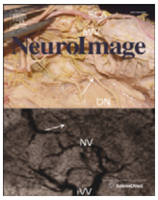
NeuroImage 59 (2012) 1745–1751

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Sleep deprivation reduces default mode network connectivity and anti-correlation during rest and task performance

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ARTICLE INFO

Article history:
Received 17 May 2011
Accepted 9 August 2011
Available online 18 August 2011

Keywords:
fMRI
Sleep deprivation
Default mode network
Resting state
Anti-correlated network
Functional connectivity

ABSTRACT

Sleep deprivation (SD) can alter extrinsic, task-related fMRI signal involved in attention, memory and executive function. However, its effects on intrinsic low-frequency connectivity within the Default Mode Network (DMN) and its related anti-correlated network (ACN) have not been well characterized. We investigated the effect of SD on functional connectivity within the DMN, and on DMN-ACN anti-correlation, both during the resting state and during performance of a visual attention task (VAT). 26 healthy participants underwent fMRI twice: once after a normal night of sleep in rested wakefulness (RW) and once following approximately 24 h of total SD. A seed-based approach was used to examine pairwise correlations of low-frequency fMRI signal across different nodes in each state. SD was associated with significant selective reductions in DMN functional connectivity and DMN-ACN anti-correlation. This was congruent across resting state and VAT analyses, suggesting that SD induces a robust alteration in the intrinsic connectivity within and between these networks.

Introduction

A single night of total sleep deprivation (SD) can result in behavioral deficits with accompanying alterations in neural activation patterns (Chee and Chuah, 2008; Goel et al., 2009). To date, the focus of most research has been on delineating the regional effects of SD on attention (Chee et al., 2008; Lim and Dinges, 2008; Tomasi et al., 2009), short-term memory (Chee and Chuah, 2007) and executive function (Nilsson et al., 2005). In contrast, far less is known about the effect of sleep deprivation on intrinsic low-frequency connectivity within the Default Mode Network (DMN) and its anti-correlated network (ACN).

The DMN is a network of brain regions that consistently deactivates in response to externally oriented tasks (Raichle et al., 2001; Shulman et al., 1997) and activates in response to numerous tasks involving internally oriented cognition (Bar, 2007; Binder et al., 2009; D'Argembeau et al., 2005; Hassabis and Maguire, 2007). The main DMN nodes—the posterior cingulate cortex (PCC), precuneus and retrosplenial cortex, the dorsal and ventral medial prefrontal cortex (MPFC), inferior parietal lobule (IPL), lateral temporal cortex (LTC), and hippocampal formation (Buckner et al., 2008)—show correlated low-frequency BOLD signal fluctuations, suggesting functional connectivity (Greicius et al., 2003).

Interestingly, these low-frequency signals are anti-correlated with several regions normally activated as a group by externally oriented tasks (Fox et al., 2005). This anti-correlated network (ACN) includes the frontal eye fields (FEF), intraparietal sulcus (IPS), middle temporal region (MT), supplementary motor area (SMA), inferior parietal lobule (also referred to as the temporoparietal junction (TPJ; Corbetta and Shulman, 2002), dorsolateral prefrontal cortex (DLPFC), and Insula (Fox et al., 2005). Switching between externally and internally oriented cognition is thought to be mediated via a competitive relationship between the ACN and DMN (Fox and Raichle, 2007; Fox et al., 2005).

Relevant to the current work, DMN connectivity and anti-correlation is diminished in many neurological and psychiatric disorders (Broyd et al., 2009; Buckner et al., 2008). Functional connectivity within the DMN is also diminished when healthy persons enter deep sleep (Horovitz et al., 2009). Both DMN functional connectivity and anti-correlation are reduced subsequent to general anesthesia (Boveroux et al., 2010; Deshpande et al., 2010), leading to the notion that diminished DMN connectivity and anti-correlation can index disrupted brain function in a variety of contexts. This motivated us to investigate if DMN connectivity and anti-correlation is altered in healthy persons undergoing a night of total SD, given the association of this state with aforementioned alterations in cognitive function.

Several SD studies evaluating short-term memory (Chee and Choo, 2004; Chee and Chuah, 2007; Choo et al., 2005) have revealed reduction in *task-related deactivation* across several nodes of the DMN. However, a recent study evaluating working memory reported *reduced* deactivation in the MPFC along with *increased* precuneus

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doi:10.1016/j.neuroimage.2011.08.026

deactivation (Gujar et al., 2010), suggesting altered functional connectivity *between DMN nodes* during SD. Indeed, recent work involving partial SD reported such reductions in DMN functional connectivity, along with reduced anti-correlation between the DMN and ACN (Sämann et al., 2010).

Functional connectivity involving the DMN has typically been evaluated using resting state data, but data acquired while participants perform tasks has also been used (Fair et al., 2007; Fransson, 2006; Greicius et al., 2003; Greicius and Menon, 2004). One approach is to regress out task-related activity before evaluating DMN functional connectivity (Fair et al., 2007). Although some studies suggest that this approach generates results comparable to those obtained from resting state data (Arfanakis et al., 2000; Fair et al., 2007), others suggest otherwise (Esposito et al., 2006, 2009; Fransson, 2006).

In the present study, we evaluated the effect of SD on functional connectivity within the DMN and anti-correlation between the DMN and ACN, both during resting state and while volunteers performed a visual attention task (VAT). This comparison is important in SD studies because sleepiness increases in the supine position (Caldwell et al., 2003) and is expected to be accentuated following sleep deprivation, particularly in the absence of task performance. As such, it might be useful to assess changes in network connectivity while a person is engaged in a task to reduce the likelihood of volunteers falling asleep.

Materials and methods

Participants

Twenty-six healthy right-handed volunteers (11 male, 22.5± 2.0 years) participated in the experiment after giving informed consent. Participants were selected from respondents to a web-based questionnaire. They 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), (4) not be of extreme morning or evening chronotype (score no greater than 22 on a modified Morningness–Eveningness scale; Horne and Ostberg, 1976), (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 two-week duration of the study, and only those whose actigraphy data indicated habitual good sleep (i.e., slept no later than 0100 h and woke no later than 0900 h) were recruited for the study.

Study procedure

Participants visited the laboratory three times. First, they attended a briefing session during which they were informed about the study protocol and practiced on the experimental task. At the end of this session, every participant was given a wrist actigraph to wear throughout the study. The second and third visits involved participating in the actual fMRI experiment. The first scanning session took place approximately one 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 separated by one week. This was to minimize the possibility of residual effects of sleep deprivation on cognition in participants whose sleep-deprivation session preceded their rested wakefulness session. The RW session took place at 0800 h. During the SD session, participants were monitored in the lab from 1900 h onward and scanning took place the next day at approximately 0500 h. 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. All participants indicated that they did not smoke or consume any medications, stimulants, caffeine or alcohol for at least 24 h prior to scanning.

Experimental task

The VAT stimuli (Fig. 1) were single large, global letters (H or S; 3.3°×2.1°) composed of several, smaller local letters (H or S; 0.6°×0.4°) (Navon, 1977). The global letter and the local letters were either congruent (i.e., a global H made up of local Hs and global S made up of local Ss) or incongruent (i.e., a global H made up of local Ss and global Ss made up of local Hs). In each trial, a single stimulus was presented centrally for 200 ms, and participants identified either the smaller, local letters or the larger, global letters by pressing one of two buttons. At the start of each run participants were told whether they would be responding to the global or local letters. For example, during a local run they were told to respond only to the local letters for the entire duration of the run. Participants performed 3 runs of the global task and 3 runs of the local task. There were 96 trials in each run, with equal numbers of congruent stimuli and incongruent stimuli. The trials were presented in a counterbalanced order that was predetermined for each participant such that there was an equal likelihood of a trial type appearing after every trial type in the design. The inter-trial interval (ITI) ranged from 3.0 to 9.0 s (mean ITI = 4.2 s) following an exponential distribution that favored short ITIs. This distribution has been shown by simulation to be efficient in uncovering differences in signal strength elicited by various experimental conditions (Hagberg et al., 2001).

Stimuli were presented with MR-compatible LCD goggles (Resonance Technology, Los Angeles, USA), and participants responded using a button box held in the right hand.

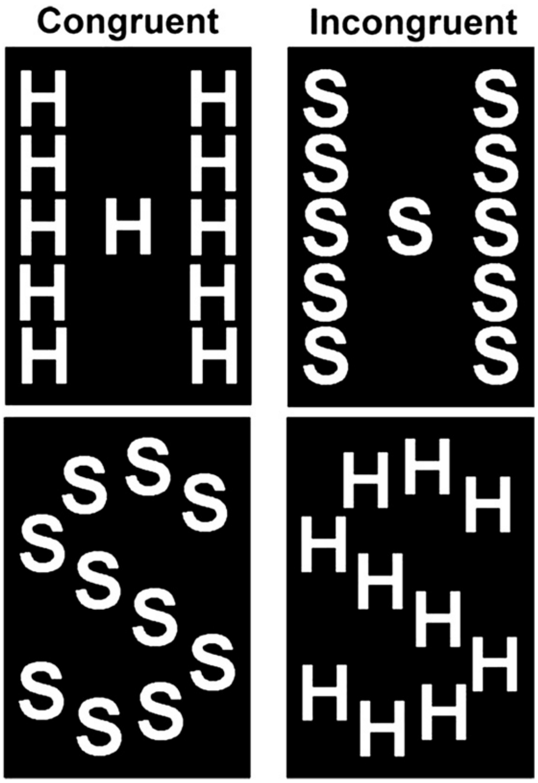

Fig. 1. Stimulus layout for VAT. Stimuli were single large, global letters made up of smaller local letters. Global and local letters were either congruent (i.e., a global H made up of local Hs) or incongruent (i.e., a global H made up of local Ss). During each trial, a single stimulus was presented centrally. Participants identified either the local or global letters by pressing one of two buttons.

Resting state run

Following the VAT, participants completed a resting state run, during which they were instructed to lie still with their eyes focused on the central fixation cross for 8 min. Participants were told to avoid head movements and swallowing.

Imaging procedure and analysis

Images were acquired on a 3T TIM Trio system (Siemens, Erlangen, Germany). A gradient echo-planar imaging sequence was used with TR of 1500 ms, field of view of 192 × 192 mm and a 64 × 64 mm pixel matrix. Twenty-eight oblique axial slices (4 mm thick with a 0.4 mm inter-slice gap) parallel to the AC–PC line were acquired. High-resolution coplanar T1 images (0.75 × 0.75 × 4.4 mm) were also obtained to facilitate coregistration. A further high-resolution anatomical reference image was acquired using a 3D-MPRAGE sequence for the purpose of Talairach normalization.

The functional images were processed using Brain Voyager QX version 1.10.3 (Brain Innovation, Maastricht, Netherlands). To correct for motion across runs, all functional images were aligned using rigid body transformation to the first image of the functional run acquired immediately before the coplanar T1-weighted image. Inter-slice timing differences attributable to slice acquisition order were adjusted using cubic spline interpolation. Gaussian filtering was applied in the spatial domain using a smoothing kernel of 8 mm FWHM for group level analyses. The functional data was coregistered to the high-resolution anatomical image using the T1 coplanar image, before being resampled to 3 mm isovoxel resolution in Talairach space using affine transformation (Talairach and Tournoux, 1988).

The main analysis involving the VAT used a single run of the task, which was truncated to have the same number of time points as the resting state analysis (318 time points). Run 3 of the VAT was selected, to minimize potential confounds such as time on task effects (Lim et al., 2010).

A band pass filter (0.009–0.09 Hz) was applied to reduce the effect of high frequency noise and very low-frequency drifts (Andrews-Hanna et al., 2007; Lowe et al., 1998; Sämann et al., 2010). For each data set, a separate general linear model (GLM) analysis was then performed including the following parameters: 1) the global brain signal (including signal from ventricular CSF), and 2) the six motion correction parameters. In addition, for the VAT data, task-related activity was modeled with finite impulse response function predictors (14 timepoints, covering 21 s). The residuals were then obtained by subtracting the estimated GLM model from the time series, and used for connectivity analyses. Previous studies have found that spontaneous synchronized activity in the DMN identified after regressing out task-related activity can yield similar results to resting state data (Fair et al., 2007).

Functional connectivity was determined in the same manner for the resting state and VAT analyses. Regions of interest (ROI) were selected independently for resting state and VAT based on RW whole-brain correlation maps with an *a priori* defined PCC seed (9 × 9 × 9 mm cube) taken from the literature (Andrews-Hanna et al., 2007). Despite independent selection, node locations were highly consistent across VAT and resting state analyses (Fig. 2; Suppl Tables 1 and 2).

Six additional DMN ROI whose time series showed maximum positive correlation with the PCC seed were selected: dorsal and ventral medial prefrontal cortices (dMPFC, vMPFC), bilateral inferior parietal lobules (LIPL, RIPL) and bilateral lateral temporal cortices (LLTC, RLTC).

Six ACN nodes were also selected based on voxels showing maximal anti-correlation with the PCC seed: bilateral insula (L Insula, R Insula), bilateral intraparietal sulcus (LIPS, RIPS) and bilateral temporoparietal junction (LTPJ, RTPJ). These specific nodes were chosen based on reports that they belong to putative sub-networks of the ACN: the insula is implicated in a salience network (Seeley et al., 2007; Sridharan et al., 2008); the IPS in the dorsal attention network; and the TPJ in the ventral attention network (Corbetta and Shulman, 2002; Fox et al., 2006a).

For RW and SD, functional connectivity during resting state and VAT analyses was assessed by computing pairwise correlations across the 7 DMN nodes and between the 7 DMN nodes and 6 ACN nodes (time series averaged across a cube of size 9 × 9 × 9 mm). The r values were Fisher-transformed (z') before further parametric statistical analyses to ensure that the data approximated a normal distribution. To determine the effect of SD on functional connectivity and anti-correlation, 2 × 2 repeated measures ANOVA were performed on the z' values obtained from each node pairing (data type; resting state vs. VAT × state; RW vs. SD). All statistics were Bonferroni corrected for multiple comparisons.

An additional analysis to investigate functional connectivity changes within the DMN across state was carried out using all 6 runs of the VAT. Here, preprocessing and analysis was the same as the above VAT analysis. However, the 6 DMN ROI were picked independently for each run. Pearson's r values for each of the node pairings in RW and SD were then averaged across the 6 runs. These averaged r values were then Fisher-transformed, before two-tailed, repeated measures t-tests between RW and SD (Bonferroni corrected) were performed on the z' values obtained from each node pairing.

Behavioral analysis

Response time was determined using only trials with correct responses (correct RT), excluding lapse trials (no response or RT > 3000 ms). The intra-individual coefficient of variation was calculated for each participant by dividing the standard deviation of correct RT by the mean correct RT. This value was then averaged across participants for each state.

Behavioral accuracy was measured using corrected recognition (Hits–False Alarms). Behavioral deficits related to SD were evaluated using paired one-tailed t-tests. SD-related functional connectivity reduction and SD-related declines in behavioral performance were then correlated to examine the functional consequences of changes in DMN connectivity and behavior.

Results

Behavioral findings

Sleep deprivation resulted in a decline in response accuracy (RW mean accuracy 89.4%, SD mean accuracy 77.8%; $t_{25} = 5.15$, $p < 0.0001$; Table 1). The number of behavioral lapses increased during SD relative to RW (12.5% vs. 2.8%; $t_{25} = 5.65$, $p < 0.0001$). SD resulted in slower responses ($RT_{correct}$ 687 ms vs. $RT_{correct}$ 632 ms; $t_{25} = 3.38$, $p < 0.01$) and increased intra-individual variability in response time (0.29 vs. 0.22; $t_{25} = 4.78$, $p < 0.0001$).

Reduced functional connectivity within DMN nodes: observed in both VAT and resting state analyses

Within the DMN, there was a main effect of state on the functional connectivity of 3 node pairs: dMPFC and LIPL; vMPFC and LIPL; PCC and LIPL (Fig. 3; Suppl. Table 3).

Reduced anti-correlation between DMN and ACN nodes: observed in both VAT and resting state analyses

A main effect of state was found on the anti-correlation between 20 DMN-ACN node pairs. The effect was mostly present between lateral nodes of the DMN, particularly IPL, and much of the ACN (Fig. 4; Suppl. Table 4).

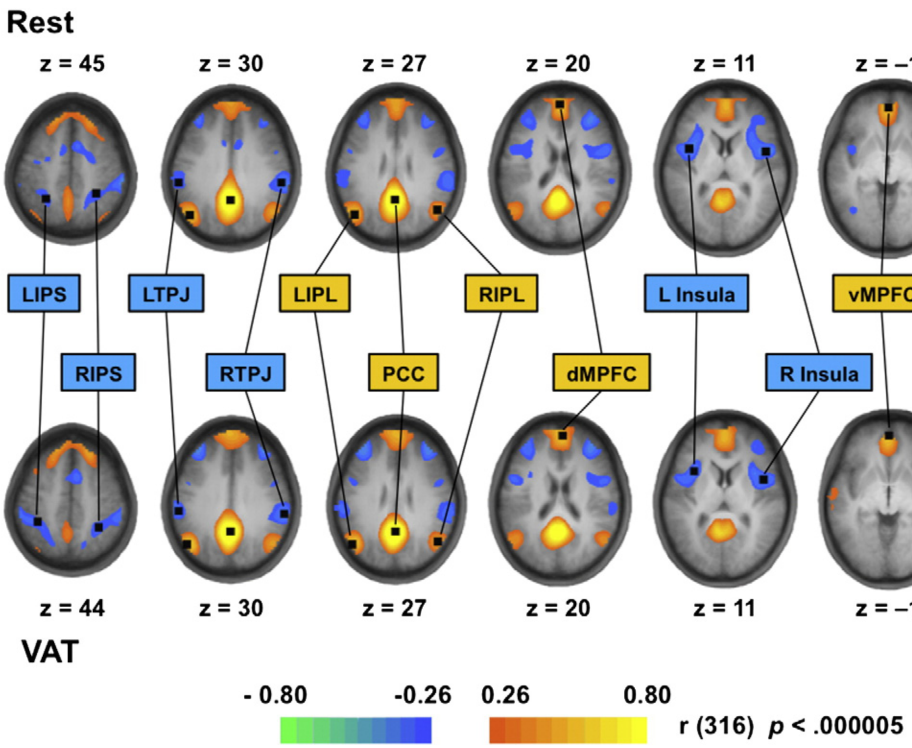

Fig. 2. DMN and ACN node location in Rest and VAT. Correlation maps between an *a priori* selected PCC seed ($9 \times 9 \times 9$ mm cube) and all other voxels in the brain. All other nodes were selected based on the *r* values ($9 \times 9 \times 9$ mm cube centered on peak voxel), 6 from the DMN (positive *r*, yellow labels), and 6 from the ACN (negative *r*, blue labels). The nodes were defined separately for the resting state and VAT data, but show a high degree of spatial overlap (Suppl. Tables 1 and 2). Black squares depict actual voxels selected for each node.

Effects of data type or interaction between data type and state

Within the DMN, no significant effects of data type, or interactions between data type and state, were found (Suppl. Table 3). Between the DMN and ACN, a single significant data type by state interaction was found between LLTC and LTPJ ($F_{1,25} = 21.00$, $p < 0.001$).

The effect of utilizing additional VAT runs

Analysis was also conducted using the average of all 6 VAT runs. Within the DMN, 14 node pairings showed a significant negative effect of SD on functional connectivity (Fig. 5).

Absence of brain-behavior correlation

The observed decline (RW-SD) in functional connectivity between 3 DMN node pairings during the resting state did not significantly correlate with any of the behavioral measures derived from the VAT (RW-SD; corrected accuracy, $RT_{corrected}$, RT variability and behavioral lapses; Suppl. Table 5). This was also true of the decline in functional connectivity within the DMN during VAT (Suppl. Table 6) and of the SD-related reduced anti-correlation, both during resting state and VAT (Suppl. Tables 5 and 6).

Table 1
Behavioral data from the VAT task after a normal night's sleep and after 22–24 h of sleep deprivation.

	RW	SD
Accuracy (%)	93.35 (6.31)	82.71 (12.02)
Lapses (%)	2.77 (4.05)	12.50 (10.88)
Correct RT (ms)	632 (102)	687 (84)
Intra-individual coefficient of variation (StdDev RT/mean RT)	0.22 (0.07)	0.29 (0.06)

SD was associated with significant reductions in performance across all behavioral measures ($p < .05$).

Discussion

We found SD to be associated with reduced functional connectivity within the DMN and reduced anti-correlation between the DMN and ACN. This was true for both resting state and VAT analyses. Declines in DMN connectivity and anti-correlation consistently affected the IPL nodes. Despite inherent differences between resting state and VAT time series, there was no significant effect of data type or interaction between data type and state when comparing data of equivalent duration. However, analyzing the data using multiple VAT runs uncovered more extensive declines in DMN functional connectivity. Finally, despite the unequivocal state changes in connectivity and

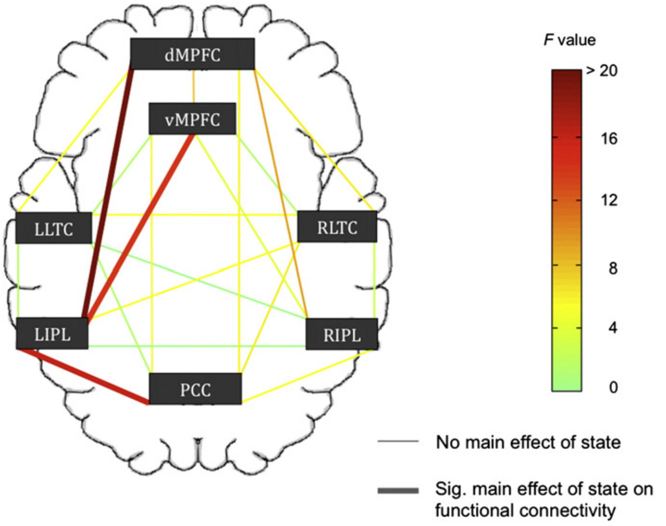

Fig. 3. Main effect of state on DMN functional connectivity. A significant main effect of state on DMN functional connectivity was found between 3 node pairs; LIPL and dMPFC, LIPL and vMPFC, and LIPL and PCC (Bonferroni corrected $p < 0.05/21 = 0.002$).

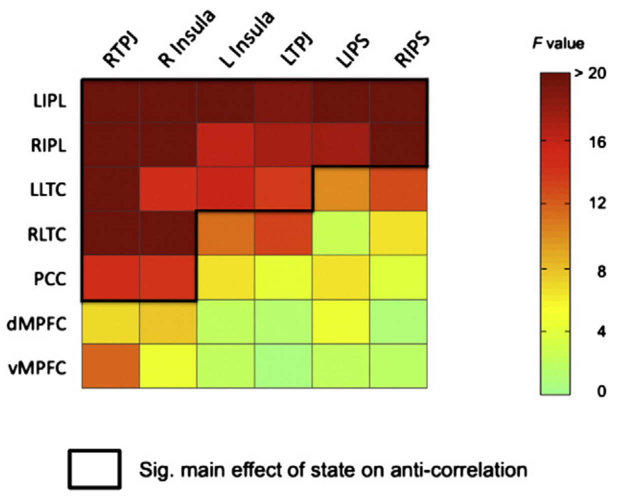

Fig. 4. Main effect of state on DMN-ACN anti-correlation. A significant main effect of state on anti-correlation was found between 20 DMN-ACN node pairs (Bonferroni corrected $p < 0.05/42 = 0.001$).

anti-correlation, there was no significant correlation between these alterations and behavioral changes induced by sleep deprivation.

SD is associated with reductions in DMN functional connectivity and anti-correlation

Reduced responsiveness to the environment is associated with declines in functional connectivity within and between brain networks. Reduced functional connectivity between anterior and posterior midline nodes of the DMN was observed during the transition into slow-wave sleep (Horovitz et al., 2009; Sämann et al., 2011). Slow-wave sleep has also been associated with reduced anti-correlation between the DMN and nodes of the ACN, such as the insula (Sämann et al., 2011). Such findings are not limited to deep sleep. They have been demonstrated during light sleep (Sämann et al., 2011) and after partial sleep deprivation (Sämann et al., 2010). Indeed, when responsiveness to the external environment is pharmacologically suppressed, connectivity between the PCC and other DMN nodes was similarly reduced (Greicius et al., 2008). Reduced anti-correlation between the DMN and parts of the ACN has also been demonstrated after Propofol-induced loss of consciousness (Boveroux et al., 2010). Moreover, these within and between network decouplings appear to be graded, with deeper anesthesia being associated with more widespread losses of connectivity (Boveroux et al., 2010; Deshpande et al., 2010).

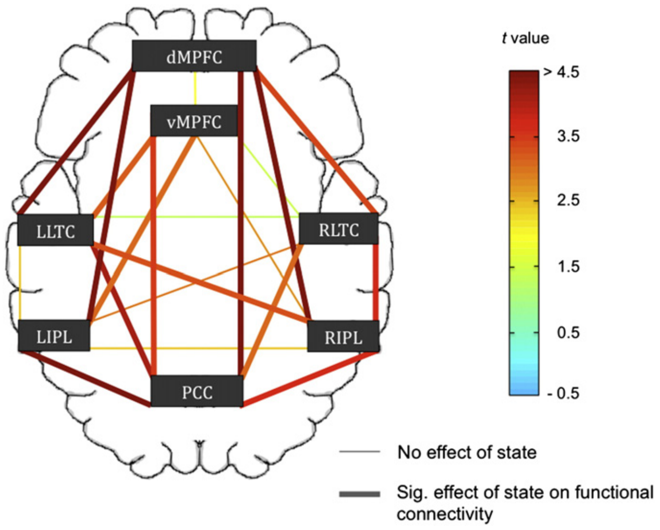

Fig. 5. Effect of state on DMN functional connectivity: average of 6 VAT runs. An analysis using an average of 6 VAT runs found extensive functional connectivity declines within the DMN after SD. t-tests showed significant effects of SD in 14 of 21 node pairings (RW>SD, Bonferroni corrected $p < 0.05/21 = 0.002$).

We found that SD-related alterations in connectivity and anti-correlation most consistently involved the IPL nodes. Previous work has found SD-related reduced IPL *deactivation* during a visual short-term memory task (Chee and Chuah, 2007), while resting state analysis has revealed reductions in IPL-MPFC functional connectivity during sleep (Horovitz et al., 2009) and after partial SD (Sämann et al., 2010). The IPL region is implicated in diverse cognitive operations (Laird et al., 2009), including bodily awareness (Felician et al., 2009), generating a sense of personal responsibility (Schaich Borg et al., 2006), and moral decision-making (Raine and Yang, 2006). These functions correspond to behaviors negatively affected by SD. Bodily connection (Giesbrecht et al., 2007), blame acceptance (Kahn-Greene et al., 2006), and responding to personal moral dilemmas (Killgore et al., 2007) are all impaired following SD. Further work is needed to explore whether this cluster of deficits maps onto SD-related reduced IPL functional connectivity and anti-correlation.

Task data compliments resting state

We explored whether the effects of SD on the DMN and ACN would be detectable in the underlying BOLD signal after regressing out task-related activity. As we sought to reduce the effect of sleep intrusions on the data, we originally anticipated this data type to be less sensitive to connectivity alterations than the resting state data. This is because performance of the VAT ensured participants maintained a higher degree of wakefulness. However, we found only a single significant interaction between data type and state, and no main effects of data type, both within the DMN, and between the DMN and ACN.

While in broad agreement with previous work comparing resting state connectivity inferred from task-related and resting state data (Fair et al., 2007), these present results differ from ICA-based studies. These latter studies have reported changes in the spatial extent of functional connectivity within the DMN with increased working memory load relative to resting state data (Esposito et al., 2006, 2009). The absence of such changes in the current study may stem from a difference in the measure of interest. Rather than focus on spatial extent, the seed-based approach used here compared correlations between spatially bounded nodes.

We found reduced DMN functional connectivity and anti-correlation during the VAT. This finding concurs with studies showing SD-related reduced DMN *deactivation* during task performance (Chee and Choo, 2004; Chee and Chuah, 2007; Choo et al., 2005). Intrinsic low-frequency activity has been postulated to influence activity at higher-frequency bands via power modulations (Buzsáki and Draguhn, 2004; Leopold et al., 2003). In support of this, intrinsic activity in motor regions has been shown to account for a significant proportion of the inter-trial variability in activity evoked by a button press task (Fox et al., 2006b), and for variance in behavioural performance (Fox et al., 2007). Thus, altered low-frequency functional connectivity within the DMN, and between the DMN and ACN, could contribute to impaired task-related DMN deactivation after SD.

Potential benefits of using multi-run task data to assess DMN connectivity

We found that using multiple VAT runs uncovered more extensive alteration in DMN functional connectivity after SD. Research on underlying correlations in low-frequency activity in the DMN and ACN often involves only resting state data, because it is straightforward to acquire, and “uncontaminated” by task activity (Fransson, 2006). Comparisons across groups or states are thus typically based on a single run of 6–10 min. Acquiring more resting state data to increase the power to detect subtle alterations between groups may decrease the signal to noise ratio due to factors such as increased head motion (Fox and Greicius, 2010). Additionally, it might be difficult to elicit the co-operation of volunteers with behavioral abnormalities, young children or those who are disposed to falling asleep. Using task data may circumvent some of these issues. Multiple runs are already collected, allowing an analysis based on markedly more data points. Critically, the present study demonstrates that task data can be used to show both equivalent results to resting state when the volume of data is matched, and more extensive effects when multiple task runs are used.

Absence of brain-behavior correlations

Despite unequivocal SD-related behavioral declines in VAT performance and reductions in both DMN functional connectivity and DMN-ACN anti-correlation, no significant correlations were found between these measures at the level of individual subjects. This was unexpected, given that stop-signal errors (Li et al., 2007) and lapses of attention (Weissman et al., 2006) have been associated with a failure to deactivate the DMN. However, little is known about how intrinsic activity interacts with task-related activity, and by extension, behavioral performance (Northoff et al., 2010). Furthermore, the few studies that do report correlations between resting functional connectivity and behavioral measures (e.g. Kelly et al., 2008) have tended to use attention-demanding tasks such as the Eriksen flanker task. Delineating the intrinsic network properties that correlate with less demanding tasks such as the VAT may require a fine-grained approach that goes beyond examining limited DMN and ACN nodes.

Limitations

Analysis was restricted to bivariate correlations between node pairs. Consequently, only relative changes between nodes could be detected. It was not possible to determine how SD affected individual nodes, or how the nodes influenced one another across states. Techniques such as ICA and Granger causality analysis could be used in the future to explore these questions. Further, the results of our task analysis were based on a single VAT. As such, they apply primarily to visual attention and cannot be generalized to other behavioural domains.

Conclusion

SD was associated with reduced DMN functional connectivity and DMN-ACN anti-correlation. This was true in the resting state and VAT analyses. The IPL node of the DMN was consistently impaired and may represent an early marker for the effects of SD, as well as an indicator of hitherto unexplored behavioural impairments. We demonstrated that task data could be used to show equivalent results to resting state when the volume of data was matched, supporting the notion that reduced deactivation after SD may be related to intrinsic DMN impairment. Moreover, we found more extensive effects of SD when multiple task runs were used, implying that under certain conditions task data may be preferable. How functional connectivity relates to behaviour and stimulus-evoked activation and deactivation of the DMN and ACN remains to be elucidated. SD is a useful assay for such questions since it represents one of the few reversible state changes that allows participants to perform relatively demanding tasks.

Acknowledgments

Grace Tang, Kavitha Dorairaj, Praneeth Namburi, Kong Danyang and Annette Chen contributed to gathering data. This work was supported by grants awarded to Dr Michael Chee from the Defense Science and Technology Agency Singapore (POD0713897) and the National Research Foundation Singapore (STaR Award).

Appendix A. Supplementary Data

Supplementary data to this article can be found online at doi:10.1016/j.neuroimage.2011.08.026.

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