Acute Partial Sleep Deprivation Negatively Affects Object Pattern Separation in Healthy Adults

Kia Puustinen [1, (2)]*, Jens Soeterboek [2], Meyra Jackson [2], & Pim Heckman [2]

[1] REVAL Rehabilitation Research Center, Hasselt University, Belgium, [2] Department of Neuropsychology & Psychopharmacology, Maastricht University, The Netherlands

Introduction

To accurately encode episodic memories, the brain must discriminate between highly similar stimuli. Functional neuroimaging has localised this process of **pattern separation** in the dentate gyrus (DG) of the hippocampus (Yassa & Stark, 2011). Utilising distinct pathways for spatial and object information, the DG allows forming distinct neural representations of convergent sensory input (Reagh & Yassa, 2014). Pattern separation is known to be impaired in several pathologies and conditions affecting the hippocampus, such as post-traumatic stress disorder, Alzheimer's disease, and ageing (Lange et al., 2017; Reagh et al., 2014; Stark et al., 2013)

Sleep deprivation has emerged as an important predictor of deficits in the medial temporal lobe (Mander et al., 2016). One night of restricted sleep is enough to hinder the neuronal connectivity of DG in mice (Raven et al., 2019) and humans (Saletin et al., 2016).While mice are known to display impaired pattern separation after half a night of extended wakefulness (Heckman et al., 2020), the novel aim of this study was to translate this finding to humans. **It was hypothesised that the participants undergoing partial sleep deprivation for one night would obtain lower scores in spatial and object pattern separation tasks than the control group sleeping normally.**

Methods

Healthy adults (18-46 years, M = 22.79, SD = 4.42) of both genders (21 males, 37 females) were randomly assigned to a control group choosing their own bedtime, or sleep deprivation group. Those unlikely to fall asleep before midnight due to their chronotype, identified as scoring <42 in the Morningness-Eveningness Scale (Horne & Östberg, 1976) were excluded. The experimental design is detailed in Figure 1.

Pattern separation capacity was tested with the **spatial mnemonic discrimination task**, and the object-based **mnemonic similarity task** (Figure 2).

2 x 5 ANOVAs were used to compare the groups and within-subject differences at each level of mnemonic interference. Bonferroni corrected *t*-tests were used for post-hoc analyses.

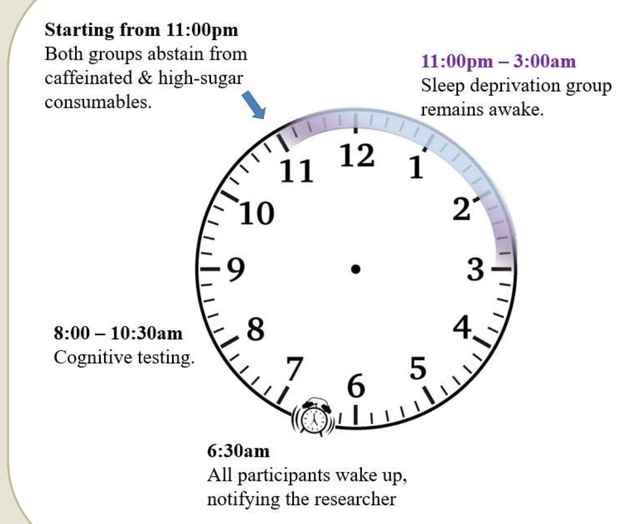

Figure 1. *The Timing of the Experimental Protocol.*

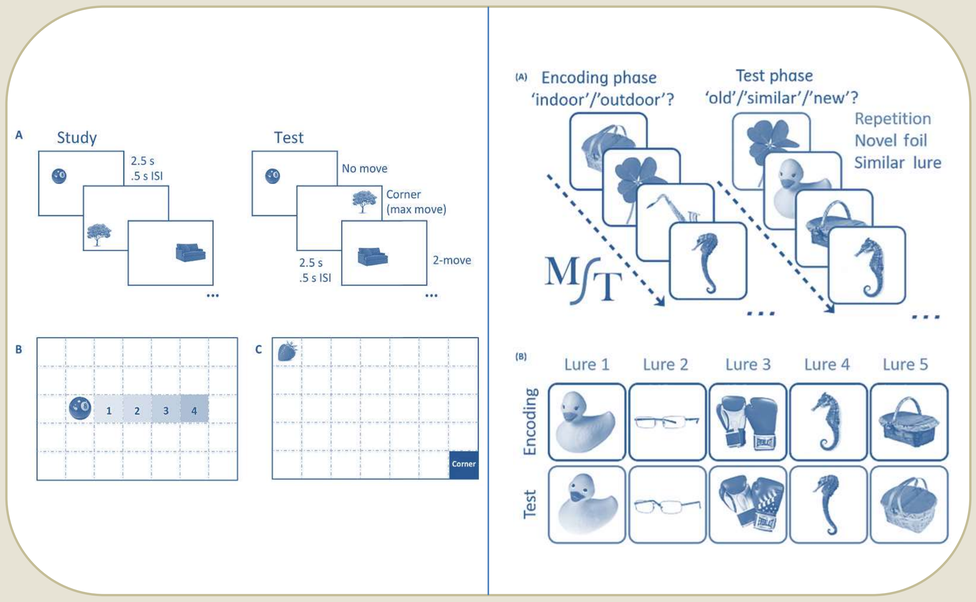

Figure 2. *Five Distinct Levels of Mnemonic Interference in Each Task*
Note. Left to right: MD-S (Reagh et al., 2014), MST (Stark et al., 2013).

Results

Spatial Discrimination (Figure 3)

- Control group was better in identifying identical locations, $t(52) = 1.95$, $p < .05$
- Assumption of sphericity was failed ($W = .59$, $p < .01$), and thus ANOVA results are reported with the Huynh-Feldt correction
- **Main effect of Lure,** $F(3.42,177.74) = 125.14$, $p < .001$, $\eta_p^2 = .71$
- No main effect of Group, $F(1,52) = .65$, $p = .42$, or interaction effect Lure*Group, $F(3.42, 177.74) = 1.61$, $p = .18$
- **Most post-hoc pairwise comparisons were significant**, $p < .001$, except for lures 3 & 4 (did not elicit significantly different scores in either group), and 4 & 5 (no difference within the control group).

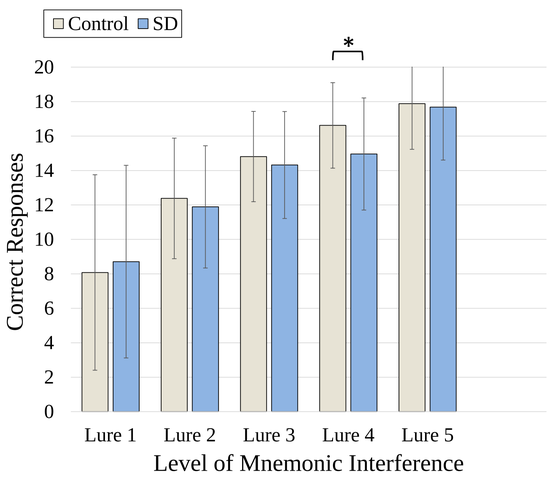

Figure 3. *Spatial Pattern Separation Performance in Each Group.*

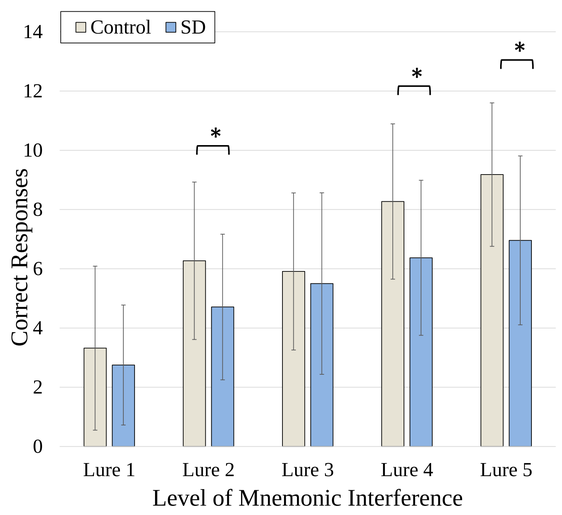

Figure 4. *Object Pattern Separation Performance in Each Group.*

Object Discrimination (Figure 4)

- **Main effect of Lure**, $F(4, 176) = 54.52$, $p < .001$, $\eta_p^2 = .55$, **and Group**, $F(1, 44) = 4.69$, $p < .05$, $\eta_p^2 = .096$, but no interaction effect Lure*Group, $F(4, 176) = 2.34$, $p = .06$.
- **Pairwise post-hoc comparisons were mostly significant**, $p < .001$, with the exception of lures 4 & 5 ($p < .05$), 2 & 3 (did not elicit significantly different scores in either group), and 3 & 4 (no difference within the experimental group).
- **The control group was found to perform better than the experimental group on lures 2, 4 and 5** ($p < .05$).

Conclusions

The hypothesis was partly supported, as sleep deprived individuals scored significantly lower in the object discrimination task. Similar conclusions cannot be made of spatial pattern separation, since the trend for inferior performance after sleep deprivation was not significant. Distinct levels of mnemonic interference were found to account for 55–71% of variation in scores. This validates pattern separation as a continuum (Yassa & Stark, 2011), where exceedingly similar stimuli are more likely to be combined into the same neural representation (pattern completion), whereas sufficiently different stimuli can be separated (pattern separation).

Performance deficits in the partially sleep deprived group allude to sleep loss disrupting the functioning of the medial temporal lobe. However, since the deficits were mostly visible in the object-based task, it is possible that the lateral entorhinal pathway used for object-based information is specifically vulnerable to sleep loss. Previous research on older adults provides evidence for such selective vulnerability, as object pattern separation (Reagh et al., 2016) and its neural correlates (Reagh et al., 2018) have been found more vulnerable to age-related decline than spatial pattern separation.

Future research should examine the specific neurological consequences of sleep deprivation using neuroimaging. Furthermore, it will be important to employ longer sleep deprivation paradigms with intermediate measurements to track the how the deficits may develop over time, along with within-subject comparisons to diminish the effect of individual differences.

Partial sleep deprivation is a concerningly prevalent public health problem in today's society, and thus uncovering its neurocognitive consequences is crucial. Our study reproduces recent rodent findings into observations about human behaviour, suggesting that even one night of insufficient sleep may cause deficiencies in creating distinct neural representations of similar stimuli, endangering accurate encoding of episodic memories.

Heckman, P. R., Kuhn, F. R., Raven, F., Bolsius, Y. G., Prickaerts, J., Meerlo, P., & Havekes, R. (2020). Phosphodiesterase inhibitors roflumilast and vardenafil prevent sleep deprivation-induced deficits in spatial pattern separation. *Synapse*, *74*(6), e22150.
Horne, J. A., & Östberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *Int J Chronobiol.*
Lange, I., Goossens, L., Michielse, S., Bakker, J., Lissek, S., Papalini, S., ... & Schruers, K. (2017). Behavioral pattern separation and its link to the neural mechanisms of fear generalization. *Soc Cogn Affect Neurosci*, 12(11), 1720-1729.
Mander, B. A., Winer, J. R., Jagust, W. J., & Walker, M. P. (2016). Sleep: a novel mechanistic pathway, biomarker, and treatment target in the pathology of Alzheimer's disease? *Trends Neurosci*, 39(8), 552-566.
Raven, F., Meerlo, P., Van der Zee, E. A., Abel, T., & Havekes, R. (2019). A brief period of sleep deprivation causes spine loss in the dentate gyrus of mice. Neurobiol Learn Mem, 160, 83-90.
Reagh, Z. M., Roberts, J. M., Ly, M., DiProspero, N., Murray, E., & Yassa, M. A. (2014). Spatial discrimination deficits as a function of mnemonic interference in aged adults with and without memory impairment. *Hippocampus*, 24(3), 303-314.
Reagh, Z. M., & Yassa, M. A. (2014). Object and spatial mnemonic interference differentially engage lateral and medial entorhinal cortex in humans. *Proc Natl Acad Sci*, 111(40), E4264-E4273.
Reagh, Z. M., Ho, H. D., Leal, S. L., Noche, J. A., Chun, A., Murray, E. A., & Yassa, M. A. (2016). Greater loss of object than spatial mnemonic discrimination in aged adults. *Hippocampus*, 26(4), 417-422.
Reagh, Z. M., Noche, J. A., Tustison, N. J., Delisle, D., Murray, E. A., & Yassa, M. A. (2018). Functional imbalance of anterolateral entorhinal cortex and hippocampal dentate/CA3 underlies age-related object pattern separation deficits. *Neuron*, 97(5), 1187-1198.
Saletin, J. M., Goldstein-Piekarski, A. N., Greer, S. M., Stark, S., Stark, C. E., & Walker, M. P. (2016). Human hippocampal structure: a novel biomarker predicting mnemonic vulnerability to, and recovery from, sleep deprivation. *J Neurosci*, 36(8), 2355-2363.
Stark, S. M., Yassa, M. A., Lacy, J. W., & Stark, C. E. (2013). A task to assess behavioral pattern separation (BPS) in humans: Data from healthy aging and mild cognitive impairment. *Neuropsychologia*, 51(12), 2442-2449.
Yassa, M. A., & Stark, C. E. (2011). Pattern separation in the hippocampus. *Trends Neurosci*, 34(10), 515-525.