if a participant did not recognize the celebrity. Overall, we separately estimated which of the 40 queried images were correctly identified as new or old and whether the participants were able to recollect the associated pet (when applicable). Importantly, feedback was never provided, neither during the retrieval task before nor after the consolidation period and thus the first retrieval task before the consolidation did not function as explicit re-learning.

To determine how memory consolidation in the vPAL paradigm is affected by sleep, we measured memory retrieval scores four times: before and after a 2.5h period when subjects were either awake or given an opportunity to sleep (Figure 2A-C). To further quantify memory effects, we computed memory consolidation (by immediate and delayed retrieval tests), and further compared consolidation scores between sleep and wake rest consolidation (Figure 2D-F). To this end, we defined three measures of memory consolidation as follows:

356 (i) Recognition discrimination = (# correct recognition / N_{trials}) - (# false recognition /N_{trials}); often referred
357 to as "hits - false alarms". Then, memory stability score (Δ Recognition discrimination stability) was
358 computed per session as the difference in % between afternoon (delayed) and morning (immediate)
359 retrieval tests: recognition memory $_{afternoon}$ - recognition memory $_{morning}$. This stability score was compared
360 between sleep and wake session. Thus, the difference between the Δ Recognition discrimination stability
361 in sleep and Δ Recognition discrimination stability in wake represents the added benefit of sleep for
362 consolidation of recognition discrimination, reflecting stabilizing effects of sleep on memory (Rasch &
363 Born, 2013; Schreiner & Staudigl, 2020; Walker & Stickgold, 2004)
364
365 (ii) Retention accuracy = # correct recognition answers / N $_{total_trials}$; can also be described as (# correct
366 recognition +# correct rejections / N $_{total_trials}$). Then memory stability score (Δ retention accuracy stability)
367 was computed per session as the difference in % between afternoon (delayed) and morning (immediate)
368 retrieval tests: retention accuracy $_{afternoon}$ - retention accuracy $_{morning}$. This stability score was compared
369 between sleep and wake session. Thus, the difference between the Δ retention accuracy stability in sleep
370 and Δ retention accuracy stability in wake represents the added benefit of sleep for consolidation of
371 memory retention, reflecting stabilizing effects of sleep on memory.
372
373 (iii) Correct associations = # correct cued recall answers / N $_{total_trials}$. Then association stability score (Δ
374 association stability) was computed per session as the difference in % between afternoon (delayed) and
375 morning (immediate) retrieval tests: association accuracy $_{afternoon}$ - association accuracy $_{morning}$. This stability
376 score was compared between sleep and wake sessions. Thus, the difference between the Δ association
377 stability in sleep and Δ association stability in wake represents the added benefit of sleep for retrieving
378 associations in a cued recall. N $_{total_trials}$ was always set to 25, including not recognized celebrities, no
379 answers and incorrectly paired pets.
380
381 **Images and visual stimulation**
382 Images of celebrities and animals were generated from copyright-free web images. We created 2 image
383 sets for vPAL experiments, each with 25 image pairs of celebrities and animals for learning, and 15
384 additional pictures of lure celebrities. Different sets were used during sleep and wake sessions such that
385 no celebrity or animal appeared twice. The set's allocation to a session was counterbalanced. Hence, each
386 image was presented an equal number of times, though in different participants. Altogether, this
387 represents a total of 130 images used in this study (80 celebrities and 50 animals). Because of the within-

subject within-session comparisons, there was no need for shuffling the learned-lure image allocation. Stimuli were presented using the psychtoolbox implementation in python (http://psychtoolbox) on a monitor placed about 50 cm in front of participants.

Sleep EEG, scoring, and characterization

Data collection. In sleep sessions, we collected polysomnographic data including high-density electroencephalogram (hd-EEG), electrooculogram (EOG), electromyogram (EMG), electrocardiogram, and video. hd-EEG was recorded using a 256-channel hydrogel geodesic sensor net (Electrical Geodesics, Inc. [EGI]). Signals were referred to Cz, amplified using an antialiasing filter and an AC-coupled high input impedance amplifier (NetAmps 300, EGI), and then digitized at 1000 Hz. Before the recording began, the electrode impedance of all sensors was confirmed to be at least below 50 kΩ.

Sleep scoring and analysis. Sleep scoring was performed according to the established guidelines of the American Academy of Sleep Medicine (Iber et al., 2007) with the aid of the sleep module in Visbrain Python package (Combrisson et al., 2019). To this end, EEG data from F3/F4, C3/C4, and O1/O2 was re-referenced to the contralateral mastoid, resampled to 250 Hz, band-pass filtered to 0.3-40 Hz and visualized in 30s epochs together with synchronized EOG from electrodes E1&E2 above and below eyebrows and EMG from submental electrode (band-pass filtered to 10-100 Hz). Successful scoring was further verified by inspecting the time-frequency representation (spectrogram) of the Pz electrode (not involved in the scoring process) superimposed with the hypnogram. Sleep was characterized, for each participant, by extracting the following measures: time in bed, duration from start to end of sleep, duration of wake within sleep, total sleep time, time in each sleep state, time in NREM sleep, latency to onset of each sleep stage, sleep onset latency, sleep efficiency (time asleep / time in bed) and sleep maintenance (time asleep / start to end sleep).

Statistical analysis

We assessed the normality of distributions with a Shapiro-Wilk test. Parametric methods for statistical testing were used if the data were normally distributed. For the analysis of the recognition answers, we used Wilcoxon signed-rank test, because the data was not normally distributed. We applied two-sided tests unless stated otherwise. Data processing and analysis were performed using custom-made R® scripts (R Core Team, 2021).

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Author contributions

Y.N., M.G.S, and I.F. conceived the research and designed experiments. Y.N. and I.F. secured funding. M.G.S., R.F., and O.S. prepared cognitive experiment. R.F., and Y.G. managed data collection. Y.G., R.F., S.Y., and FJ.S. performed sleep scoring. F.J.S., R.F., and S.Y. performed data analysis. F.J.S. and Y.N. wrote the manuscript. All authors provided ongoing critical review of results and commented on the manuscript.

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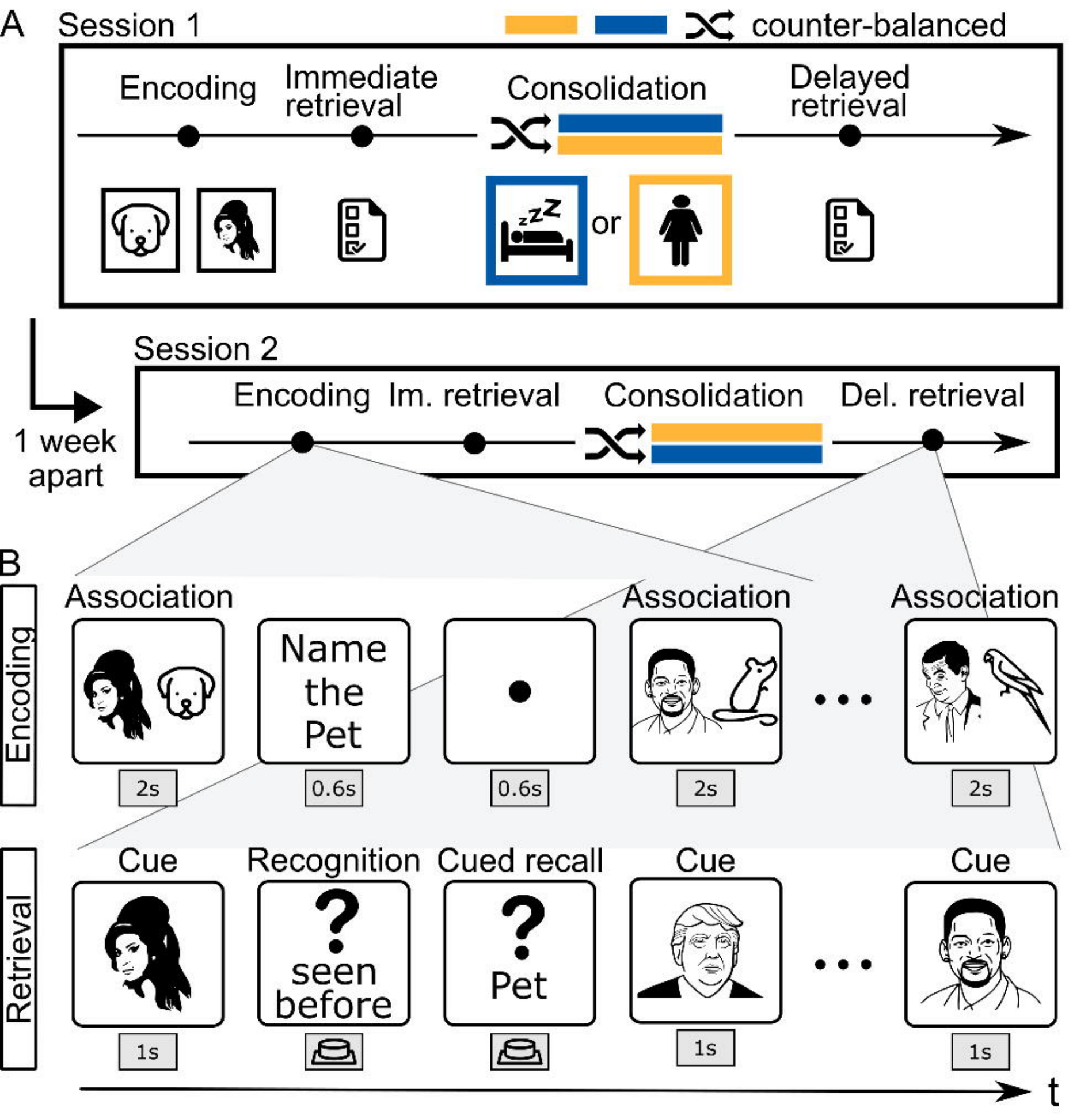
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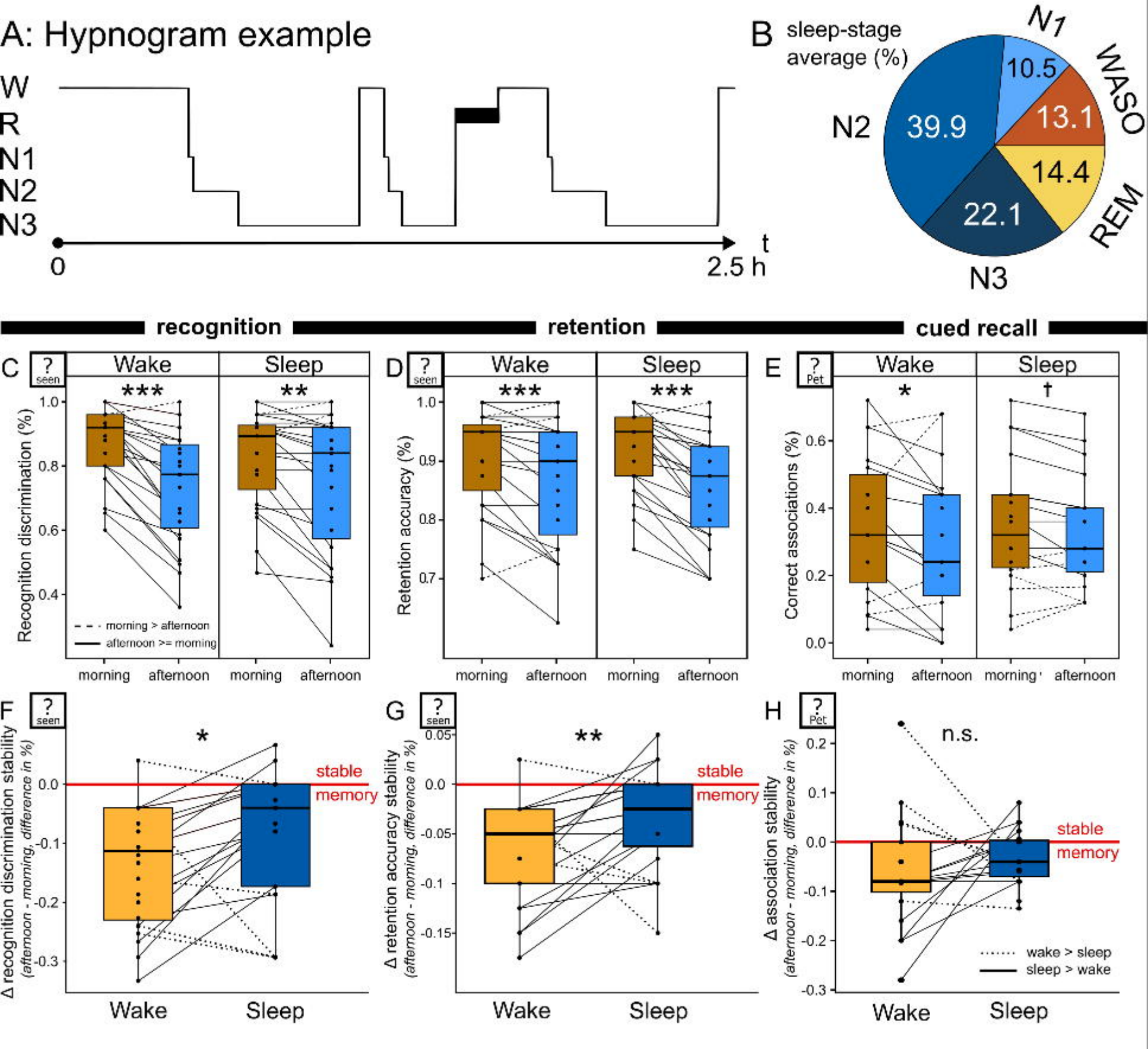
A: Hypnogram example
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Recognition discrimination (%)
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stable
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