The relationship between sleep and cognitive performance on tests of pattern separation

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Abstract

Study objectives: Sleep disturbances are considered both a risk factor and symptom of dementia. The present research aimed to identify cognitive tests in which performance is associated with objective sleep quality or quantity, focusing on cognitive tests designed to evaluate the earliest cognitive changes in dementia.

Methods: We recruited younger and older adults and remotely monitored their sleep patterns for 7 consecutive days using wrist actigraphy and sleep diaries. On day 7, participants completed a battery of cognitive tests, which included the Psychomotor Vigilance Task (PVT), the Prodromal Alzheimer's and Mild Cognitive Impairment battery from the Cambridge Neuropsychological Test Automated Battery (CANTAB), and the Mnemonic Similarity Task (MST), designed to tax pattern separation. The older adults were also assessed with the Montreal Cognitive Assessment (MoCA).

Results: The final sample included 81 younger adults (mean age: 20.12 ± 1.99) and 34 older adults (mean age: 65.56 ± 9.57). There were no significant relationships between sleep and cognitive performance in the younger adults. In the older adults, there were significant correlations between total sleep time and PVT and MST performance. MoCA scores were correlated with performance on CANTAB and MST. Total sleep time also predicted MST performance in the older adults when controlling for age and gender.

Conclusions: Performance on cognitive tests designed to assess pattern separation are sensitive to older adults' sleep duration and the early cognitive changes associated with dementia. MST should be evaluated for potential use as a clinical trial outcome measure for sleep-promoting treatments in older adults.

Keywords: Sleep/wake cognition, dementia, learning and memory, actigraphy, sleep deprivation, aging

Statement of Significance

There is growing emphasis on the importance of sleep as a potential therapeutic target for neurodegenerative diseases (e.g., Alzheimer's disease). Identifying cognitive measures that are sensitive to both sleep and the earliest cognitive changes associated with dementia are needed for use as outcome measures in clinical trials evaluating the effectiveness of sleep-promoting interventions. Our research addresses this need by investigating the relationship between sleep patterns and performance on cognitive tests designed to assess the earliest cognitive changes in dementia. Our results suggest that cognitive tests designed to assess pattern separation are uniquely sensitive to sleep quantity, particularly in older adults.

Introduction

Sleep has recently been identified as a potential therapeutic target for dementia caused by Alzheimer's disease (AD).[1] There is growing evidence from humans and preclinical mouse models that sleep can directly affect the accumulation of pathological amyloid-beta and tau proteins in the brain, both of which are the defining hallmarks of AD and are thought to drive the neuropathologic course of the disease.[1] It is estimated that by treating sleep disorders, 15% of AD cases could be delayed in onset or prevented.[2] In addition to the direct effects on neuropathology, there is evidence that sleep disruption may be the mechanistic pathway through which AD pathology affects hippocampal-dependent cognitive decline.[3] There are now a variety of interventions, from non-invasive brain stimulation (e.g., transcranial electrostimulation) to pharmacological agents (e.g., orexin receptor antagonists, melatonin, or trazodone), being evaluated for safety and effectiveness of improving sleep in individuals diagnosed with AD.[1,4,5] The ultimate goal of many of these sleep-focused trials is to improve cognition (i.e., prevent, slow, or reverse the dementia caused by AD).[5] What is now needed is to identify which of the cognitive tests would be most suitable as clinical trial outcome measures, such that the tests are sensitive to the cognitive decline associated with AD and also to sleep-associated cognitive processes.

We hypothesize that tests designed to assess pattern separation may be uniquely sensitive to sleep-associated changes in cognition, and thus may be useful as clinical trial outcome measures for testing interventions to improve sleep in older adults at risk for, or diagnosed with AD.[6] Pattern separation is a computational mechanism taking place during encoding and proposed to underlie the creation of distinct ensemble neural representations from overlapping inputs.[7,8] By transforming similar experiences into discrete neural representations, pattern

separation is postulated to increase the likelihood of accurate memory encoding and subsequent retrieval, which is fundamental to successful episodic memory.

Cognitive tests designed to assess pattern separation are sensitive to the cognitive changes associated with MCI and AD.[9–11] Performance has been shown to correlate with levels of cerebrospinal fluid amyloid-beta 42, which is a clinically validated AD biomarker.[12] Individuals with MCI and AD also have higher rates of false memories,[13–17] which is hypothesized to be caused by a failure in pattern separation leading to heightened interference amongst memories.[18]

There is also strong evidence from rodent models that sleep disruption can markedly suppress neural plasticity in the hippocampus, such as adult hippocampal neurogenesis[6] a form of plasticity that we and others have shown to play an important role in pattern separation.[19–21] We hypothesize that chronic sleep disturbance, which is a risk factor for AD, would negatively affect the hippocampal neural plasticity important for pattern separation. Indeed, a few studies in humans have shown that performance on tests designed to assess pattern separation are sensitive to periods of wakefulness and sleep deprivation.[22–24] Thus, cognitive assessments designed to assess pattern separation have been shown to be sensitive to both early stages of AD[25] and sleep.[22–24]

Here, we conducted an exploratory study examining the relationship between sleep and performance on two cognitive tests that tax pattern separation processes, the Mnemonic Similarity Task (MST)[25] and the Delayed Matching to Sample (DMS) test[26] which is part of the Cambridge Neuropsychological Test Automated Battery (CANTAB). We compared performance on these tests of pattern separation to the Psychomotor Vigilance Task (PVT), which has been previously shown to be sensitive to sleep loss and circadian misalignment[27,28] as well as performance on the other CANTAB tests that are part of the Prodromal Alzheimer's and

MCI battery. We hypothesized that shorter sleep duration and poorer sleep quality would be associated with poorer performance on PVT, MST, and CANTAB DMS.

Methods

Participants

The study was approved by the Research Ethics Board (REB) at Simon Fraser University (Protocol #30000539) in compliance with the Canadian Tri Council Policy Statement: Ethical Conduct of Research Involving Humans. Subjects were undergraduate SFU students (18 - 30 years of age) recruited via the SFU Psychology Research Participation System and advertisements, and middle-aged and older adults (50+ years of age) recruited via posters, word-of-mouth, social media platforms, and the online platform REACHBC (https://reachbc.ca/). Prior to any testing, participants completed an online consent form and a questionnaire, which collected demographic and health information. Participants needed to be able to understand and follow written and verbal instructions to be eligible to participate. There were no other exclusion criteria. Upon completion of the study, the young adults were compensated with either research credits or payment, whereas the middle-aged and older adults were compensated with payment.

Procedure

Participants were scheduled for two in-person visits. All visits took place between 10:00 and 15:00. During the first visit, participants were provided with instructions and wrist actigraphy. On the 7th day, participants returned to the lab to complete cognitive testing. Figure 1 provides an illustration of the procedure. The participants completed the PVT, then the MST, followed by the CANTAB. After CANTAB testing, the older participants completed the MoCA. The testing took ~75 min to complete.

Sleep Assessments

Sleep monitoring was performed by the participants in their home environment. All participants wore wrist actigraphy (ActTrust2 model AT20101, Condor Instruments, Sao Paulo, Brazil) on their non-dominant hand and completed an online sleep diary, hosted via Qualtrics (https://www.qualtrics.com/), for 7 consecutive days. Participants were asked to press an event button on the wrist actigraphy when going to bed and when waking up in the morning. The data were sampled in 1-min epochs. We asked the participants to follow their habitual sleep schedule and did not enforce a schedule.

Psychomotor Vigilance Task (PVT)

The PVT is designed to measure sustained attention and reaction time.[27,29] We used the 5-min PVT version developed by NASA (Version 1.2.0., Washington, D.C., USA).[30,31] The task was presented on an Apple iPad (OS 15.4.1, model A2602). The participants were instructed to attend to a small rectangular area on the dark iPad screen where a millisecond counter appeared, rapidly increasing from zero. The millisecond counter appeared at random inter-stimulus intervals (ISI), ranging from 2 to 10 s.[30] The participants were asked to tap the thumb of their dominant hand on the screen as quickly as possible when the number was shown. A practice session was completed before the experimental trials.

Mnemonic Similarity Task (MST)

The MST (Version 0.96) was used to assess pattern separation.[25] We used the 3-choice version and the pace of the task was computerized (i.e., not self-paced). The task was run using Set 1 stimuli and included two phases. Phase 1 had 128 trials and participants were sequentially presented with images of everyday objects and asked to indicate via keyboard responses whether the object was an indoor or outdoor object.[25,32] The participants were not informed about the upcoming memory test while they performed phase 1 of the task. During phase 2, which had 192

trials, the participants were sequentially presented with images of everyday objects, and the participants were asked to respond “old,” “similar,” or “new” to indicate whether the objects were a) identical to an image shown in phase 1 (i.e., old/target), b) similar to an image presented in phase 1 (i.e., similar/lure), or c) a new image not presented in phase 1 (i.e., new/foil). Of the 192 trials, one-third (64) were targets, one-third (64) were lures, and one-third (64) were foils. The lures varied by 5 levels of similarity ranging from L1 (highly similar) to L5 (least similar). All images in both phases were presented with a duration of 2000 ms with an inter-stimulus interval of 500 ms.

Cambridge Neuropsychological Test Automated Battery (CANTAB)

The Prodromal Alzheimer’s and MCI CANTAB battery included 4 cognitive tests: Delayed Matching to Sample (DMS), Paired Associates Learning (PAL), Reaction Time (RTI), and Spatial Working Memory (SWM). All tests were presented on an Apple iPad (OS 15.4.1).

The Delayed Matching to Sample (DMS) test measured visual matching ability and short-term visual recognition memory for non-verbalizable patterns. During the task, participants were shown a complex pattern (i.e., sample pattern) for 4.5 s, and four choice patterns, composed of different configurations and colors. One of the choice patterns was identical to the sample pattern and participants were asked to select one that matched. In some trials, the choice patterns and the sample pattern appeared simultaneously, whereas in other trials, there was a delay of 0, 4, or 12 s before the four choices were presented.[26]

The Paired Associates Learning (PAL) task assessed new learning and visual episodic memory [33]. During the task, boxes were shown on the screen and were opened in a randomized order for 2 s. One or more of the boxes contained a pattern. The patterns were then presented in

the center of the screen, one at a time. The participant was asked to select the box (i.e., location) in which the pattern was originally displayed.

The Reaction Time (RTI) task assessed divided attention and psychomotor speed.[34] During the task, the participant was asked to select and hold down a button at the bottom of the screen to make a yellow flash appear in one of five circles presented at the top of the screen. Once the flash appeared, the participant was instructed to react as quickly as possible by releasing the button at the bottom of the screen and touching the circle in which the yellow flash appeared.

The Spatial Working Memory (SWM) task required manipulation and retention of visuospatial information.[35] During this task, multiple boxes were presented on the screen, with one containing a hidden target. The participant was asked to select the empty boxes until only one box remained that contained the hidden target.

The Montreal Cognitive Assessment (MoCA)

The older adults completed the MoCA Duo (MoCA Montreal) administered on an Apple iPad (OS 15.4.1, model A2602 with a 260.6 x 174.1 mm screen size).[36] MoCA Duo is an automated version of the standard MoCA questionnaire.[37] The MoCA measures 6 cognitive domains including executive function, memory, attention, visuospatial skills, language, and orientation.[36] The test is a 30-point scale and a total score of less than 26 can indicate MCI. An extra point is added to participants who have fewer than 12 years of formal education. The administration time of the test was approximately 10 min.

Data analysis

Wrist actigraphy

Wrist actigraphy data were extracted and analyzed using ActStudio software (Version 2.2.0, Condor Instruments, Sao Paulo, Brazil). Only nocturnal sleep was assessed. Average total

sleep time (TST) across the week was used as a measure of sleep quantity and average sleep efficiency across the week was used as a measure of sleep quality. A minimum of 5 nights of complete wrist actigraphy data were required for each participant to be included in the analyses. Sleep diaries were used to confirm bed and wake times. We also used Clocklab (Version 6.1.11, Actimetrics, Wilmette, USA) to run a cosinor analysis to estimate acrophase, amplitude, interdaily stability (IS), and intradaily variability (IV) of the daily activity rhythms.

PVT

We calculated the slowest 10% reaction times for all PVT trials, which has previously been shown to be sensitive to sleep loss.[38,39]

MST

For the MST analysis, the Memory Recognition scores (REC) were calculated as [p(correct old response to repeated images) - p(incorrect old response to foils)].[25] The Lure Discrimination Index (LDI) was calculated as [p(correct similar response to lures) - p(incorrect similar response to foils)].[40] We also assessed performance for the L1 and L2 specific lure bins, which have the highest levels of similarity between the lures and the repeated images, and thus are most taxing on pattern separation. For L1 and L2, we assessed *Accuracy*, as the probability of correctly identifying the lure as similar, and *False Memory Error Rate*, as the probability of falsely identifying the lure as a repeated image.

CANTAB

CANTAB data were analyzed using the CANTAB software.[41] The key performance measures included in our analyses were:

DMS. We calculated DMS Pattern Errors (All Delays), as the number of times the participant initially chose the distractor stimulus with different physical attributes (i.e., an

incorrect pattern), but matching color elements, calculated across all trials with a delay component.

PAL. The number of times a participant selected the correct box on their initial attempt while recalling the pattern locations (PAL First Attempt), and the number of times a participant selected the incorrect box with an adjustment to allow for a comparison of error rates across all participants (PAL Adjusted Errors).

RTI. The average duration elapsed from the moment a participant let go of the response button until they selected the target stimulus.

SWM. The number of times a participant revisited a box where a token was previously found (SWM Between Errors) and the number of times the participant started a new search pattern from the same initial box in trials with 6-8 boxes (SWM Strategy).

Montreal Cognitive Assessment

The MoCA total score calculated out of 30 points.

Statistical analyses

The relationships between sleep measures and cognitive performance were assessed with Pearson's correlation analyses, using JMP Student Edition 18.2.1 (JMP Statistical Discovery LLC, North Carolina, USA). Correlations between data that violated the assumption of normality were conducted using Spearman's rank correlation (ρ). Significant correlations between sleep and cognitive performance were further examined using multiple linear regression analyses, to account for age and gender as potential confounding variables. The residuals of the models were normally distributed, centered around zero with constant variance and were not affected by outliers. Observations were independent shown by the Durbin Watson's test ($p > .05$). We did not include ethnicity in our model as our sample size did not allow for equal distribution of

different ethnic groups. The cut-off used for statistical significance was $p < 0.05$ (two-tailed) for all measures. As this was an exploratory study, we did not control for multiple comparisons.

Results

Sample characteristics

Of the 89 younger adults and 40 older adults recruited, 8 younger adults and 6 older adults were excluded from all analyses, due to unreliable or missing sleep data (n = 6), distractions during testing (n = 1), not understanding task instructions (n = 2), poor performance or malfunction on both MST and CANTAB (n = 4), and outside recruitment age range (n = 1). The remaining 81 younger adults (mean age: 20.12 ± 1.99) and 34 older adults (mean age: 65.56 ± 9.57) were included in the analyses. Table 1 shows the participant demographic information and Table 2 shows the average sleep and circadian rhythm parameters.

For the task-specific analyses, an additional 1 younger adult and 4 older adults were excluded from PVT analyses due to reporting major distractions during task performance (n = 2) or failing to keep their thumb still in between trials, leading to unintentional screen taps (n = 3). Eleven younger adults and 9 older adults were excluded from MST analyses due to errors in MST administration or malfunction (n = 5), mixing up button presses (n = 1), not understanding the task indicated by using the similar response less than 10 times (n = 7),[42] not complying with task instructions (n = 3), and a REC score below the cut-off value of .50 (n = 4). Five younger adults were excluded from CANTAB analyses due to technical error (n = 2) and not complying with the protocol (n = 3). No older adults were excluded from CANTAB analyses. Two older and 28 younger adults were excluded from circadian analyses as they did not have 5 or more consecutive days of continuous wrist actigraphy-wearing.

Performance on PVT is correlated with sleep in the older adults but not in the younger adults

There were no significant relationships between average total sleep time or sleep efficiency and PVT performance in the younger adults ($p > .05$; Supplementary Table S1). In the older adults, there were significant correlations between average TST and mean slowest 10% RT ($\rho(28) = -0.38$, $p = .04$). There were no significant correlations between average sleep efficiency and PVT performance ($p > .05$). There were no significant correlations between PVT and circadian parameters in the younger or older adults ($p > .05$; Supplementary Table S2).

Performance on a cognitive test of pattern separation is correlated with sleep in the older adults, but not in the younger adults

In the younger adults, there were no statistically significant correlations between TST or sleep efficiency and performance on the MST ($p > .05$, Figure 2) or CANTAB ($p > .05$). When evaluating the relationship between circadian rhythm parameters and MST performance, there was a significant correlation between amplitude and CANTAB RTI ($\rho(46) = -0.30$, $p = .04$). No other tests were correlated with circadian parameters ($p > .05$). See Supplementary Tables S1 and S2 for additional statistical results.

In the older adults, there were statistically significant correlations between sleep and MST performance; specifically, TST and L1 Accuracy ($\rho(23) = 0.42$, $p = .04$) (Figure 2g), and between TST and L1 False Memory Error Rate ($r(23) = -0.41$, $p = .04$) (Figure 2k). There were no statistically significant correlations between sleep and performance on the CANTAB battery ($p > .05$). There were no significant relationships between MST or CANTAB tests and circadian parameters in the older adults ($p > .05$). See Supplementary Tables S1 and S2 for additional statistical results.

MoCA performance was not correlated with sleep or circadian parameters but was correlated with cognitive performance measures in the older adults

There were no relationships between the MoCA total score and TST or sleep efficiency, or circadian parameters ($p > .05$). The PVT was also not significantly correlated with the MoCA ($p > .05$). For the MST, the MoCA total score was significantly associated with L1 Accuracy ($\rho(23) = 0.45$, $p = .02$) (Figure 3c) and L1 False Memory Error Rate ($r(23) = -0.43$, $p = .04$) (Figure 3e). For CANTAB, the MoCA total score was significantly correlated with PAL First Attempt ($r(32) = 0.51$, $p = .002$), PAL Adjusted Errors ($r(32) = -0.42$, $p = .01$), and the SWM measure SWM Between Errors ($\rho(32) = -0.53$, $p = .001$). See Supplementary Table S3 for the remaining results.

Performance on cognitive test of pattern separation is predicted by total sleep time in the older adults

When controlling for age and gender, the multiple linear regressions showed a significant overall model for L1 Accuracy ($F_{3,21} = 10.65$, $p = .0002$) and L1 False Memory Error Rate ($F_{3,21} = 5.11$, $p = .008$) in the older adults. Age was a significant covariate for L1 Accuracy ($t_{1,21} = -4.52$, $p = .0002$) and for L1 False Memory Error Rate ($t_{1,21} = 2.75$, $p = .01$). TST predicted L1 Accuracy ($t_{1,21} = 3.34$, $p = .003$) and L1 False Memory Error Rate ($t_{1,21} = -3.03$, $p = .006$). A sensitivity analysis supported these findings. See Supplementary Tables S4 and S5 for additional statistical results.

Discussion

It is well-established that sleep is important for optimal cognition and that sleep disturbances are often associated with psychiatric and neurological conditions that affect cognition. Recently, sleep has garnered attention as a potential therapeutic target for AD.[1] Here, we aimed to identify the cognitive tests that are most sensitive to sleep quantity and quality, focusing on those tests shown to be sensitive to the early cognitive changes associated with

dementia. Clinical trials evaluating the effectiveness of sleep-promoting interventions in older adults at risk for or diagnosed with dementia, require cognitive tests that are sensitive to sleep to be used as clinical trial outcome measures.[5]

We hypothesized that performance on tests designed to assess pattern separation (i.e., MST and CANTAB DMS) would be most sensitive to sleep quantity and quality.[6] The hallmark symptom of AD is impaired episodic memory. Importantly, failure in episodic memory does not always reflect forgetting, but instead the specific memory impairment exhibited by patients with MCI or AD may reflect false memory, because episodic memory is particularly vulnerable to interference.[13,14] Pattern separation is a computational mechanism that plays an integral part in decreasing interference among similar memory representations.[18] In the MST task, a failure in indicating lures as "similar" and instead judging lure images as "old" (false memory) may suggest ineffective pattern separation during encoding. Correctly judging lures as "similar" would indicate that effective pattern separation had taken place during encoding.[43] In the DMS task, the participant has to differentiate between patterns that vary in similarity, thus, vary in the need for effective pattern separation.

Our results show that MST is sensitive to sleep quantity in older adults. Specifically, we found a significant correlation between longer sleep duration in the older participants and better discriminative performance on MST trials with the highest level of similarity between the lures and target images (i.e., L1). We also examined the probability of false memory on the MST lure trials with the highest similarity. We found that the older adults with the longest sleep duration were less likely to have a false memory (i.e., falsely recognize an L1 Lure as a repeated image). Additionally, when controlling for age and gender, sleep duration predicted performance on MST lure trials with the highest similarity in the older adults.

Of the 5 CANTAB tests that are part of the Prodromal AD and MCI battery, none of the CANTAB tests were correlated with sleep. Most of the CANTAB tests, however, were correlated with MoCA total score, specifically PAL and SWM. This is consistent with previous studies showing the high sensitivity of PAL at detecting the earliest cognitive changes associated with dementia.[44] It also importantly highlights that not all tasks validated for detecting the earliest cognitive changes associated with MCI and dementia are equally as sensitive to sleep-associated cognitive performance.

Our results also show significant relationships between performance on MoCA and MST in older adults. Specifically, our analyses showed that lower MoCA scores were associated with poorer performance on MST trials with the highest level of similarity between the lures and repeated images (i.e., L1). Our results complement but do not replicate previous work that showed that the MoCA score predicted LDI performance.[45] In reviewing the graphical display of our data, there does appear to be a non-significant association between the MoCA score and LDI, which might suggest that our study was unpowered to detect this relationship. Since L1 lures tax pattern separation the most, our analyses suggest that L1 lure discrimination and false memory errors may be more sensitive than overall LDI to dementia-related decline and sleep-related impairments. These findings support previous reports that MST is sensitive to AD-associated cognitive decline[40] and can be an effective outcome measure in clinical trials interested in measuring memory improvement in patients with dementia.[46] Importantly, our results highlight that while both PAL and MST are correlated with MoCA scores, only MST (and not PAL) was also correlated with and predicted by sleep quantity in the older adults.

Performance on the PVT was also associated with sleep quantity in the older adults. While the PVT is sensitive to sleep, it was not correlated with MoCA scores or other cognitive

measures indicative of dementia. The ideal clinical outcome measure for sleep targeting therapeutics for AD would be a cognitive measure sensitive to both sleep and AD-associated cognitive decline.

The current research had strengths. We used both wrist actigraphy and self-report measures to achieve an estimation of rest and activity. We also used cognitive tests that have been validated to assess cognitive domains known to decline in prodromal MCI and AD. The study is novel in that it examined how tests of pattern separation may be uniquely sensitive to sleep measured with wrist actigraphy in older adults.

The current research also had limitations. Our study did not include direct measures of sleep or measures that allowed for sleep staging (e.g., polysomnography or at-home EEG). Additionally, caffeine intake may have affected performance as we did not control for caffeine consumption. Caffeine is an adenosine-inhibitor that can prevent impairments in hippocampal long-term potentiation caused by sleep deprivation.[22] Thus, any effects of poor nighttime sleep may have been masked by effects of daytime caffeine consumption in our participants, particularly because MST performance has been shown to improve following caffeine intake.[47] Finally, the older adult sample size was small, thus findings must be interpreted carefully. The small sample size also did not allow us to examine ethnic differences in terms of sleep and cognition. The ethnic make-up of our older adult sample was predominantly white, thus, our findings may not be generalizable to other ethnic groups. Future research should aim to recruit a larger sample size to allow for analysis of the effect of different demographic variables.

Conclusion

To summarize, our research suggests that not all cognitive tests sensitive to impairments associated with MCI and dementia may be appropriate outcome measures for clinical trials

evaluating sleep-promoting treatments in older adults. In our study, the cognitive measure that was most sensitive to sleep quantity in older adults was the test designed to assess pattern separation performance (i.e., MST). Future studies are needed to assess whether cognitive tests designed to tax pattern separation are sensitive enough to detect cognitive improvements associated with sleep-targeting therapeutics.

Data availability

Data will be available upon request.

Conflict of Interest Statement

The authors listed in this manuscript confirm that they have no affiliations or involvement with any organization or entity that has a non-financial interest (e.g., personal or professional affiliations, relationships, beliefs, or knowledge) or financial interest (e.g., honoraria, stock ownership, expert testimony, or patent-licensing arrangements) that are related to the materials and content presented and discussed in this manuscript.

Disclosure Statement

a) Financial disclosure: There are no financial conflicts of interest to disclose.

b) Non-financial disclosure: The authors state that their submission has been posted as a preprint.

Ethics approval statement

The research study was reviewed and approved by the Research Ethics Board at Simon Fraser University (Protocol #30000539). All participants provided written informed consent to participate in the research.

Acknowledgements

This work was funded by SFU New Faculty Start-up grant (Project Number: 13-2720-00000-N000844, B.A.K.), Canada Research Chairs (Project Number: CRC-2020-00047, B.A.K.), and Canada Foundation for Innovation (CFI-41428, B.A.K.). We would like to thank the following research assistants who assisted with data collection and analyses: Julia Mugliston, Kashish Mehta, Japneet Kaur, Arman Virk, Olivia Braziller, Karthikha Sri Indran, Hannah Chute, Tina Shehata, Vanessa Salzano, Sara Tam, Liliane Tansley, Robert Gibson, Alex Nash, and Miranda Chang. We would also like to thank Craig Stark (University of California, Irvine) for his invaluable advice and assistance in using the Mnemonic Similarity Task, and Ian Berkovitz (SFU) for helpful statistical consultations.

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Tables

Table 1. Participant characteristics

	Younger adults	Older adults
Age		
Age range	18-30	51-84
Mean	20.12 ± 1.99	65.56 ± 9.57
Sex		
Female	50	18
Male	31	16
Education		
Years of education	1-2nd year university student	16.60 ± 3.56 years
>12 years of education	100%	87.7%
Ethnicity		
Indigenous	0	1
Hispanic	2	0
Middle Eastern	9	0
Black	2	0
Asian	43	3
White	19	29
Mixed ethnicity	6	1
Medical history		
Mental health disorder		
Anxiety	7	2
Depression	3	5
ADHD	1	0
PTSD	1	1
Comorbid	7	2
Not specified	1	0
Neurological condition		
Concussion	4	2
Brain surgery	0	1
Dysautonomia	1	0
Migraine	0	1
Sleep disorder		
Sleep apnea	0	4
Insomnia	1	1

Comorbid	1	2
AD family history		
Yes	-	4
No	-	22
Not sure	-	8
Consumption of psychoactive substances		
Caffeine		
≥ Once a day	18	10
≥ Once a week	15	-
Nicotine		
≥ Once a day	2	0
≥ Once a week	1	0
Marijuana		
≥ Once a day	2	1
≥ Once a week	4	0
≥ Once a month	4	0
≥ Once a year	0	1
Alcohol		
≥ Once a day	0	1
≥ Once a week	10	11
≥ Once a month	6	0
≥ Once a year	0	1
Not specified	7	2
MoCA total score		
Mean	-	25.74
Range	-	19-30
Time-zone crossing within the past month		
≥1 time-zones:	0	4
Not specified	4	1
Working nightshifts:		
Currently:	8	0
In the past:	11	16

Table 2. Summary of sleep and circadian rhythm parameters

Participants	Bedtime	Wake-up time	TST (h)	Sleep efficiency (%)	SOL (h)	WASO (h)	Amplitude	Acrophase (h)	IV	IS
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Older adults	23.08 ± 1.38	7.01 ± 1.22	7.18 ± 0.98	90.55 ± 4.21	0.06 ± 0.02	0.65 ± 0.34	1.67 ± 0.66	14.22 ± 1.85	1.14 ± 0.31	0.42 ± 0.14
Younger adults	01.54 ± 1.48	8.95 ± 1.36	6.63 ± 0.84	89.48 ± 4.97	0.06 ± 0.02	0.68 ± 0.39	1.66 ± 0.61	17.22 ± 1.86	1.05 ± 0.28	0.39 ± 0.10

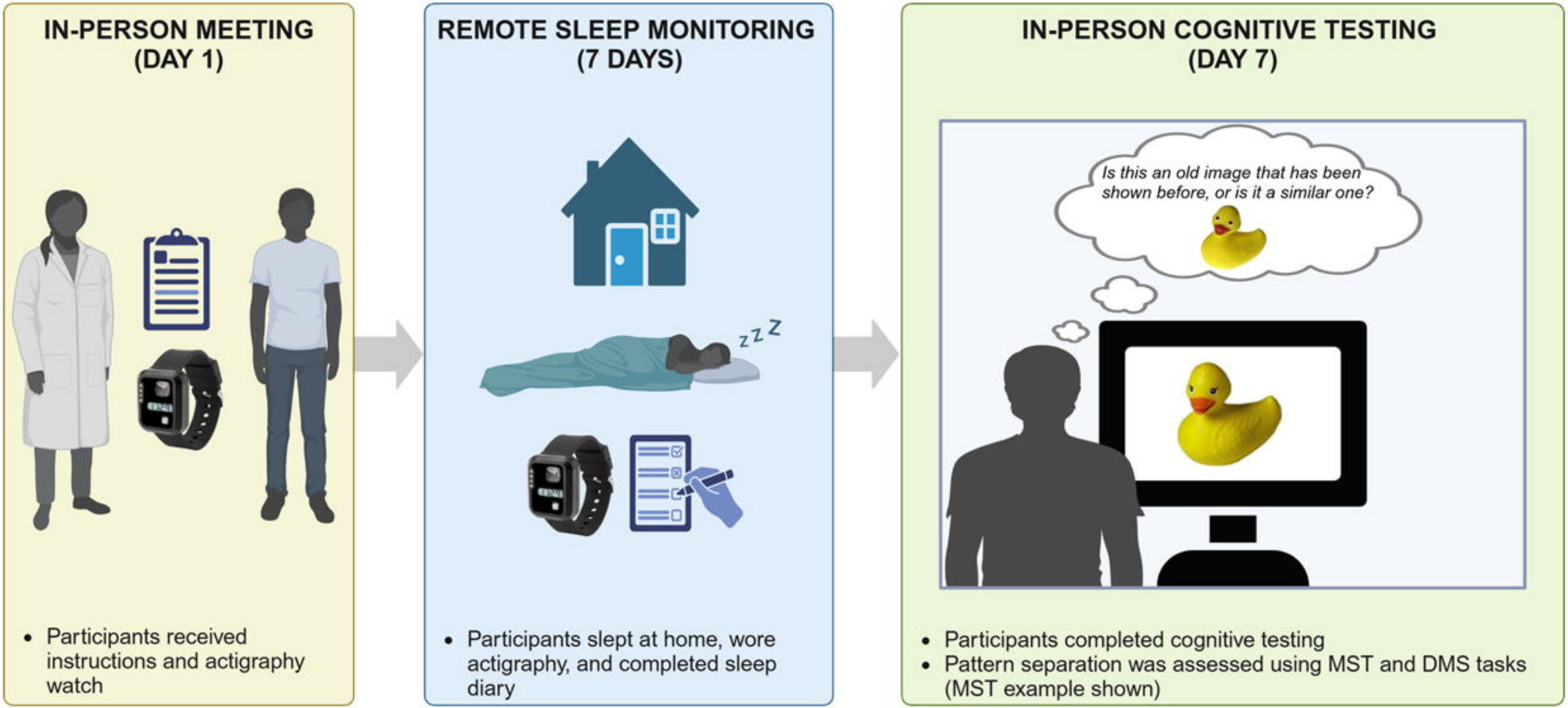
Abbreviations: TST, Total Sleep Time; SOL, Sleep Onset Latency; WASO, Wake After Sleep Onset; IV, Intradaily Variability; IS, Interdaily Stability. Bedtime, Wake-up time, TST, SOL, WASO, and acrophase are displayed in decimal time.

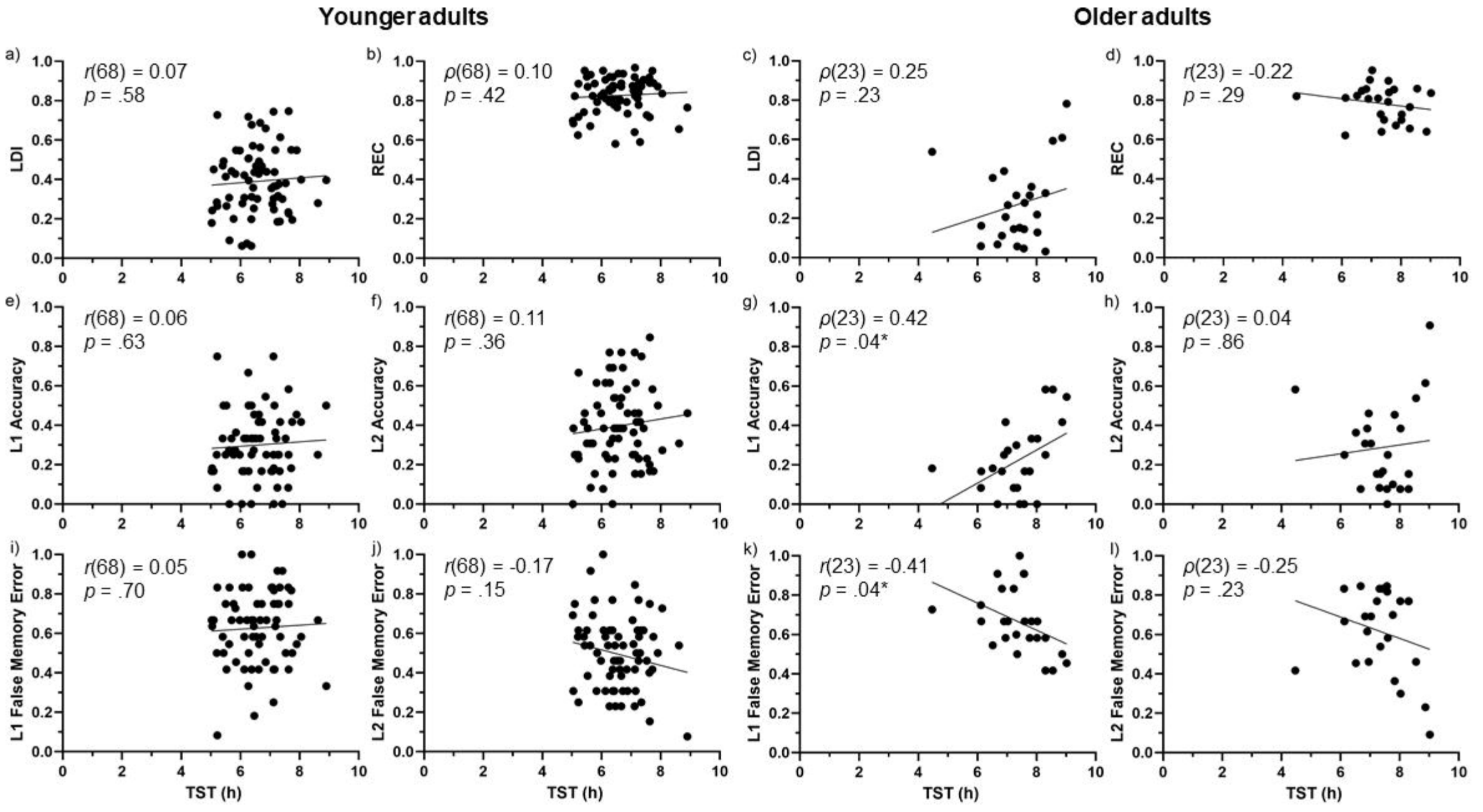
Figures

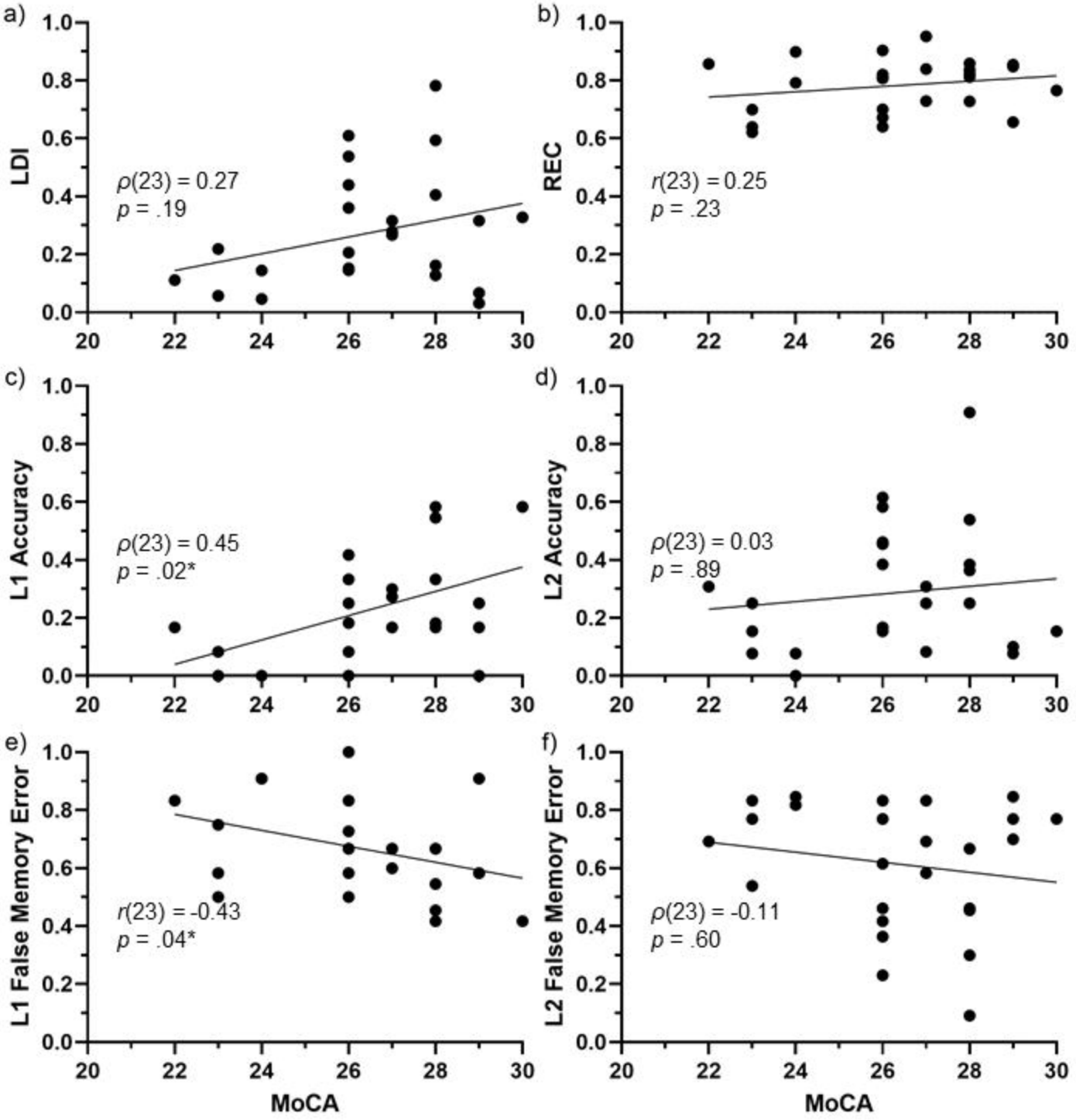
Figure 1. Illustration of the procedure, including two example images used in the MST.[25] Created with BioRender.com. Abbreviations: MST, Mnemonic Similarity Task; DMS, Delayed Matching to Sample.

Figure 2. Scatterplots showing the relationship between TST and MST performance: LDI (a, c), REC (b, d), L1 Accuracy (e, g), L2 Accuracy (f, h), L1 False Memory Error Rate (i, k), and L2 False Memory Error Rate (j, l). The left two columns (a, b, e, f, i, j) show data collected from the younger adults. The right two columns (c, d, g, h, k, l) show data collected from the older adults. Each black dot represents an individual participant. Pearson's (r) or Spearman's (ρ) correlation, * = $p < 0.05$. Abbreviations: TST, total sleep time; LDI, Lure Discrimination Index; REC, Recognition Memory; L1, Lure Bin 1; L2, Lure Bin 2.

Figure 3. Relationship between performance on MoCA and MST in older adults. Scatterplots showing the relationship between MoCA total score and a) LDI, b) REC, c) L1 Accuracy, d) L2 Accuracy, e) L1 False Memory Error Rate, and f) L2 False Memory Error Rate. Each black dot represents an individual participant. Pearson's (r) or Spearman's (ρ) correlation, * = $p < 0.05$. Abbreviations: MoCA, Montreal Cognitive Assessment; LDI, Lure Discrimination Index; REC, Recognition Memory; L1, Lure Bin 1; L2, Lure Bin 2.


IN-PERSON MEETING
(DAY 1)
• Participants received instructions and actigraphy watch
REMOTE SLEEP MONITORING
(7 DAYS)
zzz
• Participants slept at home, wore actigraphy, and completed sleep diary
IN-PERSON COGNITIVE TESTING
(DAY 7)
Is this an old image that has been shown before, or is it a similar one?
• Participants completed cognitive testing
• Pattern separation was assessed using MST and DMS tasks (MST example shown)


Younger adults
Older adults
a)
r(68) = 0.07
p = .58
LDI
b)
ρ(68) = 0.10
p = .42
REC
c)
ρ(23) = 0.25
p = .23
LDI
d)
r(23) = -0.22
p = .29
REC
e)
r(68) = 0.06
p = .63
L1 Accuracy
f)
r(68) = 0.11
p = .36
L2 Accuracy
g)
ρ(23) = 0.42
p = .04*
L1 Accuracy
h)
ρ(23) = 0.04
p = .86
L2 Accuracy
i)
r(68) = 0.05
p = .70
L1 False Memory Error
j)
r(68) = -0.17
p = .15
L2 False Memory Error
k)
r(23) = -0.41
p = .04*
L1 False Memory Error
l)
ρ(23) = -0.25
p = .23
L2 False Memory Error
TST (h)


a)
LDI
ρ(23) = 0.27
p = .19
b)
REC
r(23) = 0.25
p = .23
c)
L1 Accuracy
ρ(23) = 0.45
p = .02*
d)
L2 Accuracy
ρ(23) = 0.03
p = .89
e)
L1 False Memory Error
r(23) = -0.43
p = .04*
f)
L2 False Memory Error
ρ(23) = -0.11
p = .60
MoCA
MoCA