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Degradation of cortical representations during encoding following sleep deprivation

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A B S T R A C T

A night of total sleep deprivation (TSD) reduces task-related activation of fronto-parietal and higher visual cortical areas. As this reduction in activation corresponds to impaired attention and perceptual processing, it might also be associated with poorer memory encoding. Related animal work has established that cortical columns stochastically enter a 'down' state in sleep deprivation, leading to predictions that neural representations are less stable and distinctive following TSD. To test these predictions participants incidentally encoded scene images while undergoing fMRI, either during rested wakefulness (RW) or after TSD. In scene-selective PPA, TSD reduced stability of neural representations across repetition. This was accompanied by poorer subsequent memory. Greater representational stability benefitted subsequent memory in RW but not TSD. Even for items subsequently recognized, representational distinctiveness was lower in TSD, suggesting that quality of encoding is degraded. Reduced representational stability and distinctiveness are two novel mechanisms by which TSD can contribute to poorer memory formation.

Introduction

Sleep plays an important role in the formation and consolidation of declarative memories (Gais et al., 2006, 2007; Rasch and Born, 2013; Stickgold, 2005) and its deprivation results in poorer memory of previously learned material (Chernik, 1972; Gais and Born, 2004; Gais et al., 2006; Plihal and Born, 1997). Reduced hippocampal activation possibly from saturation of storage capacity, is a possible mechanism for poorer declarative memory formation following sleep deprivation (Van Der Werf et al., 2009; Yoo et al., 2007). To date, research on sleep and memory (Diekelmann and Born, 2010; Paller and Voss, 2004) has primarily focused on how sleep facilitates the gradual transfer of memories from the hippocampus to long-term storage in neocortical areas. However, in addition to its role as a short-term memory store, the hippocampus also indexes and binds cortical representations of memories (Nadel and Moscovitch, 1997, 1998). Relative to the multiple studies on consolidation, far less attention has been directed to the effect of sleep on memory encoding, and specifically, how neocortical inputs to the hippocampus and their disruption following sleep deprivation might be contributory.

Given these points, a clearer understanding of neocortical contributions to memory encoding in sleep-deprived persons might benefit from exploring the ramifications of reduced task-related cortical activation. Reduced activation occurs in fronto-parietal areas that mediate top-down control of attention, and in higher visual cortex responsive to these control signals (Chee and Chuah, 2007; Chee et al., 2011; Tomasi et al., 2009). Insofar as cortical activation in higher visual areas corresponds to the deployment of selective attention and its resultant enhancement of perceptual processing (Corbetta and Shulman, 2002), higher visual cortical activation might also result in more robust memory formation. Conversely, reduced activation in higher visual areas might correspond to a less durable memory of a stimulus.

Beyond activation magnitude, another potential influence on the durability of memory is the stability with which a given ensemble of neurons is consistently recruited during task performance (Ward et al., 2013; Xue et al., 2010). In the sleep-deprived brain, lower task-related activation has been taken to indicate fewer neurons being active at any given time (Chee and Chuah, 2007; Chee et al., 2011). Critically, activated neurons in the sleep-deprived brain appear to change from moment to moment, there being random dropout of neural activity involving different cortical columns at different times (Vyazovskiy et al., 2011). This 'local sleep', where different cortical columns randomly enter a 'down state' is accompanied by an increase in behavioral lapses in sleep-deprived animals (Vyazovskiy et al., 2011), and has also been recently reported in humans (Bernardi et al., 2015;

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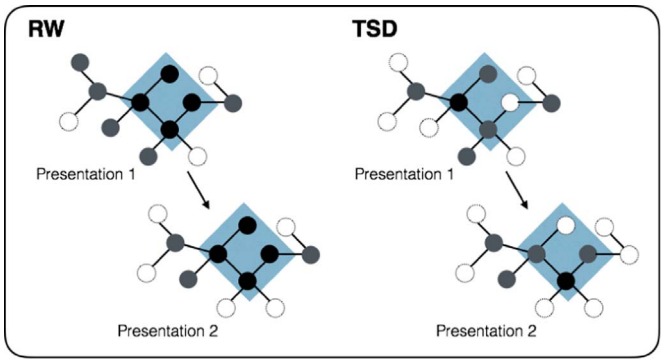

Fig. 1. Schematic showing how local sleep can affect neural activation patterns. In RW, a higher number of functional nodes gives rise to more robust perceptual representations. In TSD, a reduced number of functional units/nodes could degrade the quality of a sensory representation. The stochasticity of local sleep can result in reduced representational stability across repeated presentations of the same stimulus. Activated nodes are depicted by filled circles, with a darker fill reflecting stronger activation. The highlighted area indicates units/nodes that are crucial for primary task performance.

Hung et al., 2013). Sleep deprivation might therefore reduce the stability of neural activation patterns elicited by repeated presentation of the same stimulus (Fig. 1).

While behavioral measures have shown a quantitative reduction in items well encoded following sleep deprivation (Yoo et al., 2007), it remains unclear how memory for learned material is *qualitatively* inferior to items encoded in the well-rested state. Fine-grained neuroimaging measures of neocortical representations might shed light on how sleep deprivation affects the quality of memory encoding. To this end, we utilized two measures associated with multivoxel pattern analysis of fMRI data to measure the 'quality' of memories encoded in sleep-deprived persons.

The first measure, pattern similarity (PS), examines the correlation in neural responses across repetition of the same stimulus (Xue et al., 2010, 2013) and can be considered as an index of stability in neural activation patterns. PS has been shown to be predictive of subsequent encoding, and is thought to benefit memory through the provision of consistent input to the hippocampus (Xue et al., 2013). The second measure, 'exemplar distinctiveness' evaluates item-specific (as distinct from category-specific) differences in activation when different pictures within the same category are shown. This was evaluated by comparing each item's self similarity (PS) to its similarity to other exemplars from the same category. We hypothesized that sleep deprived participants would show both lower pattern similarity and exemplar distinctiveness within scene selective cortical regions during encoding, contributing to poorer subsequent recognition performance compared to participants who slept normally.

To test these predictions, we studied healthy young adult participants following a night of normal sleep or after a night of total sleep deprivation. While undergoing fMRI, they made categorical judgements on scene pictures that were repeated after a few trials. Recognition memory was evaluated via a surprise recognition test administered approximately 45 min after the last scan. We examined three scene selective ROIs (PPA: Parahippocampal place area (Epstein and Kanwisher, 1998), TOS: Transverse occipital sulcus (Hasson et al., 2003) and RSC: Retrosplenial cortex (Maguire, 2001), and their associated neural activation patterns for pattern similarity and item distinctiveness across the two groups.

Materials and methods

Participants

Forty-eight healthy right-handed adult participants were recruited after giving informed consent concerning a study protocol approved by the Institutional Review Board of the National University of Singapore. These participants were then randomly assigned to Rested Wakefulness (RW) or Total Sleep Deprivation (TSD) groups but this information was given to them only after they entered the laboratory for their test session. Eligible participants had to be without any history of psychiatric, neurological and/or sleep disorders and did not exhibit strong morningness or eveningness preference. They were required to maintain a regular sleep-wake schedule (6.5–9 h of sleep a night, sleeping before 0030 h and waking before 0900 h) for the entire duration of the study. Adherence to the sleep schedule and total sleep time was measured by wrist actigraphy (Actiwatch, Philips Respironics, USA). All participants adhered to the sleep schedule. There was no significant difference in total sleep time (TST) ($t(43)=-0.38$, $p=0.71$, $d=0.11$; RW: M=6.93 h, SD=0.61 h; TSD: M=6.99 h, SD=0.56 h) or sleep efficiency ($t(43)=-0.58$, $p=0.57$, $d=-0.08$; RW: M=86.3%, SD=6.5%; TSD: M=87.5%, SD=6.8%) between RW and TSD groups immediately prior to imaging. Participants abstained from caffeine, medication and alcohol 24 h prior to their experimental session.

Procedure

Participants visited the laboratory on three separate occasions, with each session separated from another by at least one week. The first session was a briefing session, where participants were informed about the study procedures and requirements. They then underwent a functional localizer scan and wore a wrist actigraph for the entire duration of the study.

Participants assigned to the RW group entered the lab at 2000 h and had a 9 h sleep opportunity (2200–0700 h) before their experimental session (Total Sleep time: M=7.6 h, SD=0.65 h; Sleep efficiency: M=85.7%, SD=7.8%). Participants in the TSD group entered the lab at 1900 h and were kept awake under constant supervision by research personnel until the end of the session.

Incidental encoding task

Materials

320 colored scene images were selected for this experiment from the LabelMe image database (Russell et al., 2007), with 160 Indoor scenes (Living rooms and Restaurants) and 160 outdoor scenes (Forests and City streets). The images were divided into 2 sets of 160 images (40 from each scene category), with half designated as targets, and the other half as foils. Image sets were counterbalanced across participants.

Experimental task

The fMRI experiment, utilized a slow event related design, with each trial lasting 12 s. The long interval between events was intended to reduce collinearity in model estimation, allowing for the examination of activation patterns of individual events (De Martino et al., 2008).

Each trial started with the presentation of a scene image for 3 s. Participants were required to make an indoor/outdoor judgment by pressing one of two buttons with their index or middle finger (counterbalanced across participants). This was followed by a sensorimotor baseline task (Stark and Squire, 2001), where arrows were presented for 200 ms each (ISI: 1300 ms), and participants indicated the direction of the arrow via a button press with the index (left arrow) or middle (right arrow) finger of their right hand (Accuracy–RW: M=98.5% SD=1.3%; TSD: M=89.8% SD=4.1%). The arrow judgment task sought to limit further encoding of the scene images (Ward et al., 2013) and served as the baseline for fMRI analysis (Fig. 2A).

Participants underwent 10 scanning runs each lasting 398 s, during which they were presented with 160 scene images (16 in each run), each presented twice with 3–8 trials (M=6.5) between repeated presentations. No images were repeated across runs. Each run lasted 398 s.

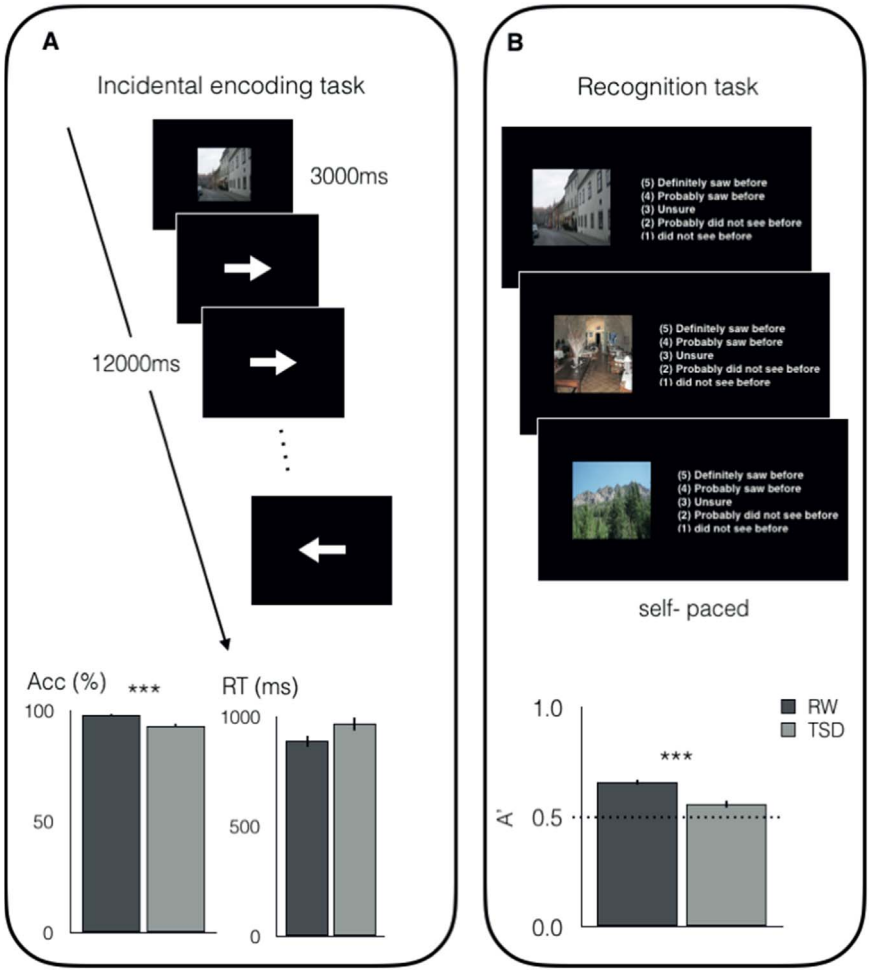

Fig. 2. Task schematics and behavioral results. In the encoding task (A, upper panel) participants indicated whether they saw an indoor or outdoor scene. They then indicated the direction of sequentially presented arrows (200 ms each, 1300 ms ISI). Accuracy of indoor/outdoor judgments during the encoding task was significantly higher in the RW group; RT was similar across groups (A, lower panel). During recognition (B, upper panel), participants indicated on a 5-point scale how confident they were that the image presented was one they had seen earlier during scanning. Recognition was measured using A' (B, lower panel) and was significantly above chance for both the RW and TSD groups. As expected, the RW group performed significantly better than the TSD group. Error bars reflect +/− 1 SEM. *** $p < 0.001$.

Post-scan behavioral task

A surprise recognition test was conducted approximately 45 min after the final scan (An additional recognition test was conducted 1 week after the encoding session, but further analysis was not performed as recognition in the TSD group was at chance level). During the recognition task, participants were shown a total of 160 scene images (80 old and 80 category matched novel foils). They were required to rate the presented images on a scale of 1–5 (1: Did not see before, 3: Unsure, 5: Definitely saw before), indicating how confident they were that a given scene was shown during scanning (Fig. 2B).

To ensure that forgetting was not simply a result of attentional lapses during encoding, subsequent analyses included only images that were correctly responded to on *both* encoding presentations. During recognition, items with ratings of 4 and 5 were classified as hits, while items rated 1 or 2 were classified as misses. Items that were rated as 3 ('Unsure') were excluded from subsequent analyses. Recognition performance was measured using a sensitivity index A', where a value of 0.5 indicates chance performance in the separation of Old and Novel items (Stanislaw and Todorov, 1999).

Functional localizer task

A separate functional localizer scan was acquired to identify participant-specific PPA, RSC and TOS. The functional localizer task utilized a block design where alternating blocks of faces or scenes were presented with an interval of 16 s. Each block lasted for 16 s, and 8 images were presented for 400 ms each with an ISI of 1600 ms. Participants were required to indicate if the Faces were male or female, and if the Scenes were indoor or outdoor. Scene images used were selected from categories not used in the memory tasks to minimize interference effects.

Image acquisition and preprocessing

MR images were acquired on a 3 -Tesla MAGNETOM Prisma systems (Siemens, Erlangen, German). Ten runs comprising 199 functional-MRI volumes each (first 4 volumes were discarded for T1-stabilization), were acquired for each participant using a gradient echo-planar imaging (EPI) sequence with 36 axial slices (slice thickness 3mm), using the following parameters: TR, 2000 ms; TE, 30 ms; flip angle 90°; FOV 192*192 mm; matrix 64*64; voxel size, 3.0 mm isotropic. Duration 398 s/run.

The same EPI sequence was used for the functional localizer scan, with the sole difference being the number of volumes collected (257 volumes). High-resolution anatomical reference images were acquired using an MPRAGE sequence (TR 2300 ms; TI 900 ms; flip angle 9°; BW 240 Hz/pixel; voxel size 1.0 mm isotropic).

Images were realigned to the first image of the functional run using

rigid body transformation. Trilinear and sinc interpolation implemented in SPM2 (Wellcome Department of Cognitive Neurology, London, UK) were then used for slice-time correction. Functional data was co-registered to cortical surface of individual T1 scans (Fischl et al., 1999) using FreeSurfer (http://surfer.nmr.mgh.harvard.edu), and the co-registered images were transformed into MNI152 space, and were smoothed with a 5mm FWHM smoothing kernel. Details of this processing pipeline can be obtained from Yeo et al. (2011).

fMRI analysis

Data from 3 participants were excluded due to excessive movement during the fMRI session (> 1.5mm displacement in multiple runs), resulting in a final sample consisting of 45 participants (N=24 for RW (12 Female); N=21 for TSD (11 Female)) between the ages of 19 and 30 (RW: M=23.8, SD=2.9; TSD: M=22.2, SD=2.2). Motion parameters of the final sample did not differ between the RW and TSD group ($t(43) = 0.53$, $p = .60$).

Analyses were confined to scene-selective PPA, RSC and TOS defined based on the independent functional localizer. All ROIs were identified individually for each subject with a Scene > Face contrast. A threshold of $p < 0.05$ FWE was used for the PPA and TOS, and *uncorrected* $p < 0.001$ for the RSC (Fig. 3a). Different thresholds were used to ensure reasonably sized ROIs and similar procedures have been described in prior work examining scene selective regions (Epstein and Higgins, 2007; Epstein et al., 2007). While the RSC is selective for scene processing, it tends to be more strongly activated when navigation is required (Vann et al., 2009). As participants in our study were only required to make indoor/outdoor judgments, RSC activation was relatively weak and a more lenient threshold was therefore used. Boundaries for each ROI were defined based on the scene selective ROIs derived in Julian et al. (2012). As three subjects (all three participants from RW group) did not show reliable bilateral activations within RSC clusters, they were excluded from analyses involving the RSC.

We specified the GLM within SPM8 (Wellcome Department of Cognitive Neurology, London, UK). All trials were modeled with a separate regressor, resulting in a design matrix with 320 regressors of interest (160 images * 2 presentations). All regressors were created by convolving relevant events with a canonical HRF. Additionally, we included 8 covariates of no interest (error and missed trials from the baseline task, and 6 motion parameters), together with dummy variables, which were included to account for differences across runs.

For each participant, a vector of *t*-values was created for each ROI, based on the pattern of BOLD activation related to each event.

A significance level of $p < 0.05$ was applied for all statistical testing, and when comparisons were performed across all 3 ROIs, a corrected threshold of $p < 0.017$ was used to account for multiple comparisons.

To replicate findings from prior work (Yoo et al., 2007), we performed a whole-brain level analysis comparing activation in RW and TSD across i) all encoding trials, and ii) trials with subsequently remembered images. For this analysis, the statistical threshold used was similar to that adopted in the original study (uncorrected $p < 0.001$, $k=15$).

Category level Information representation

Cross-correlation was used to determine if the selected ROIs contained information discriminating different scene *categories* (Haxby et al., 2001). A ROI containing information discriminating scene categories was one that showed higher *within- than between-* category correlations.

Pairwise Pearson's correlations were computed for the activation patterns elicited on every trial. Within-category correlation was determined by averaging the correlation values for all pairs belonging to the *same* category (i.e. *corr*(Indoor, Indoor) & *corr*(Outdoor,

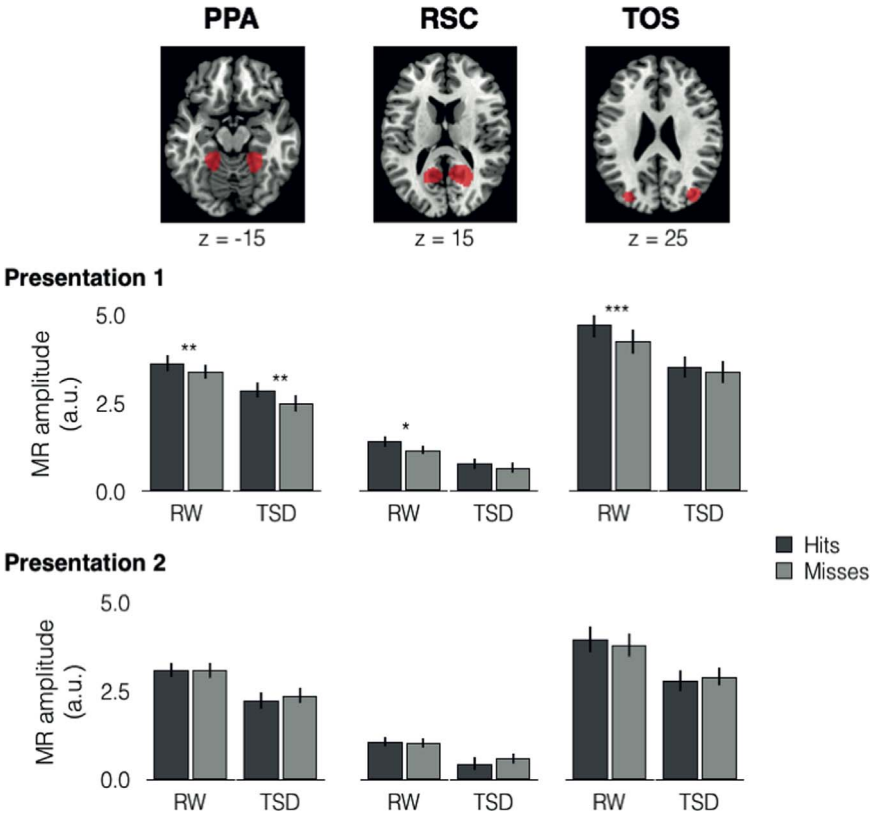

Fig. 3. Activation magnitude in the three ROIs for the first and second presentations of subsequently remembered and forgotten items. On the first presentation of pictures, the RW group showed significantly greater activation for subsequently remembered items in the PPA and TOS. In the TSD group, this difference (Dm effect) was only evident in the PPA. Error bars depict +/−1 SEM. ** $p < 0.01$; *** $p < 0.001$.

Outdoor)). Between-category correlation was derived by averaging the correlation values for all pairs belonging to *different* categories (i.e. *corr*(Indoor, Outdoor)).

A one-sample *t*-test was performed on the difference in within- and between- category correlation (i.e. $corr_{Within} - corr_{Between}$); values significantly greater than 0 indicate that the ROI contained information allowing distinction of the 2 categories.

To reduce the likelihood that a significant difference was driven by task specific demands (different button presses for indoor and outdoor), a similar comparison was performed for the subcategories (Indoor: Living Room & Restaurant; Outdoor: City & Forest).

Subsequent memory (Dm) effects in fMRI signal amplitude

BOLD signal amplitude predicts subsequent memory (Brewer, 1998; Wagner, 1998). Corresponding to the expectation that higher signal amplitude within the ROI speaks to greater processing of the presented stimulus, we expected greater BOLD signal amplitude for subsequently remembered items than forgotten items.

Signal amplitude for each trial was computed by averaging the beta estimates across all voxels within an ROI. Each trial was then separated based on subsequent memory, and the difference in signal amplitude between subsequently remembered and forgotten items was examined with a 2x2×2 mixed-ANOVA. State was the between-subject factor; Presentation and Subsequent memory were within-subject factors.

Stability in neural activation: within-item pattern similarity

Pattern similarity (PS) is a measure of distance in state space, with greater pattern similarity reflecting shorter distance between states (Davis and Poldrack, 2013; Xue et al., 2010). Within-item pattern similarity was calculated as the pairwise Pearson's correlation of the vectors for each item across presentations as follows:

$$Within - item \;\; PS(i) = corr(A_{i1}, A_{i2}), \tag{1}$$

where A_{i1} corresponds to activation pattern elicited by the initial presentation of the i^{th} item and A_{i2} corresponds to activation pattern elicited by the second presentation of that item. This was separately averaged for subsequently remembered (hits) and forgotten items (misses) and across groups.

Item-Specific distinctiveness within the PPA

To examine the distinctiveness of activation patterns for remembered items, we contrasted within-item pattern similarity to between-item (category) similarity.

Item-specific distinctiveness was computed by subtracting the between-item similarity from the within-item PS. If activation patterns elicited across repetition of a stimulus were more similar to each other than activation patterns elicited by other items of the same category, this would suggest reinstatement of item-specific activation (Xue et al., 2010). While distinctiveness is related to within-item PS, the two measures are at least partially dissociable. For example, if attention is consistently directed to processing of gist information, high within-item PS and high between-item PS will co-exist, resulting in low distinctiveness. Between-item PS can be represented as follows:

$$Between - item\, PS = \sum_{j=1}^{K} corr(A_{i1}, \; A_j) \;\; /K, \tag{2}$$

where A_j corresponds to the initial activation pattern for each item *j* in the set *K*, comprising of items in the same category as item *i*. Item-specific distinctiveness was thus defined as:

$$Distinctiveness = (Within - item \;\; PS) - (Between - item\, PS) \tag{3}$$

Lower fidelity of encoding would give rise to less item-specific reinstatement of activation patterns, resulting in lower item-specific distinctiveness (i.e. lesser self-similarity and greater category similarity). Statistical analyses were performed on Fisher's z-transformed correlation values.

Results

Scene encoding

Performance of indoor/outdoor judgments during incidental encoding was evaluated using accuracy and RT. The RW group showed better accuracy than the TSD group ($t(43)=5.70$, $p < 0.001$, $d=1.70$; RW: M=98.2%, SD=1.3; TSD: M=93.3%, SD=4.1), and also showed marginally faster response time ($t(43)=-2.00$, $p=0.051$, $d=-0.6$; RW: M=889 ms, SD=127 ms; TSD: M=967 ms, SD=134 ms).

Recognition memory

Recognition of old items (A') was significantly above chance in both RW ($t(23)=12.49$, $p < 0.001$, $d=5.21$) and TSD groups ($t(20)=3.77$, $p=0.001$, $d=1.69$). Only items that were correctly responded to during incidental encoding were eligible for the subsequent evaluation of recognition performance. This was done to reduce the possibility that encoding of test items were affected by momentary lapses in attention. Despite this adjustment, picture recognition was still significantly poorer following TSD ($t(43)=4.85$, $p < 0.001$, $d=1.45$; Fig. 2B). There was no significant difference in RT across groups and trial types during recognition (Supp Table 1).

Reduced task related activation in hippocampus following sleep deprivation

Before examining neural representations within neocortical ROIs of interest, we first determined if we could replicate the prior finding of reduced hippocampal activation following TSD (Yoo et al., 2007). The TSD group showed lower task-related activation of the right hippocampus (Peak coord: 20, −28, −4; t=4.90; Supp Fig. 1) across all encoding trials. In addition to the hippocampus, fronto-parietal and higher visual areas were also affected by sleep deprivation, exhibiting lower task-related activation (Supp Table 2). This result also held when only remembered trials were analyzed.

Information representation in PPA, RSC & TOS

To determine if the ROIs contained information discriminating different scene categories, we utilized cross-correlation to show that a ROI containing information discriminating scene categories exhibited higher *within-* than *between-* category correlations (Haxby et al., 2001). Activation patterns within the three ROIs carried sufficient information to facilitate the discrimination of different scene categories. This was evidenced by significantly higher within-category compared to between-category correlations in all three ROIs in both RW (PPA: $t(23)=5.98$, $p < 0.001$, $d=2.45$; RSC: $t(20)=3.76$, $p=0.012$, $d=1.68$; TOS: $t(23)=4.73$, $p < 0.001$, $d=1.97$) and in TSD (PPA: $t(20)=5.43$, $p < 0.001$, $d=2.43$; RSC: $t(20)=2.92$, $p=0.008$, $d=1.31$; TOS: $t(20)=3.18$, $p=0.005$, $d=1.42$; Supp Fig. 2). This finding held up in the PPA and TOS for within and between sub-category correlations involving comparisons between living room and restaurant pictures, as well as between city and forest pictures (Supp Fig. 2). The latter finding is important because it indicates that the category information within the ROIs was unlikely to be a result of task differences related to the identification indoor and outdoor scenes (as opposed to stimulus driven differences).

Signal amplitude in the PPA was greater for subsequently Remembered than Forgotten items

We compared signal amplitudes for subsequently remembered and forgotten items and found a significant subsequent memory or Dm effect in favor of remembered items in the PPA ($F(1,43)=7.70$, $p=0.008$, $\eta_p^2=0.152$). This Dm effect was present only upon the initial presentation of images and not following their subsequent presentation as evidenced by a significant interaction of presentation and subsequent memory ($F(1,43)=9.74$, $p=0.003$, $\eta_p^2=0.185$).

In the PPA, the Dm effect was present in both RW (Pre1: $t(23)=3.84$, $p=0.001$, $d=0.96$; Pre2: $t(23)=0.11$, $p=0.917$, $d=0.02$) and TSD groups (Pre1: $t(20)=2.63$, $p=0.016$, $d=0.58$; Pre2: $t(20)=-1.26$, $p=0.221$, $d=-0.28$) (Fig. 3). In TOS, the Dm effect was significant in RW ($t(23)=4.45$, $p<0.001$, $d=0.94$) but not TSD ($t(20)=0.99$, $p=.336$, $d=0.22$). In the RSC, Dm effect trended towards significance in RW ($t(20)=2.40$, $p=0.026$, $d=0.53$) but was absent in TSD ($t(20)=1.03$, $p=0.314$, $d=0.23$). Higher PPA signal, but not TOS or RSC signal for remembered pictures across states, is consistent with its role in encoding environmental scenes (Epstein et al., 1999).

Pattern similarity and subsequent memory

In well-rested (RW) participants, pattern similarity in the PPA for remembered items was significantly higher than for forgotten items ($t(23)=3.38$, $p=0.003$, $d=0.69$) suggesting that PS in this region was informative about subsequent memory. Pattern similarity was irrelevant to subsequent memory of the scene images in the other two ROI. This was true of both states.

TSD was accompanied by significant lowering of PS in the PPA ($F(1,43)=16.66$, $p<0.001$, $\eta_p^2=0.28$), pointing to less stable neural representations following sleep deprivation. Lowered PS in the TSD state was similar for remembered and forgotten items ($t(20)=-1.37$, $p=0.185$, $d=-0.32$; Fig. 4).

Quality of encoded information: distinctiveness of Item representation

Finally, to examine the quality of encoded information, we examined item-specific distinctiveness of neural representations. We confined this analysis to the PPA as it showed the greatest sensitivity to differences in subsequent memory, indexed by both univariate Dm and within-item PS. The analysis was confined to subsequently remembered items to reduce uncertainty regarding what might be depicted in forgotten or non-encoded items. The RW group showed significantly greater item-specific distinctiveness than the TSD group ($t(43)=2.92$, $p=0.006$, $d=0.87$; Fig. 5).

Discussion

Sleep deprivation prior to learning can affect memory formation through its effect on the hippocampus (Yoo et al., 2007). An alternative mechanism demonstrated here is deficient neural representation within neocortical regions that feed into the hippocampus. Well-rested participants showed neural representations within the PPA that were stable across picture repetition, with higher pattern similarity for items that were subsequently remembered relative to those that were forgotten. Sleep deprivation impaired picture recognition and lowered pattern similarity to a level below that of forgotten items in the rested group. Finally, pattern information associated with remembered items was less distinct following sleep deprivation.

Activation in cortical areas responsible for mediating and responding to selective attention is reduced following sleep deprivation, likely as a result of cortical columns in these regions spontaneously and stochastically entering a 'down state' (Vyazovskiy et al., 2011). Particularly relevant to the current work, this lowered neural activation is accompanied by increased variability of behavioral responses.

Pattern similarity is thought to reflect consistency in feature processing and may benefit subsequent memory through the provision of stable inputs to the hippocampus (Xue et al., 2013). This is supported by the observation that greater pattern similarity in the well-rested group was associated with superior subsequent memory. While it is unclear why pattern similarity did not differ between subsequently remembered and forgotten items in the TSD group, it is likely that activation patterns, even for remembered items, were already too unstable in TSD to provide any substantial mnemonic benefits.

The present results concerning reduced pattern similarity in sleep deprived persons complement prior work showing that sleep deprivation reduces perceptual processing capacity (Kong et al., 2011), and impairs selective attention (Kong et al., 2012; Lim et al., 2010; Tomasi et al., 2009). In a nutshell, reduced processing of stimulus features during sleep deprivation results in less stable input into the hippocampus from the PPA, contributing to weaker encoding, resulting in poorer recognition memory.

In support of the account that sleep-deprivation compromises the 'quality' of stimulus encoding even for subsequently remembered items, the neural distinctiveness of remembered items within the

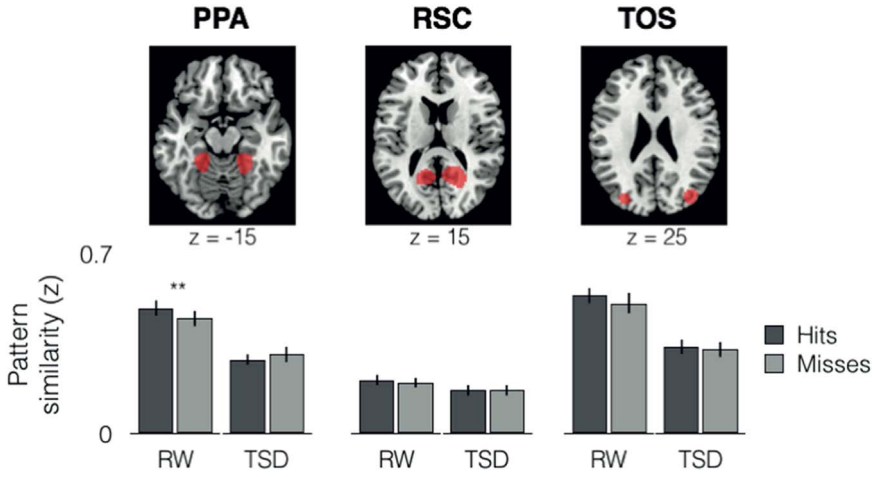

Fig. 4. Pattern similarity for subsequently remembered items was greater in the PPA for the RW group but not the TSD group. No difference in pattern similarity between subsequently remembered and forgotten item was observed in the RSC and TOS. Error bars indicate +/−1 SEM. ** $p<0.01$.

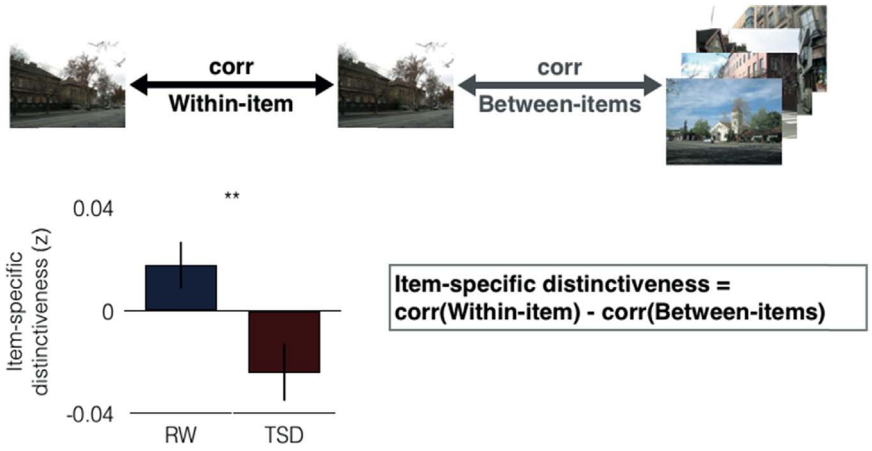

Fig. 5. Item-specific distinctiveness in the PPA. Distinctiveness was defined as the difference between within-item pattern similarity and between-item similarity (including only items within the same category). Subsequently remembered items showed greater item-specific distinctiveness in neural activation patterns in the RW group than in the TSD group. Error bars indicate +/−1 SEM. ** $p < 0.01$.

PPA was found to be reduced under sleep deprivation.

Distinctiveness in activation patterns has been used to indicate reinstatement of item-specific activation patterns (Xue et al., 2010). In the present work, greater distinctiveness refers to being able to distinguish the neural representation of a specific exemplar from a visual category from other exemplars within the same category. This was evaluated through the comparison of within-item similarity (PS) and between-item similarity. Two potential mechanisms could account for the reduction in distinctiveness following sleep deprivation.

Decline in visual processing following sleep deprivation may be a result of reduced cholinergic drive and lowered arousal (Chuah and Chee, 2008). Conversely, higher cholinergic drive might increase perceptual selectivity in visual processing regions by increasing the signal to noise ratio of sensory neural responses. In turn, this may give rise to a more distinct visual percept and more robust encoding (Furey et al., 2000).

An alternative explanation for how lower distinctiveness relates to poorer memory relates to the redundancy of information capture at the time of encoding. In our study, participants performed indoor/outdoor judgment of scene images. This only required attending to category information and not exemplar information. When participants were well rested, they showed higher distinctiveness for remembered items than sleep-deprived participants, suggesting that despite being task irrelevant, rested participants encoded additional exemplar information, giving rise to more distinctive representations. In contrast, the reduced distinctiveness displayed in TSD participants, points to reduced processing of exemplar information. This resulted in representations that bore greater similarity to exemplars from the same category. Such degraded memory representations might have been sufficient for supporting successful recognition of some scene images but with less feature redundancy that could be referenced for confident recognition, resulting in overall poorermemory.

Computational models of memory formation have suggested that the generation of distinctive memory traces is a function of hippocampal pattern separation mechanisms (McClelland et al., 1995; O'Reilly and Norman, 2002). As such, reduced representational distinctiveness could potentially be driven by degraded input to the hippocampus or reduced hippocampal function. Indeed, prior findings have shown that hippocampal lesions reduce one's ability to distinguish similar memoranda (Brock Kirwan et al., 2012). High-resolution fMRI studies, have also demonstrated the role of hippocampal subregions in producing distinctive neural representations (Lacy et al., 2011). Unfortunately the spatial resolution of our scans made reliable inquiry of hippocampal pattern representations unfeasible, limiting possible examination of hippocampal-neocortical interactions during encoding.

Conclusion

In sum, degraded representation of visual sensory information in the PPA contributes to poorer memory encoding in sleep deprived young adults and subsequently reduces recognition performance.

Author contributions

J.H. Poh designed and planned the study, conducted the experiments, analyzed the data and wrote the manuscript. M.W.L. Chee designed and planned the study, analyzed the data and wrote the manuscript.

Competing interests statement

Both authors declare no competing financial interests.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.neuroimage.2017.01.080.

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