

Sleep deprivation and its effects on object-selective attention

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ABSTRACT

Sleep deprivation (SD) affects attention but it is an open question as to whether all subtypes of attention are similarly affected. We investigated the effects of 24 h of total SD on object-selective attention. 26 healthy, young adults viewed quartets of alternating faces or place scenes and performed selective judgments on faces only, scenes only or both faces and scenes. Volunteers underwent fMRI following a normal night of sleep and again following approximately 24 h of total sleep deprivation in a counterbalanced fashion. Sleep deprivation resulted in slower and less accurate picture classification as well as poorer recognition memory for scenes. Attention strongly modulated activation in the Parahippocampal Place Area (PPA). Task-related activation in the fronto-parietal cortex and PPA was reduced in SD, but the relative modulation of PPA activation by attention was preserved. Psychophysiological interaction between the left intra-parietal sulcus and the PPA that was clearly present after a normal night of sleep was reduced below threshold following SD suggesting that PPI may be a more sensitive method of detecting change in selective attention. Sleep deprivation may affect object-selective attention in addition to exerting a task-independent deficit in attention.

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Introduction

A single night of total sleep deprivation (SD) can impair cognitive performance (Durmer and Dinges, 2005) in a manner that contributes to industrial and transportation accidents as well as medical errors (Barger et al., 2006; Dinges, 1995; Mitler et al., 1988; Philip and Akerstedt, 2006). While the degradation of “attention” is an important contributor to cognitive decline and this has been explored using functional brain imaging (Chee et al., 2008; Drummond et al., 2001; Mander et al., 2008; Portas et al., 1998; Tomasi et al., 2008) as well as behavioral studies (Doran et al., 2001; Santhi et al., 2007) it remains an open question as to whether all facets of attention are similarly diminished by SD. Several behavioral studies have suggested that despite overall decline in response speed, feature based visual search (Horowitz et al., 2003) and alerting may be preserved (Versace et al., 2006).

Multiple studies have shown that on behavioral and neurophysiological levels, attention is not a unitary construct. As such, it is important to clarify the use of this term in the present study. William James’s conceptualization of attention: “Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others...” highlights the

construct central to the present study, that of input selection. Selectively attending to the “thing of interest” (Desimone and Duncan, 1995; Johnston and Dark, 1986) has been studied through experiments evaluating spatial (Corbetta and Shulman, 2002; Hopfinger et al., 2000; Kastner et al., 1999), feature (Liu et al., 2003) and object-based (Serences et al., 2004) attention.

Adaptively focusing on task-relevant stimuli results in enhanced perception at attended locations (Bashinski and Bacharach, 1980; Posner, 1980). Accompanying these behavioral benefits are increases in the firing rate of neurons within the receptive field of these attended locations (Reynolds and Chelazzi, 2004) and the inhibition of neuronal firing to non-attended locations. These changes in neural activity are driven by top-down or bottom-up (stimulus salience) influences that have been well studied in humans using non-invasive techniques (Corbetta and Shulman, 2002; Hopfinger et al., 2000; Kastner and Ungerleider, 2000).

Here, we explored the effects of SD on the behavioral and neuroanatomical correlates of object-selective attention—a form of selective attention that relates to how the visual system can select *particular targets* even if they spatially overlap, or are partially occluded by other non-target items (Duncan, 1984; Serences et al., 2004). The degradation of this faculty in the setting of sleep deprivation could contribute to an ICU nurse, an air traffic controller, or a security officer failing to detect a critical signal amidst competing pieces of visual information that they typically encounter.

Critically, although spatial and object-selective attention can be dissociated behaviorally, the cognitive control regions that support

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them overlap considerably (Serences et al., 2004; Wojciulik and Kanwisher, 1999). As such, it may be difficult or impossible to disambiguate the effects of a manipulation (like sleep deprivation) that could impair one type of attention without affecting the other. Ascertaining how object-based attention could contribute to SD-related performance decline could therefore benefit from an experimental design that evaluates the output of the relevant attention system—i.e. the effect or result of object selection in the brain, as opposed to evaluating top-down control signals.

Towards this goal, volunteers were asked to make perceptual judgments on either faces or outdoor scenes that alternated within the same spatial location (Fig. 1). As attending to scene or face stimuli maximally activates spatially separate regions in the ventral visual cortex, we are able to differentiate the effects of object-selective attention. For instance, selectively attending to scenes elicits higher parahippocampal place area (PPA) activation (Gazzaley et al., 2005a) and more pronounced repetition suppression (Yi and Chun, 2005) than attending to faces. In contrast, both tasks would be expected to activate similar fronto-parietal cognitive control areas that bias attention to the task-relevant object or face.

The extent to which activity in object selective ventral visual areas is modulated by task demands has functional significance. For example, a reduced difference in PPA activation between attend and ignore conditions was related to performance impairment in elderly subjects who were less able to ignore distracting stimuli (Gazzaley et al., 2005b).

In the present study, we investigated the effect of SD on the imaging correlates of object-selective attention by examining both its effect on activation in cognitive control and ventral visual areas as well its effect on the psychophysiological interaction (PPI) between the parietal control regions and visual cortex. PPI (Friston et al., 1997) detects a significant difference in the regression co-efficient (effectively the slope) of fMRI signal in a reference region and a functionally connected region as a function of a psychological variable—here object specific attention; and provides a second measure for evaluating state related change in neural engagement. Studying such functional

connectivity could provide information about the interaction between top-down control regions and sensory cortex that may not be evident from inspecting changes in activation alone.

Materials and methods

Participants

Twenty-six healthy young adults took part in the experiment (14 females, mean age 20.7 years, SD 1.9 years). Participants were selected from respondents to a web-based questionnaire posted on a university website. Volunteers had to: (1) be right-handed, (2) be between 18 and 35 years of age, (3) have habitual good sleeping habits (sleeping no less than 6.5 h each night for the past one month), and (4) were not extreme morning types on a modified Morningness–Eveningness scale (Horne and Ostberg, 1976). This was to reduce variance in behavioral and imaging findings arising from chronotype differences, (5) not be on any long-term medications, (6) have no symptoms associated with sleep disorders, and (7) have no history of any psychiatric or neurologic disorders.

The sleeping habits of all participants were monitored throughout the 2-week duration of the study and only those whose actigraphy data indicated habitual good sleep (i.e., slept no later than 1:00 AM and woke no later than 9:00 AM) were recruited for the study following informed consent. All participants indicated that they did not smoke, consume any medications, stimulants, caffeine or alcohol for at least 24 h prior to scanning.

Study procedure

Participants made three visits to the laboratory. During the first visit, they were briefed on study protocol and sleep habit requirements, and practiced the study task. At the end of this session, every participant was given a wrist actigraph (Actiwatch, Philips Respironics, USA) to wear throughout the study. The second and third visits involved MR imaging. The first scanning session took place

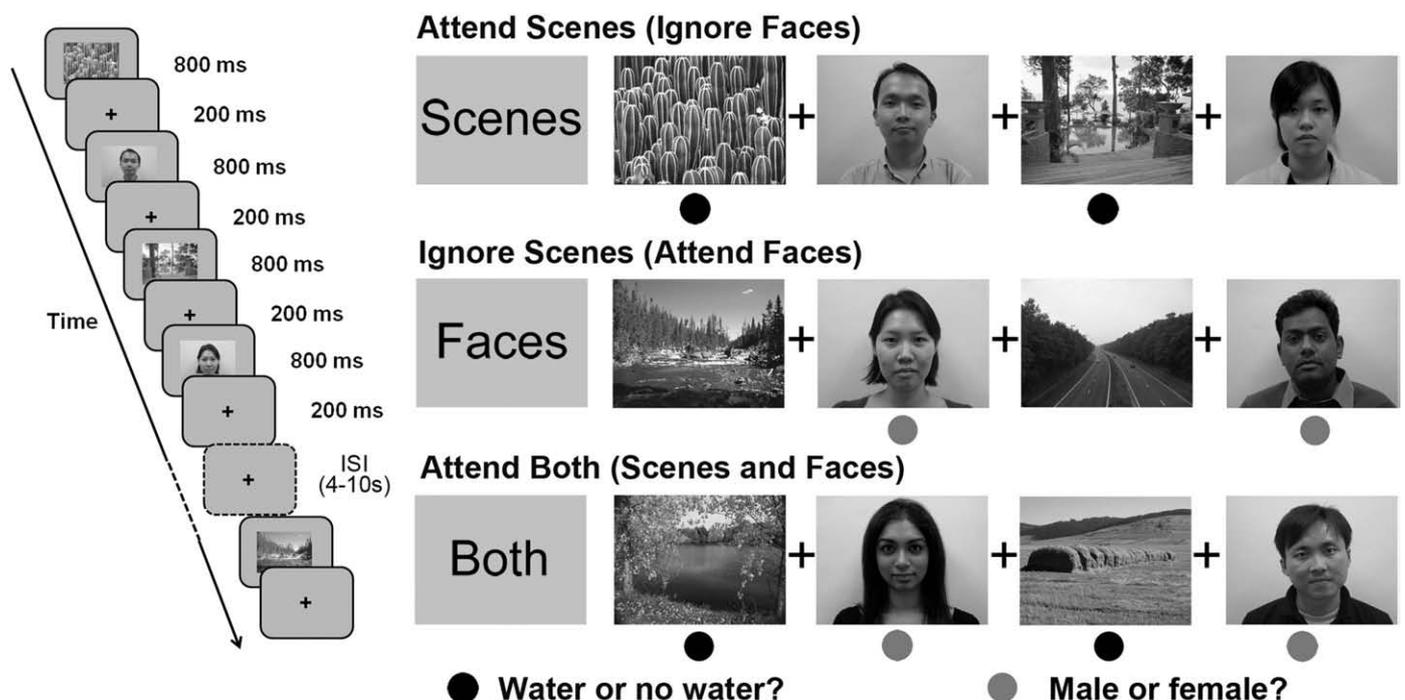


Fig. 1. Schematic of the selective attention task. Face and scene images were presented for 800 ms each, with an interstimulus interval of 200 ms. Participants were instructed to attend to the scenes (AS), attend to faces (and ignore scenes; IS) or to attend to both. In the AS condition they indicated if there was water in the scene. In the IS condition, they indicated if the face was female. In the AB condition, both tasks were performed together.

approximately 1 week after the initial visit. The order of the two sessions (rested wakefulness (RW) and sleep deprivation (SD)) was counterbalanced across all the participants and the sessions were separated by 1 week. This was to minimize residual effects of sleep deprivation on cognition for participants who underwent the sleep-deprivation session first. The RW session took place at 8:00 AM. For the SD session, participants arrived at the lab at 7:00 PM after staying awake the whole day without napping. Participants were monitored overnight and scanning took place the next day at approximately 5:00 AM. During the SD session, participants were allowed to engage in non-strenuous activities such as reading and watching videos. Vigorous physical activity prior to the scans was not permitted.

Scanning took place at approximately 5:00 AM, around the circadian nadir for most persons. While this time is not identical to the one used during RW scans, carefully conducted studies have shown that the difference in sustained attention performance between 5:00 AM and 9:00 AM after a night of sleep deprivation is small (Dorrian et al., 2005). Finally, we chose this time because most vehicular accidents following SD occur most frequently at 2:00 AM and 6:00 AM (Horne and Reyner, 1995).

Experimental tasks and imaging procedure

This experiment was modeled after one that evaluated the effects of selective attention on ventral visual cortex activation (Gazzaley et al., 2005a). We modified the original design by having volunteers make perceptual judgments on the stimuli to enable us to selectively analyze trials where the subject was known to be attentive. We eliminated the working memory component of the experiment, as we were concerned that concurrently evaluating working memory would confound the assessment of activation attributable to selection signals.

Participants viewed task stimuli using MR-compatible LCD goggles (Resonance Technology, Los Angeles, CA, USA) and responded with a button box held in the right hand. The task stimuli were grayscale images of faces and scenes (Fig. 1). Scenes comprised gray scale photographs of outdoor scenes, half of which contained water. Equal numbers of male and female faces with neutral expressions were presented. Although the specific level of luminance was not measured, care was taken to ensure comparability of luminance of the photos to reduce the likelihood of visual transient effects. Each trial comprised a sequence of 2 faces and 2 scenes. Each stimulus within the quartet appeared for 800 ms separated by 200 ms of fixation. Scenes or faces could appear first with equal probability and they appeared only once in the entire imaging experiment.

Each picture subtended a visual angle of 12 degrees in the horizontal direction and 9 degrees in the vertical direction. The pictures were followed by an inter-trial interval (ITI) that ranged from 4 to 10 s, in accordance with a distribution that favored the shorter ITIs (Hagberg et al., 2001).

Each experimental session (RW, SD) comprised three runs, and each run comprised 20 quartets. There were three task conditions (1) Attend scenes (AS; or ignore faces), in which participants indicated if the scene contained water or not by pressing one button for scenes that contained water and another if it did not, (2) Ignore scenes (IS; or attend faces), where they indicated if a male or female face was presented; as with scenes, choice was signaled by pressing one of two buttons (3) Attend Both (AB; attend both scenes and faces) in which participants responded to both scenes and faces in the manner just described. This third task was added to evaluate the effect of task load on brain activation.

The order of task presentation was counterbalanced across participants. Each of the 3 runs lasted 246 s. Between 10 and 15 min after completion of imaging, volunteers were given a recognition memory test in which they viewed faces and scenes (160 novel, 240 previously viewed) and made “new” or “old” judgments.

At the end of recognition memory testing, a functional localizer scan was conducted. This was used to define the PPA and FFA for each individual independent of the object-selective attention experiment. The functional localizer comprised two runs, each of which comprised eight stimulus blocks interleaved with eight fixation blocks. Each run lasted 6 min 16 s each. During each run participants passively viewed four 18-s blocks of scene and four blocks of face stimuli, that comprised 18 pictures per block; making up a total of 72 scenes and 72 faces per run.

Images were acquired on a 3-Tesla Tim Trio system (Siemens, Erlangen, Germany). A gradient echo-planar imaging sequence with TR 2000 ms, TE 35 ms, FA 90 degrees, FOV 192 × 192 mm and a 64 × 64 pixel matrix was used. Twenty-eight oblique axial slices (4 mm thick with a 0.4 mm inter-slice gap) parallel to the AC-PC line were acquired. Inline motion correction was applied. High-resolution coplanar T1 anatomical images were also obtained. For the purpose of image display in Talairach space, a further high-resolution anatomical reference image was acquired using a 3D-MPRAGE sequence.

Behavioral data analysis

To reduce the likelihood of including trials that included random responses or those in which the subject was momentarily asleep, we only analyzed valid trials—ones in which subjects made responses to the target stimuli. For example, an AS trial which contained a response to faces was rejected. AS and IS valid trials had to have 2 responses and AB trials 4 responses. As it might be difficult to detect the presence of a small water-containing feature in a scene, we did not penalize incorrect answers as long as a response was made.

Reaction time (RT) for each trial was computed from the mean RT of all the attended stimuli within each trial. Subsequent recognition performance was evaluated using A' , a well-established, non-parametric measure of memory performance based on hit and false alarm rates (Snodgrass and Corwin, 1988). The effects of attention and sleep deprivation on online task performance and subsequent memory were evaluated using a 2 (state: RW vs. SD) by 3 (attention: Attend scenes, Attend Both, Ignore scenes) repeated-measures ANOVA using SPSS 16.0 (SPSS Inc, Chicago IL).

Image analysis

The functional images were processed using Brain Voyager QX version 1.8.6 (Brain Innovation, Maastricht, The Netherlands). 3-dimensional rigid-body motion correction across runs was performed using the first image of the second functional run as the reference image. Inter-slice timing differences attributable to slice acquisition order were adjusted using tri-linear interpolation. Gaussian filtering was applied in the spatial domain using a smoothing kernel of 8 mm FWHM for group level activation maps. Following linear trend removal, a high-pass filter of period 80 s was applied. The T1 images were used to register the functional data set to the volunteers' own 3D image and the resulting aligned dataset transformed into Talairach space.

Functional imaging data was analyzed using a general linear model with 7 block predictors, one for each attention condition (Attend scenes, Ignore scenes, Attend Both) in each of the two states. Invalid trials (defined earlier) and omissions were modeled separately by a seventh predictor and did not enter the analysis. The predictors, represented by a boxcar function, were convolved with a canonical hemodynamic response function.

To account for baseline drifts across runs and between experimental sessions, z-transformation of the signal time-courses for each run was performed. A mixed effects model was used for data analysis where the first level analysis involved a fixed effects estimation of beta weights for the predictor variables relevant to each subject. The

beta values for each predictor in every individual served as the input for a second-level, random effects analysis.

To control for Type I error, voxels were processed using an iterative cluster size thresholding procedure (Goebel et al., 2006) that considered the spatial smoothness of functional imaging data when generating activation maps based on a corrected cluster threshold ($p < 0.05$). Subsequent to this a voxel-level threshold of at least $p < 0.001$ (uncorrected) for t maps and $p < 0.001$ (uncorrected) for F maps was applied.

The effects of interest were (1) how object selective attention modulated ventral visual cortex activation, (2) how object selective attention modulated frontal and parietal activation, and (3) how these findings were altered by SD. Analysis of object-selective attention within the ventral visual cortex was region-of-interest (ROI) based. The Parahippocampal Place Area (PPA) and Fusiform Face Area (FFA) were defined by a separately conducted localizer scan performed for each individual as described previously. A PPA ROI comprised a $10 \times 10 \times 10$ mm cube of voxels that surrounded the one showing maximum difference in activation between scene and face blocks (thresholded at $p < 1.0 \times 10^{-9}$; uncorrected; Suppl Fig. 1).

As the PPA has been shown to yield the clearest selectivity data (Gazzaley et al., 2005a; Yi and Chun, 2005), we focused our evaluation on this region. As there was no hemispheric asymmetry of PPA activation, activation magnitude data for all conditions (AS, IS, and AB) was obtained from both left and right PPA and averaged (Fig. 2). To quantify the effects of attention on PPA activation across state, an attention modulation index (AMI) was computed for each participant. This was the difference in PPA activation between AS and IS conditions (and between AB and IS conditions).

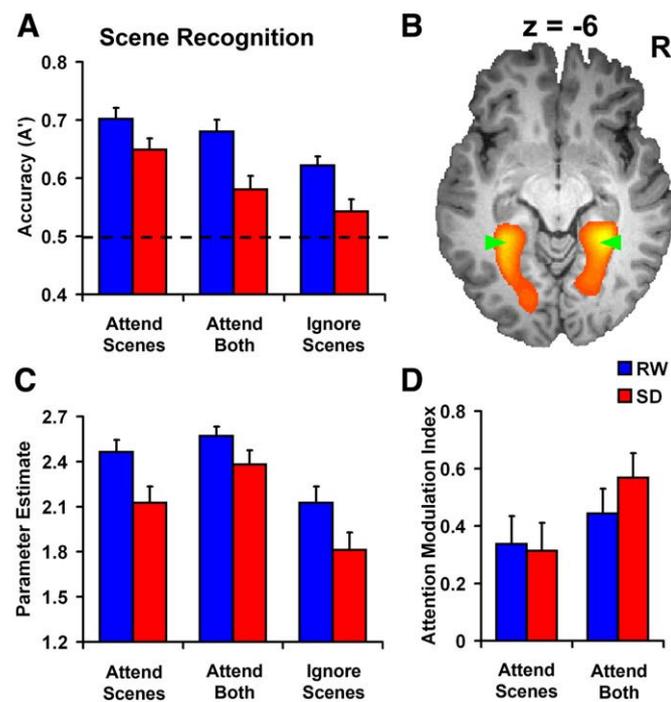


Fig. 2. Recognition performance for scenes, Parahippocampal Place Area (PPA) activation and its modulation by attention across a normal night of sleep (RW) and following sleep deprivation (SD). (A) Recognition memory measured by A' after a normal night's sleep (RW) and after 24 h of sleep deprivation (SD). There was a significant decrease in recognition performance when participants ignored scenes and when they were sleep deprived. (B) Activation map based on the functional localizer scans, thresholded at $p < 0.001$ showing the region showing sensitivity to scenes in the PPA averaged across 26 participants for display purposes. Note that in the analysis, individual maps were considered. (C) Activation in the PPA corresponding to the three different task conditions in each of the two states. (D) Index measuring the strength of attention modulation of PPA activity in the AS and AB conditions.

Fronto-parietal regions that could mediate the effects of object attention were identified from the conjunction of areas showing task-related activation across all three conditions (AS, IS, AB) in the RW state (Suppl Fig. 1). This was intended to select the minimum set of the possible regions activated by any of these three tasks (Nichols et al., 2005). The rationale for selecting activation at RW as the basis for comparison was previously elaborated on (Chee et al., 2006; Choo et al., 2005). Magnitude of activation across task and state was evaluated using ANOVA.

Psychophysiological interaction (PPI) analysis (Friston et al., 1997; Gitelman et al., 2003) was performed by extracting the time-series of activation from a 10 mm cubic region surrounding the "peak voxel" within the left IPS (Fig. 4). This region was selected as the seed because prior work has suggested the left IPS to be casually involved in the control of object-based visual attention (Serences et al., 2004).

The IPS peak voxel showed activation in all three conditions (Suppl Fig. 1). The linear model used in the PPI predicted the time course in target brain regions to be the sum of three regressors: the time course of activity in the seed region, a vector coding the item attended to (AS vs. IS) at any given time and the PPI term. To construct the PPI term, the deconvolved IPS (seed) time-course was multiplied with a vector containing the psychological variables of interest (AS & IS). This product was then re-convolved with a canonical hemodynamic response function (Gitelman et al., 2003). Separate whole-brain analyses were computed for each subject and for each state. AB runs were excluded from consideration in this analysis. To obtain connectivity maps, a two-tailed, one-sample t -test was conducted on the parameter estimates for the PPI (interaction) term in a second level analysis. Finally, these parameter estimates were contrasted using a two-tailed, paired t -test to determine if the connectivity between the IPS and target regions changed significantly across state.

Results

Behavioral findings

There was a strong main effect of task on response time ($F_{(2,50)} = 74.54$, $p < 0.001$), whereby the attend both (AB) condition elicited slower responses than either the attend scenes (AS) or ignore scenes (IS, where faces were attended). This might be expected from the increased processing load when having to attend to both faces and scenes.

Sleep deprivation resulted in a greater number of invalid responses for all three conditions indicative of increased behavioral lapses ($F_{(1,25)} = 9.29$, $p < 0.01$). SD was also associated with slower ($F_{(1,25)} = 4.50$, $p < 0.05$), less accurate performance ($F_{(1,25)} = 11.56$, $p < 0.01$) and greater intraindividual coefficient of variation of RT ($F_{(1,25)} = 4.42$, $p < 0.05$; Table 1). There was no interaction between state and task condition for response times ($F_{(2,50)} = 1.68$, n.s., Table 1).

Table 1

The proportion of valid trials (%), performance accuracy (%) and mean reaction time (RT) across the three attention tasks after a normal's night sleep (RW) and after 24 h of sleep deprivation (SD).

	RW			SD		
	Valid trials %	Accuracy %	RT ms	Valid trials %	Accuracy %	RT ms
Attend scenes	96.4 (6.1)	90.0 (7.3)	695 (92)	86.4 (12.5)	73.6 (15.6)	731 (116)
Attend both	96.5 (5.1)	85.2 (6.7)	703 (88)	91.9 (9.8)	78.5 (16.5)	734 (91)
Attend faces	94.6 (7.5)	91.8 (7.6)	616 (77)	89.8 (10.6)	88.1 (15.0)	630 (78)

Figures in parentheses indicate standard deviation. Note that the Attend Faces condition is the equivalent of the Ignore Scenes condition in the imaging portion of the analysis. Sleep deprivation was associated with slower, less accurate and temporally more variable responses in all three conditions.

Table 2

Recognition performance as measured by *A'* for scenes and faces as a function of attention condition after a normal night's sleep (RW) and after 24 h of sleep deprivation (SD).

	RW			SD		
	Attended	Ignored	Both	Attended	Ignored	Both
Scenes	0.70 (0.11)	0.62 (0.08)	0.68 (0.11)	0.65 (0.11)	0.54 (0.11)	0.58 (0.13)
Faces	0.62 (0.11)	0.58 (0.09)	0.59 (0.11)	0.63 (0.12)	0.54 (0.10)	0.57 (0.12)

Numbers in parentheses indicate standard deviation. Object-selective attention was associated with significantly better recognition of attended objects in both states. This was true for both scenes and faces. Sleep deprivation affected recognition of scenes but not faces.

Attention benefitted memory for scenes and faces in both states as reflected by *A'* scores for scenes ($F_{(2,50)} = 19.85, p < 0.001$) and faces ($F_{(2,50)} = 7.12, p < 0.01$). Sleep deprivation lowered recognition scores for scenes under all task conditions ($F_{(1,25)} = 13.88, p < 0.001$). However, face recognition was not found to be adversely affected by sleep deprivation ($F_{(1,25)} = 0.52, n.s.$) suggesting that it may be more automatic (Table 2). There was no interaction between task condition and state for recognition memory ($F_{(2,50)} = 1.18, n.s.$).

Although the pictures were not explicitly cued like in experiments evaluating orienting attention, the appearance of a subsequent place scene or face could be anticipated following the appearance of the first stimulus in the quartet. This was evident by the large main effect of stimulus order on RT ($F_{(1,25)} = 83.08, p < 0.001$). Interestingly, there was interaction between stimulus order and state ($F_{(1,25)} = 7.61, p < 0.01$) indicating that the benefit of cueing was greater in the sleep deprived state (Versace et al., 2006).

Attention and sleep deprivation modulate parahippocampal place area (PPA) activation

As with the behavioral data, only valid trials were analyzed. In agreement with prior work regarding attentional modulation of PPA activation (Gazzaley et al., 2005a; Yi and Chun, 2005), we found PPA activation to be more spatially consistent across subjects than Fusiform Face Area (FFA) activation. Additionally, sleep deprivation did not appear to affect face recognition. As such, our analysis concerning the effects of selective attention and state were focused on the PPA and scene processing.

After a normal night of sleep, the attend scenes (AS) condition elicited higher PPA activation than the ignore scenes (IS) condition consistent with the influence of object-selective attention ($t_{(25)} = 2.69, p < 0.05$; Fig. 2). Sleep deprivation resulted in significantly lower

Table 3

Talairach co-ordinates of cognitive control regions that showed significant task-related activation in a conjunction of Attend Scene, Ignore Scene and Attend Both conditions.

	BA	Talairach co-ordinates			<i>t</i> value	
		x	y	z		
					RW	SD
L precentral gyrus	6/8	-46	2	34	13.05	7.77
R precentral gyrus	6/8	37	2	32	14.01	10.29
L middle frontal gyrus	10	-28	40	22	8.07	4.84
R middle frontal gyrus	46	48	29	19	6.89	3.93
L medial frontal cortex	6	-9	2	49	13.65	10.92
R medial frontal cortex	6	6	11	43	11.71	8.37
L anterior cingulate cortex	32	-12	8	37	13.47	8.42
R anterior cingulate cortex	32	6	11	43	11.71	8.37
L insula	13	-30	20	11	13.85	7.12
R insula	13	27	17	7	11.47	6.06
L intraparietal sulcus	7	-30	-52	40	14.38	10.38
R intraparietal sulcus	7	24	-57	40	12.92	8.79

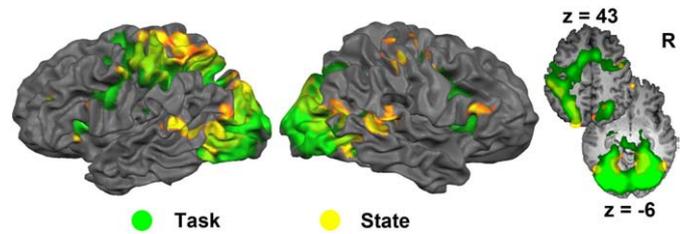


Fig. 3. Brain regions showing effects of task and state. Conjunction map thresholded at $p < 1.0 \times 10E-6$ (uncorrected) showing areas activated in all three task conditions during RW (in green-blue) together with areas showing a main effect of state thresholded at $p < 0.001$ (uncorrected) showing reduced activation during SD (red-yellow).

PPA activation in both AS and IS conditions ($F_{(1,25)} = 15.92, p < 0.001$), scaled in a manner that preserved the difference between AS and IS activation ($t_{(25)} = 2.99, p < 0.05$). This was reflected in the lack of significant change in the Attention Modulation Index (AMI) which measures the difference in PPA activation between AS and IS conditions as well as between AB and IS conditions across states ($F_{(1,25)} < 1, p = n.s.$; Fig. 2).

The comparable magnitude of PPA activation in the AB and AS conditions (there was a non-significant trend for higher activation in the AB condition) suggests that the dual task condition was not as taxing as previously reported (Gazzaley et al., 2005a) possibly because in the current experiment, there was not a demand on working memory unlike in the original design.

Attention and state effects in cognitive control regions

There was a significant effect of task condition on parietal activation following a normal night of sleep, consistent with the cognitive control function attributed to this region (bilateral but asymmetric, clear on the left side, L Parietal; $F_{(2,50)} = 3.85, p < 0.05$; Table 3, Fig. 4). This was driven primarily by the contrast between the AB and IS conditions ($t_{(25)} = 2.62, p < 0.05$), there being no statistically significant difference between AB and AS or between AS and IS, consistent with the comparable levels of attention engagement for AS and IS.

Sleep deprivation resulted in bilaterally reduced parietal (asymmetric, with effect being more pronounced in the left hemisphere; L parietal: $F_{(1,25)} = 6.53, p < 0.05$; Fig. 4) and inferior frontal activation ($F_{(1,25)} = 6.97, p < 0.05$). The difference in parietal activation between conditions was not significant in SD. There was no effect of task in bilateral inferior frontal regions in either state ($F_{(2,50)} < 1, n.s.$).

There was an overlap of areas activated during the performance of all three tasks and areas showing reduced activation following sleep deprivation (Fig. 3). Hence, the areas we reported as showing SD-

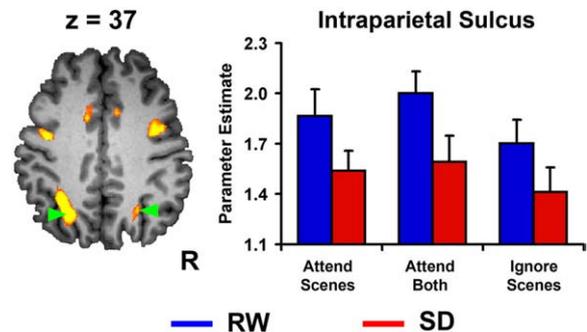


Fig. 4. Intraparietal sulcus (IPS) activation across task and state. Activation map thresholded at $p < 1.0 \times 10E-9$, showing the conjunction of task-related signal change in the cognitive control regions for all three tasks (IPS highlighted by green arrowheads). (B) Task-related signal change in the IPS after RW and after SD. There was a main effect of state on task-related activation across all three tasks.

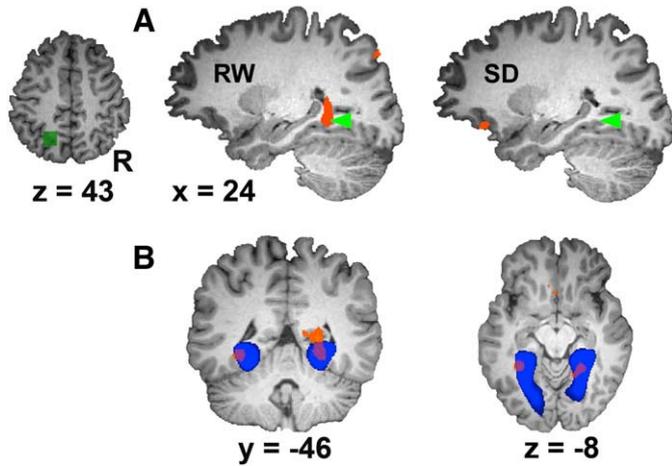


Fig. 5. Psychophysiological interaction between IPS and PPA. (A) PPI maps thresholded at $p < 0.05$ showing the interaction between the reference left IPS region (indicated by a green square) and right PPA. PPI was observed between these regions after a normal night's sleep but not after SD. (B) Overlap between "place/scene" sensitive regions identified by an independent localizer (blue) and the regions showing PPI during RW (orange).

related change in activation were those engaged during task performance and are functionally meaningful.

Effective connectivity changes across states

The psychophysiological interaction (PPI) analysis evaluated functional linkage between the parietal and ventral visual regions across states in an unbiased manner as it was conducted at a whole brain level (Fig. 4). PPI detects a significant difference in the regression coefficient (effectively the slope) of fMRI signal in a reference region and a functionally connected region as a function of psychological variable—object specific attention in this case (Friston et al., 1997).

The PPI analysis revealed significant functional connectivity between the IPS and the PPA + retrosplenial cortex following a normal night of sleep ($t_{(25)} = 2.70$, $p < 0.01$; Fig. 5; Table 4A), but not following SD ($t_{(25)} = 0.32$, n.s.). The PPI map created using a direct contrast between the interaction terms across states concurred with the above findings (Table 4B). Recent work has shown that the PPA contains a contextually local representation of scenes whereas the retrosplenial cortex taps into a view invariant more integrative representation of the scene (Epstein et al., 2007; Park and Chun, 2009). The direct comparison of PPI across state for the PPA/retrosplenial cortex was also significant ($t_{(25)} = 3.31$, $p < 0.01$).

Imaging findings in the thalamus

We neither observed an increase (Chee and Chuah, 2008; Portas et al., 1998; Tomasi et al., 2008), nor a decrease (Chee and Choo, 2004;

Table 4A

	Talairach co-ordinates			t value	
	x	y	z	RW	SD
R parahippocampal gyrus	23	-46	-8	2.70**	0.32
L parahippocampal gyrus	-31	-44	-8	2.70**	0.36
R lateral occipital complex	54	-58	-2	3.16**	-0.59
L fusiform gyrus	-36	-13	-22	2.54*	-1.699
L precuneus	-28	-71	25	2.50*	-0.57

This table shows PPI determined separately in each state. Talairach co-ordinates of regions that showed significant state differences in psychophysical interaction with the seed left IPS region (Talairach co-ordinates -30, -52, 40; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

Table 4B

	Talairach co-ordinates			t value
	x	y	z	RW>SD
R parahippocampal gyrus	31	-35	-9	3.31**
R lateral occipital complex	52	-59	-9	2.68*
L lateral occipital complex	-53	-62	-9	2.68*
L inferior frontal gyrus	-31	30	10	2.99**
L fusiform gyrus	-38	-12	-17	4.25***

This table shows the results of the contrast in PPI values computed when data from both RW and SD were included in the same model. Talairach co-ordinates of regions that showed significant state differences in psychophysical interaction with the seed left IPS region (Talairach co-ordinates -30, -52, 40; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

Choo et al., 2005) in task-related thalamic activation across state in any of the three conditions ($F_{(1,25)} = 0.05$, n.s.). This suggests that for this task, performance differences across state are less likely to have been due to differences in arousal mediated via the thalamus.

Discussion

We found that sleep deprivation resulted in slower and less accurate picture classification as well as poorer recognition memory. SD lowered task-related activation within the ventral visual area (represented by the PPA/retrosplenial cortex) as well as fronto-parietal control regions across all conditions. Although SD did not reduce the extent to which attention modulated PPA activation, it was associated with reduced psychophysiological interaction between the left intraparietal sulcus (IPS) and the PPA during object selection.

Functional connectivity changes suggest derangement of object selective attention during sleep deprivation

As illustrated here, in some contexts, understanding the neural underpinnings of state related change in behavior might benefit from looking beyond a simple examination of increases or decreases in task-related activation that can yield conflicting results requiring careful interpretation. For example, whereas many studies including our own (Bell-McGinty et al., 2004; Chee et al., 2006, 2008; Chee and Chuah, 2007; Lim et al., 2007; Mu et al., 2005) have found lower task-related parietal activation to accompany performance decrements in SD, several studies (Drummond et al., 2000, 2001, 2005) have shown otherwise.

Inter-individual differences in response to sleep deprivation can account for some of the differences in findings between studies (Chee et al., 2006; Chuah and Chee, 2008; Mu et al., 2005). At other times, relative preservation or even increase in region-specific, task-related activation during SD has often been attributed to "compensation." This is certainly appropriate when task performance in a given individual is preserved at some levels of cognitive load (Chee and Choo, 2004) or task difficulty but not at others (Drummond et al., 2005).

However, examining task activation alone may fail to accommodate the possibility that within the same patch of association cortex, cognitive operations may be unequally affected during SD. For example it has been shown that a speed-accuracy tradeoff occurs in sleep deprived persons engaged in visual search tasks (Horowitz et al., 2003; Santhi et al., 2007) and that less efficient engagement of neural circuitry and slower responding may drive activation in cognitive control regions in opposite directions (Chee et al., 2008). Such effects may not be separable when only one level of cognitive load or task difficulty is assessed or when the cognitive comparison of interest relates to category selection which does not modulate processing load, as in the case of the present study.

Functional connectivity may prove useful in the latter context or when the target cortical region performs several cognitive operations of which only one is of interest. In the current experiment, cortex surrounding the IPS could be involved in sustaining attention, attending

to scenes, or contributing to the encoding of stimuli into long-term memory. The PPI analysis clarified by showing that an elevation of parietal signal was associated with a greater increase in PPA activation in the AS condition compared to the IS condition after a normal night's sleep. Since the cognitive demands related to sustaining attention and encoding were arguably similar across AS and IS, we can reasonably conclude that PPI reflects the action of selective attention rather than a more general task-independent effect we later discuss. Additionally, we can infer that the attenuation of this PPI following sleep deprivation reflects the diminution of object-based attention perhaps as a result of a change in neural synchrony across state. While we acknowledge that fMRI does not have the temporal resolution to reveal differences in synchronization, PPI analyses consider the interaction in MR signal between seed and target regions at a finer grained level (each block in this case) and may be more sensitive to attention modulation than the AMI, which measures the average activation differences between “attend” and “ignore” blocks.

Finally, prior behavioral work has shown that orienting attention—where response time is reduced by the provision of an informative cue prior to target appearance, is spared in short duration total sleep deprivation whereas there is concurrent decrement of vigilant (sustained) attention, as reflected by slower responses to infrequent, unheralded stimuli (Versace et al., 2006).

In our experiment, because the appearance of a scene or a face is followed by the subsequent appearance of these stimuli in a predictable manner, the effect of SD may have been ameliorated to the point where it was detectable only by PPI, arguably a more sensitive measure of functional change than AMI. This cue-like facilitation of response time was evident in the interaction between state and stimulus order (Suppl. Table 1).

Functional connectivity analyses have proven informative in research related to sleep and memory consolidation (Sterpenich et al., 2007; Yoo et al., 2007) but have not been widely applied in the setting of SD studies (Bell-McGinty et al., 2004).

Sleep deprivation also exerted task-independent effects on sustained attention

In addition to the deficit in object-based attention, sleep deprivation also resulted in greater variation in RT and increased behavioral lapses. These were evenly distributed across the three task conditions and are consistent with a loss of sustained (vigilant) attention. Accompanying these behavioral changes was a reduction in inferior frontal and parietal (IPS) activation associated with both AS and IS following sleep deprivation, consistent with prior studies from our laboratory (Chee and Chuah, 2007; Chuah and Chee, 2008; Lim et al., 2007). The task-independent decrease in top-down control could explain the lowering of PPA activation in both AS and IS conditions during SD.

Had sleep deprivation solely affected object selective attention, we would have observed a failure to attenuate PPA activity in the IS condition with little impact on activation in AS. This latter pattern was observed in healthy elderly and was attributed to a reduced ability to suppress task-irrelevant visual stimuli (Gazzaley et al., 2005b).

At first, it would seem contradictory to report task-specific as well as task-independent effects of sleep deprivation on the control of attention in the same experiment. However, deficits in selective and sustained attention can co-exist following sleep deprivation (Santhi et al., 2007). Whether top-down control mechanisms generalize across a wide range of sensory representations or are specific to task relevant information is another issue that continues to be debated, but the current findings are consonant with a recent imaging study that found evidence for both generalized and specialized components of attentional control within the same subjects with considerable overlap between areas controlling different stimulus types of cues (Slagter et al., 2007a).

A clearer understanding of how attention is affected by sleep deprivation is motivated by recent findings that different forms of mental training can improve performance in attention demanding tasks (Slagter et al., 2007b, 2008). Knowing what faculties are most vulnerable and in which individuals (Van Dongen et al., 2004) may aid in the design of more efficient strategies to maintain adequate attention in sleep deprived persons (Santhi et al., 2007) using the cognitive training, light (Santhi et al., 2008) or pharmacologic measures (Bodenmann et al., 2009; Wesensten et al., 2005).

Isolating selective attention—some suggestions

In the current results AB elicited similar magnitude of PPA activation compared to AS, whereas in the original study that used a similar design, AB elicited less PPA activation than AS, as might be expected from competition for limited processing resources (Gazzaley et al., 2005a,b). This variation in results might have arisen because we used larger pictures than in the original study making the AB task perceptually less difficult, and reducing demands on having to divide attention between faces and scenes. Stronger isolation of selective attention might be realized by increasing the rate of rapid serial visual presentation (Yi and Chun, 2005) or by using overlapping, transparent stimuli (O'Craven et al., 1999). Finally, to investigate the possibility that the provision of a cue could reduce the impact of SD on attention demanding tasks, one could present target pictures unheralded by prior cues and in a temporally unpredictable fashion.

Conclusion

In summary, while we found that in a task requiring object selective attention, one night of total sleep deprivation affected functional connectivity between the IPS and PPA without altering the attention modulation index in the PPA. This can be interpreted as evidence that PPI is a more sensitive marker of selective attention, enabling us to differentiate its contribution to reduced cognitive function from a more generalized, task-independent effect attributable to reduced vigilance. It remains to be seen if more pronounced specific deficits in selective attention may be drawn out by tasks that place stronger demands on selection or by eliminating informative cues as to the appearance of target stimuli.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2009.08.067.

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