Sleep Deprivation Elevates Expectation of Gains and Attenuates Response to Losses Following Risky Decisions

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Study Objectives: Using a gambling task, we investigated how 24 hours of sleep deprivation modulates the neural response to the making of risky decisions with potentially loss-bearing outcomes.

Design: Two experiments involving sleep-deprived subjects were performed. In the first, neural responses to decision making and reward outcome were evaluated. A second control experiment evaluated responses to reward outcome only.

Participants: Healthy right-handed adults participated in these experiments (26 [mean age 21.3 years] in Experiment 1 and 13 [mean age 21.7 years] in Experiment 2.)

Measurements and Results: Following sleep deprivation, choices involving higher relative risk elicited greater activation in the right nucleus accumbens, signifying an elevated expectation of the higher reward once the riskier choice was made. Concurrently, activation for losses in the insular and orbitofrontal cortices was reduced, denoting a diminished response to losses. This latter finding of reduced insular activation to losses was also true when volunteers were merely shown the results of the computer's decision, that is, without having to make their own choice.

Conclusions: These results suggest that sleep deprivation poses a dual threat to competent decision making by modulating activation in nucleus accumbens and insula, brain regions associated with risky decision making and emotional processing.

Keywords: Functional neuroimaging, risk taking, decision making, nucleus accumbens, orbitofrontal cortex

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SLEEP DEPRIVATION HAS GROWN INCREASINGLY COMMON IN DEVELOPED COUNTRIES.[1] LACK OF ADEQUATE SLEEP IMPAIRS VIGILANCE, FLEXIBLE THINKING, working memory, and executive functioning.[2-5] These cognitive changes may combine to impair the ability to make favorable decisions under conditions of risk.

Understanding why we make poorer decisions when sleep deprived is important, not only because of the increasing numbers of persons affected, but also because of unprecedented opportunities to incur damaging losses by means such as online gambling.[6] Indeed, sleep-deprived participants have been shown to choose higher-risk decks and exhibit reduced concern for negative consequences when performing a variant of the Iowa Gambling Task.[3,7] Well-rested participants learn to avoid high-risk decks and to choose from the advantageous decks, but sleep-deprived participants tend to continue to choose from the risky decks as the game progresses.[3,7]

Two aspects of decision making are particularly likely to be affected by sleep deprivation: the ability to ascertain risk as well as the ability to learn emotionally from the consequences of decisions.[8] The former involves harnessing prior knowledge of potential rewards and their valuation to make decisions and involves activation of the dorsolateral prefrontal cortex and the striatum.[9] The effects of sleep deprivation on dorsolateral prefrontal cortex activation in non-gambling tasks have been well characterized. They vary with task,[10,11] as well as across individuals,[12,13] with relatively preserved task performance being associated with either higher activation[15,16] or only modest activation decline.[14] In contrast, the effect of sleep deprivation on the engagement of striatal regions remains unexplored. Work to date on healthy, non sleep-deprived adults suggests that the ventral striatum participates in both the anticipation and the receipt of reward,[17,18] whereas the dorsal striatum has been associated with the processing of experienced reward magnitude and valence.[19]

Recent findings suggest that emotion also plays an important role in decision making.[20] As an example, choices made in a gambling task after 49 hours of sleep deprivation are similar to those of patients with lesions in the ventromedial prefrontal cortex,[7] a brain region (in conjunction with the neighboring orbitofrontal cortex) that is associated with emotional experiences of gains and losses.[9] Work involving a non-gambling task has also shown reduced glucose metabolism in the orbitofrontal region following sleep deprivation,[21] but the link between risky behavior following loss of sleep and orbitofrontal engagement has not been explicitly demonstrated.

In Experiment 1, we characterized the effect of sleep deprivation on putative substrates for risk-reward ascertainment (dorsolateral prefrontal cortex and striatum), as well as emotional learning (ventral and orbitofrontal cortex), using a gambling task (Figure 1a). Only a few gambling experiments involving functional magnetic resonance imaging have evaluated decision making, anticipation, and reward processing concurrently,[22,23] and none of those have used a sleep deprivation manipulation.

We separated decision and reward phases of the task in Experiment 1, but a potential concern was that the relatively slow evolution of the BOLD response could cause activation associated with decision making to influence the peristimulus baseline in the reward phase. A further concern in Experiment 1 was a limited number of loss trials, particularly for the risk-averse individu-

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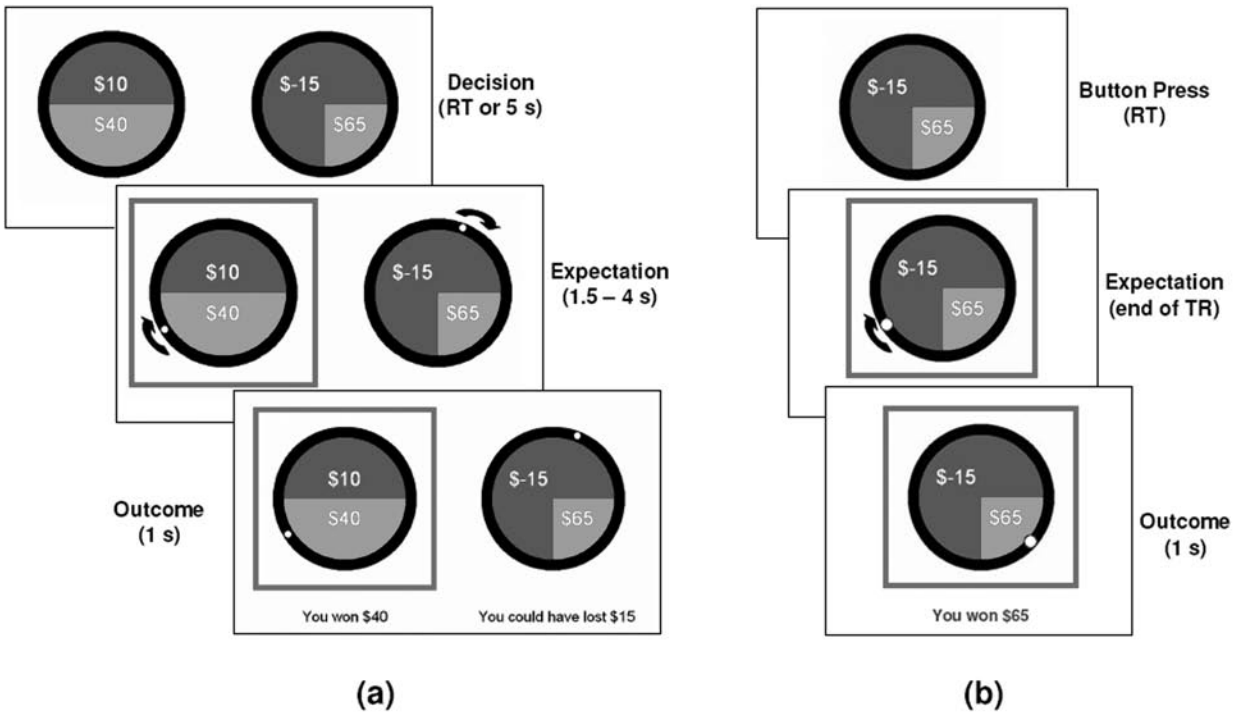

Figure 1—(a) A schematic of the gambling task used in Experiment 1, illustrating paired Low-Risk (left) and High-Risk (right) gambles. In each trial, subjects were presented with a pair of gambles and chose between them by pressing 1 of 2 buttons within 5 seconds. A red rectangle immediately appeared around the chosen gamble followed by small white balls, which spun around the perimeter of each gamble for between 1.5 to 4 seconds. The outcome of each gamble was indicated by the final position of the balls and reinforced by text messages that appeared for 1 second. This was then followed by a variable fixation of 1.5 to 6.5 seconds prior to the next trial. (b) A schematic of the task used in the Experiment 2, based on a High-Risk gamble. In each trial, subjects pressed a button as soon as the gamble appeared on the screen. In contrast to Experiment 1, the duration of the expectation phase was restricted to the completion of the current TR. Other aspects of the experiment were identical to Experiment 1.

als. To alleviate these concerns, we ran a second experiment that involved the presentation of passive gambles in which decision making was rendered unnecessary by having the computer make predetermined choices (consisting of equal number of losses and gains; Figure 1b).

METHODS

Participants

Twenty-six right-handed, healthy adults (12 women, mean age = 21.3, SD = 1.6 years) participated in Experiment 1 and a further 13 adults (3 women, mean age = 21.7, SD = 1.5 years) participated in Experiment 2. Wrist actigraphy was used to monitor the sleeping habits of the participants over the duration of the study (approximately 2 weeks). The actigraphy data of all the participants indicated habitually good sleep (ie, they usually went to sleep no later than 1:00 AM and woke no later than 9:00 AM). Participants refrained from smoking and did not ingest medications, stimulants, caffeine, or alcohol for at least 24 hours prior to scanning. The study was approved by the Singapore General Hospital Institutional Review Board, and informed consent was obtained from all participants.

Study Procedure

Participants visited the laboratory 3 times. They first attended a briefing session during which they were informed of the study protocol and requirements and were practiced on the study task. At the end of this session, every participant was given an actigraph to wear throughout the study. The first scanning session took place approximately a week later. The order of the 2 sessions (rested wakefulness and sleep deprivation) was counterbalanced across all the participants and separated by 1 week. This was to minimize the possibility of residual effects of sleep deprivation on cognition for those participants whose sleep-deprivation session had preceded their rested-wakefulness session.[24] The rested-wakefulness session took place at 8:00 AM. For the sleep-deprivation session, participants were monitored in the lab from 6:30 PM onward, and scanning took place the next day at 7:00 AM. During the sleep-deprivation session, participants were allowed to engage in non-strenuous activities such as reading and watching videos.

Experiment 1: Procedure

Three gamble types (Certain, Low-Risk and High-Risk) were arranged in 2 possible pairings: Certain/Low-Risk and Low-Risk/High-Risk. All gambles were depicted on a pie chart in 2 neutral colors (brown and light green), highlighting the contrast between the 2 options in a risky gamble. A Certain gamble was associated with a 100% chance of winning the indicated sum. Risky gambles consisted of a choice between 2 rewards associated with paired probabilities of 25% and 75% or 50% and 50%. Volunteers always stood to gain in a Low-Risk gamble, whereas a High-Risk gamble involved the pairing of a loss with a significantly higher reward.

The reward magnitude in a risky gamble was determined by taking into account the associated probabilities. The expected values were only approximately matched between the 2 pairs of gambles presented in individual trials, but they were balanced across all trials in the experiment. The reward values varied between $4 and $30 for Certain gambles (mean expected value = $15), between $2 and $40 for Low-Risk gambles (mean expected value = $16 in Certain/Low-Risk pairs and $15 in Low-Risk/High-Risk pairs), and between $30 and $70 for High-Risk gambles (mean expected value = $14). No trial was repeated within a session, but the same gamble pairs were used in both sessions.

Each session consisted of 6 runs. Each run started with a 15-second fixation interval, the first 10 seconds of which was discarded to allow for attainment of a steady state of scanner magnetization. Each run consisted of 10 trials of each of the 3 experimental conditions and lasted a total of 305 seconds. At the beginning of each trial, 2 gambles were presented, and subjects had to choose 1 of them by pressing the appropriate button on the response box within a 5-second interval (Figure 1). A ball then appeared on each of the gambles and spun along the circumference of the circles for 1.5 to 6.5 seconds. The payout on each of the gambles was determined according to where the ball stopped. A text message then appeared, stating the amount won, as well as what would have been won had the alternative decision been taken. This message appeared for 1 second and was replaced by a variable (1.5, 4, or 6.5 seconds) inter-trial fixation interval. All 20 trial types were randomized within each run for each session and for each subject. After 20 trials (or 290 seconds from onset of the run), a fixation cross appeared and remained till the end of the run.

In the event that the subject failed to respond within 5 seconds, the trial was classified as a lapse. In such an event, the balls proceeded to spin, and messages indicating potential earnings for each gamble appeared. Across the entire cohort, there were a total of 20 such trials during the rested-wakefulness session and 28 such trials following sleep deprivation. These lapse trials were modeled as separate nuisance predictors but were not analyzed.

Experiment 2: Procedure

In our analysis of imaging data from the first experiment, we found that interesting differences in the neural responses to different gamble outcomes manifested as negative deflections relative to baseline. To evaluate the possibility that this was a result of inadequate temporal separation of the BOLD response to the decision-making and reward-outcome phases of the trials, we modified the original experiment to capture the effects of reward processing while omitting decision making.

Each trial involved the presentation of a single Certain or a High-Risk gamble (Figure 1b). Subjects were instructed to respond to every gamble by pressing a single button as soon as the gamble appeared, thus maintaining a motor-response requirement but eliminating the decision phase. Following a response, a ball appeared and spun around the gamble for the remaining part of the current TR. The predetermined outcome of each trial, selected at random, was presented as a 1-second text message. Inter-trial intervals (fixation) varied between 1.5 to 6.5 seconds. Twenty trials of the Certain gamble and 40 trials of the High-Risk gamble, half of which resulted in losses and the other half in gains, were presented. These trials, with the same range of reward values as used for Experiment 1, were presented over 2 runs in each state. We were interested only in the response to the outcomes for the High-Risk gambles in this study.

Imaging Procedure

Imaging was performed on a Siemens 3T Allegra system (Siemens Allegra, Erlangen, Germany). Stimuli were rear projected (Epson EMP 7250) and participants viewed them using an angled mirror fastened to the head coil. A bite-bar was used to reduce head motion. Thirty-six oblique axial slices were acquired in both experiments, approximately parallel to the AC-PC line, using a T2* weighted gradient-echo EPI sequence (TR = 2500 ms; effective TE = 30 ms; matrix = 64 × 64; FOV = 192 × 192 mm; 3.0-mm thickness, 0.3-mm gap). High-resolution anatomic reference images were obtained using a 3-dimensional MP-RAGE sequence. A high-resolution T1-weighted coplanar image was acquired in an identical orientation to the functional magnetic resonance data to facilitate registration of the functional runs to the 3D anatomic image.

Data Analysis

In Experiment 1, functional images from each subject were preprocessed and analyzed using BrainVoyager QX version 1.5.2 (Brain Innovation, Maastricht, Netherlands). Motion correction was performed. Inter-slice timing differences attributable to slice acquisition order were adjusted using linear interpolation. In the spatial domain, data were smoothed with a Gaussian smoothing kernel of 8 mm FWHM. A temporal high-pass filter of period 100 seconds was applied following linear trend removal. The functional images were aligned to coplanar high-resolution images, and the image stack was then aligned to a high-resolution 3D image of the brain. The resulting realigned data set was transformed into Talairach space.

Functional analysis at a voxel-by-voxel level was performed using a General Linear Model (GLM) with a total of 8 predictor variables (regressors) in each state (rested wakefulness, sleep deprivation). Four regressors were created for each decision type Certain/Low-Risk, Certain/Low-Risk, Low-Risk/High-Risk, Low-Risk/High-Risk). A fifth regressor (Expectation) was used to model the expectation phase, when the subjects had selected the gamble and were waiting for the results to be displayed. Three more regressors—Loss, Low-Gain, and High-Gain—were used to model the reward phase, depending on whether the actual winning was a loss, a small gain (less than $25), or a large gain, respectively. Each regressor was convolved with a hemodynamic response function and its first temporal derivative. Because there were a large number of trials that fell under the small gain category, only the parameter estimates for Loss and High-Gain predictors were used in analyzing the effect of outcome. Voxel-by-voxel repeated-measures analysis of variance (ANOVA) was performed on both the decision-making and outcome predictors across states, and a region was considered significantly active if it survived a threshold of $P < 0.001$.

Functional data from Experiment 2 were preprocessed and analyzed in an identical fashion to Experiment 1. Functional analysis at a voxel-by-voxel level was performed using a GLM with a total of 3 predictors: Certain, Gain, and Loss in each of the states. Additional region-of-interest analyses were carried out in regions that showed a significant state-by-outcome interaction in the first

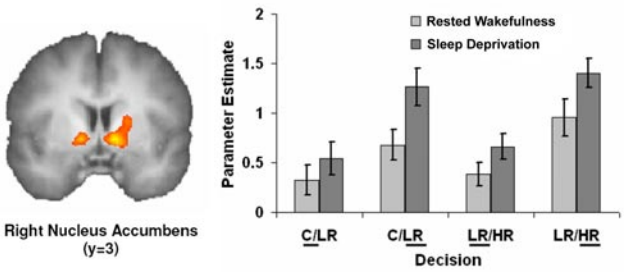

Figure 2—A significant effect of decision was found in the bilateral nucleus accumbens and caudate. The mean parameter estimates (± SEM) depict how activation in the right nucleus accumbens varied according to the decision made in different gambles: (i) choosing the Certain option in a Certain/Low-Risk gamble (C/LR), (ii) choosing the Low-Risk option in a Certain/Low-Risk gamble (C/LR), (iii) choosing the Low-Risk option in a Low-Risk/High-Risk gamble (LR/HR), and (iv) choosing the High-Risk option in a Low-Risk/High-risk gamble (LR/HR). Within each gamble pair, there was greater activation of the right nucleus accumbens for decisions involving greater risk.

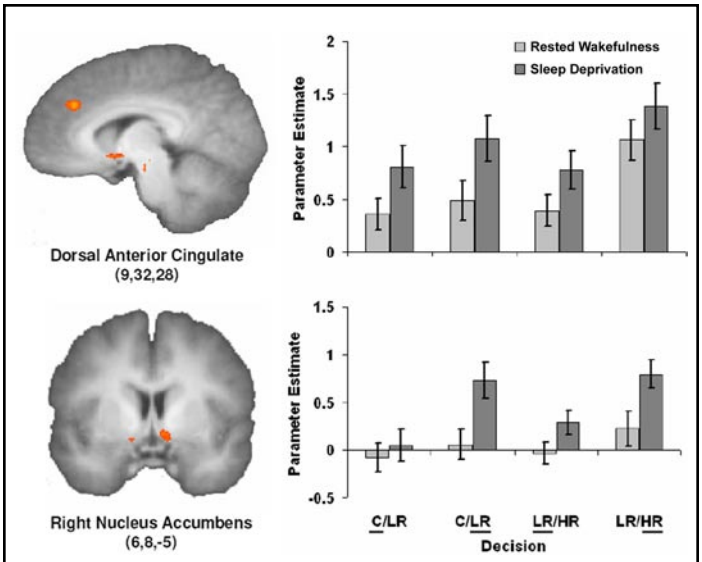

Figure 3—A significant effect of state in relation to decision making was present in the dorsal anterior cingulate, suggesting higher demands associated with resolving conflict when sleep deprived There was higher right nucleus accumbens activation for riskier decisions following sleep deprivation, suggesting a greater expectation of being rewarded for these risky decisions when sleep deprived. The mean parameter estimates (± SEM) depict how activation varied according to each decision in each state.

experiment, namely left anterior insula and left orbitofrontal cortex.

RESULTS

Experiment 1: Behavioral Results

A 4 (decision: Certain/Low-Risk, Certain/Low-Risk, Low-Risk/High-Risk, Low-Risk/High-Risk) by 2 (state: rested wakefulness, sleep deprivation) repeated-measures ANOVA on reaction times revealed significant main effects of decision ($F_{1,25}$ = 20.1, P < 0.001) and state ($F_{1,25}$ = 7.69, P = 0.01) but no interaction ($F_{1,25}$ = 1.77, NS). Participants took longer to make decisions following sleep deprivation (Table 1). Subjects also took less time to choose the Low-Risk option in both gamble pairs, indicating that this was the default option for most decisions.

We defined risk preference for each session as the number of times that the participant selected the riskier options: Certain/Low-Risk, Low-Risk/High-Risk. There was no significant difference in risk preference between the 2 states. Subjects earned an average bonus of $35.50 (SD = $6.71) for the rested-wakefulness session and $35.70 (SD = $10.08) for the sleep-deprivation session.

Experiment 1: Neural Correlates of Decision Making

Consistent with other studies, decision making in both states activated a common network of regions.[25,26] This included bilateral activation of dorsolateral prefrontal cortex, anterior insula, precentral gyrus, thalamus, anterior cingulate cortex, intraparietal sulcus, and inferior parietal lobule. A 4 (decision) by 2 (state) repeated-measures voxel-by-voxel ANOVA revealed significant effects of risk in the bilateral nucleus accumbens, anterior insula and right caudate (greater activation for risky compared to conservative decisions, Figure 2a) and significant effects of state in the right nucleus accumbens and dorsal anterior cingulate (greater activation following sleep deprivation). Posthoc tests of nucleus accumbens activation showed that there was significantly greater activation following sleep deprivation only for riskier decisions (Figures 2b and 3; Table 2).

Contrary to some prior studies,[10,27] sleep deprivation did not

Table 1—Reaction times of decisions and the percentage of risky decisions made for each gamble type during normal sleep and following sleep deprivation

	Results		t-value (Sig.)
	Normal Sleep	Sleep Deprivation	
Reaction Time, ms			
Certain/Low-Risk	1660 ± 362	1827 ± 390	2.54 (.018)
Certain/Low-Risk	1509 ± 382	1636 ± 454	2.98 (.006)
Low-Risk/High-Risk	1745 ± 441	1777 ± 452	0.89 (NS)
Low-Risk/High-Risk	1821 ± 518	1946 ± 568	2.13 (.043)
Percentage of Risky Choices, %			
Certain/Low-Risk	65.51 ± 13.1	68.91 ± 14.0	1.53 (NS)
Low-Risk/High-Risk	41.98 ± 14.8	40.51 ± 10.1	0.64 (NS)

Data are presented as mean ± SEM. The t values represent the effect of state on these measures, investigated using paired-samples tests.

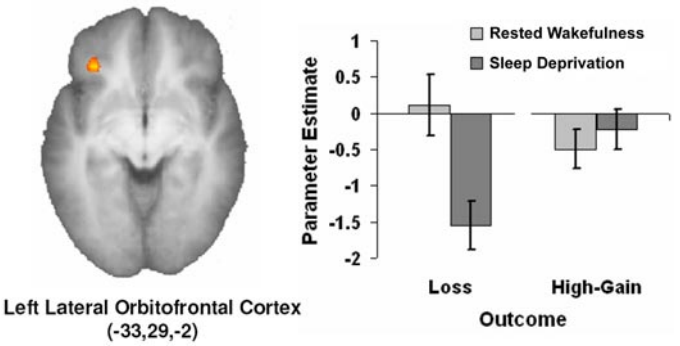

Figure 4—Mean parameter estimates (± SEM) of activation in the left lateral orbitofrontal cortex showing an effect of state as well as an interaction between state and outcome in Experiment 1. The greater activation in this region following normal sleep might reflect a signal to avoid subsequent disadvantageous decisions.

have an effect on activation in the dorsolateral prefrontal cortex, an area important for maintaining task goals.[28] There was also a notable paucity of performance lapses compared with our prior studies that tested working memory and inhibition,[12,29] attesting to higher motivation levels associated with the reward-bearing nature of the gambling task.

Experiment 1: Neural Correlates of Reward Processing

A 2 (outcome: Loss, High-Gain) by 2 (state) repeated-measures voxel-by-voxel ANOVA showed that sleep deprivation significantly reduced activation in both right and left anterior insula, as well as ventrolateral prefrontal cortex, left orbitofrontal cortex, and right superior frontal gyrus. Independent of state, greater activation for losses relative to gains occurred in bilateral anterior insula, anterior cingulate cortex and intraparietal sulcus. Greater activation for gains compared to losses was observed in the ventral striatum, including the nucleus accumbens and anterior medial prefrontal cortex. A significant state-by-outcome interaction was also present in the left anterior insula, left orbitofrontal cortex, and right superior frontal gyrus (Figures 4 and 5, Table 3).

Table 2—Talairach coordinates of regions that demonstrate significant (P < 0.001) effects of decision or state in a 4 (decision) by 2 (state) voxel-by-voxel repeated-measures analysis of variance for decision making

Region of Interest	Hemisphere	Peak Talairach Coordinates			F value
		x	y	z	
Effect of Decision					
Nuclues Accumbens	L	-12	2	-2	20.48
	R	9	-1	-4	21.21
Caudate	R	18	8	10	18.34
Anterior Insula	R	33	23	4	12.92
Thalamus	L	-3	-16	7	10.24
Effect of State					
Dorsal Anterior Cingulate	R	9	32	28	15.28
Nucleus Accumbens	R	6	8	-5	13.01
	L	-15	5	-8	9.09*

*P < 0.005

Experiment 2: Reward Processing without Decision Making

Parameter estimates from regions of interest in left anterior insula, right superior frontal gyrus, and left orbitofrontal regions, defined by the activation mask obtained from Experiment 1, were subjected to a 2 (Outcome: Loss, Gain) by 2 (State) repeated-measures ANOVA. A significant outcome by state interaction was obtained for the left anterior insula (Figure 5) but not for the right superior frontal gyrus and left orbitofrontal cortex. These findings corroborated our earlier observation pertaining to a reduced activation for losses following sleep deprivation in left anterior insula. The absence of significant effects in the left orbitofrontal cortex and right superior frontal gyrus could be attributed to a lack of need to adapt future decisions based on feedback from the current trial.

DISCUSSION

The present findings illustrate how sleep deprivation modulates the neural substrate for decisions that involve tradeoffs between

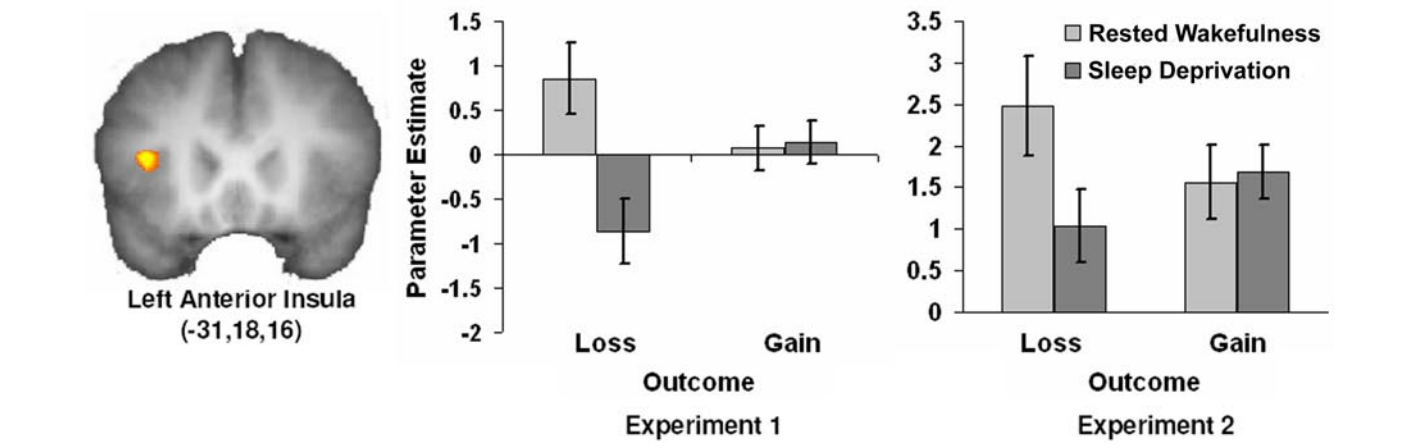

Figure 5—Mean parameter estimates (± SEM) of activation in the left anterior insula, showing an effect of state as well as a significant interaction between state and outcome in both experiments. The significantly reduced activation to losses following sleep deprivation indicates reduced response to losses incurred from risky decisions.

Table 3—Talairach coordinates of regions that demonstrate significant ($P < 0.001$) effects of outcome or state in a 2 (outcome: loss, high-gain) by 2 (state) voxel-by-voxel repeated measures analysis of variance for decision outcomes

Region of Interest	Hemisphere	Peak Talairach Coordinates			F value
		x	y	z	
Effect of Outcome					
Anterior Cingulate	R	6	14	37	71.85
Medial Prefrontal Cortex	L	-6	41	-5	61.74
Precentral Gyrus	R	42	2	37	37.11
Anterior Insula	R	33	14	1	33.75
	L	-33	17	1	31.84
Nucleus Accumbens	L	-12	5	-2	29.86
	R	18	2	-5	24.83
Intraparietal Sulcus	L	-30	-67	40	20.17
	R	33	-66	34	18.49
Effect of State					
Anterior Insula	L	-36	20	13	22.85
	R	30	26	4	12.37
Lateral Orbitofrontal Cortex	L	-30	32	-2	11.63
Inferior Frontal Gyrus	R	27	32	16	13.45
	L	-25	47	13	11.85
Superior Frontal Gyrus	R	21	29	42	13.86
State × Outcome Interaction					
Anterior Insula	L	-31	18	16	29.39
Lateral Orbitofrontal Cortex	L	-33	29	-2	39.53
Superior Frontal Gyrus	R	20	38	43	25.32

potentially higher gains associated with the risk of a loss. Historically, although several studies have shown sleep deprivation to be associated with increased risk-taking behavior, these have involved at least 36 hours of sleep deprivation.[3,7] Here, we found that 24 hours of sleep deprivation modulated neural systems associated with decision making in the absence of (and plausibly prior to) behaviorally manifest changes in risk preference. Our findings suggest that imaging data might lead standard behavioral measures in detecting this cognitive phenomenon.

Effects of Sleep Deprivation on Decision Making

Following sleep deprivation, greater activation of the dorsal anterior cingulate was observed in the decision-making phase irrespective of the type of decision made. The contributions of the cingulate to cognitive control include the detection of errors as well as monitoring for response conflict,[31] and the present findings may reflect greater effort in resolving the conflict between maximization of expected value and minimization of regret when sleep deprived.[32]

Activation of the nucleus accumbens is typically associated with gain prediction and has been shown to correlate with the magnitude of anticipated gains.[17,18] Recently, activation in this region was shown to precede risky choices in a financial decision-making task.[33] In this study, we observed increased activation in this region for the riskier decisions in both states. Additionally, choosing gambles with higher risk relative to the alternative gamble elicited significantly greater activation in the right nucleus accumbens following sleep deprivation.

We hypothesize that this increased activation could represent an increased expectation of winning the higher payout associated with the riskier decision. Thus, whereas sleep-deprived volunteers faced with any decision show behavioral and imaging features of heightened response conflict, only making a relatively higher risk choice is accompanied by a greater expectation for being rewarded.

Effects of Sleep Deprivation on Reward Processing

The flip side to the emotional high of being rewarded for a gamble is being able to learn from disadvantageous decisions. As this involves processing of emotions related to loss and regret, we evaluated the influence of sleep deprivation on emotional responses to decision outcome by comparing activation associated with losses and gains across the states.

In both experiments, selectively attenuated responses for loss in the insula may correspond to reduced disappointment in response to losses. The insular cortex, through its afferent and efferent connections to the medial and orbital prefrontal cortex, anterior cingulate, and amygdala, is thought to evaluate the emotional significance of a stimulus and generate an appropriate affective response.[34] In contexts that do not involve counterfactual reasoning, as in Experiment 2, the insula appears to respond to both positive and negative outcomes. However, only the response to losses appears to be consistent across experiments, corroborating accounts that this region is important in signaling disappointment.[35,36]

The lateral orbitofrontal cortex appears to be sensitive to the magnitude of punishment.[37,38] Reduced activation in this region to losses under conditions of sleep deprivation in Experiment 1 suggests a state-dependent impairment of the learning of negative reward associations. Damage to the orbitofrontal cortex is thought to impair learning and the ability to reverse reward associations, perhaps by disrupting the ability to use emotional markers to guide decisions.[39] Regret following poor decisions is 1 such emotional marker. In Experiment 1, losses elicited significant lateral orbitofrontal cortex activation when subjects were sleep deprived, possibly reflecting learning to avoid subsequent bad decisions.[22] As regret (distinct from disappointment) and response learning are contingent on being able to influence outcome through choice, it is possible that the lack of effect in the orbitofrontal region in the second experiment could stem from the predetermined nature of outcomes.

CONCLUSIONS

Sleep deprivation was associated with increased activation in the nucleus accumbens for risky decisions, indicating a possible shift toward risk-seeking behavior.[33] Additionally, there was decreased activation in the anterior insula following losses when sleep deprived. Finally, the attenuation of activation in the orbitofrontal cortex suggests that, in addition to altering risk preferences, sleep deprivation may also diminish the ability to learn from the negative consequences of risky behavior.

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REFERENCES

1. NSF-survey. National Sleep Foundation's Sleep in America Poll. Available at: http://www.sleepfoundation.org/press/index.php?secid = &id = 290. Accessed on: 23 May 2006.
2. Durmer JS, Dinges DF. Neurocognitive consequences of sleep deprivation. Semin Neurol 2005;25:117-29.
3. Harrison Y, Horne JA. The impact of sleep deprivation on decision making: a review. J Exp Psychol Appl 2000;6:236-49.
4. Pilcher JJ, Huffcutt AI. Effects of sleep deprivation on performance: a meta-analysis. Sleep 1996;19:318-26.
5. Roehrs T, Greenwald M, Roth T. Risk-taking behavior: effects of ethanol, caffeine, and basal sleepiness. Sleep 2004;27:887-93.
6. AGA-survey. The AGA Survey of Casino Entertainment. American Gaming Association 2006:24-30. Available at: http://www.americangaming.org/survey/index.cfm. Accessed on: 23 May 2006.
7. Killgore WD, Balkin TJ, Wesensten NJ. Impaired decision making following 49 hours of sleep deprivation. J Sleep Res 2006;15:7-13.
8. Kerr A, Zelazo PD. Development of "hot" executive function: the children's gambling task. Brain Cogn 2004;55:148-57.
9. Trepel C, Fox CR, Poldrack RA. Prospect theory on the brain? Toward a cognitive neuroscience of decision under risk. Brain Res Cogn Brain Res 2005;23:34-50.
10. Choo WC, Lee WW, Venkatraman V, Sheu FS, Chee MWL. Dissociation of cortical regions modulated by both working memory load and sleep deprivation and by sleep deprivation alone. Neuroimage 2005;25:579-87.
11. Drummond SP, Brown GG. The effects of total sleep deprivation on cerebral responses to cognitive performance. Neuropsychopharmacology 2001;25:S68-73.
12. Chee MW, Chuah YML, Venkatraman V, et al. Functional imaging of working memory following normal sleep and after 24 and 35 hours of sleep deprivation: correlations of fronto-parietal activation with performance. Neuroimage 2006;31:419-28.
13. Mu Q, Mishory A, Johnson KA, et al. Decreased brain activation during a working memory task at rested baseline is associated with vulnerability to sleep deprivation. Sleep 2005;28:433-46.
14. Chee MW, Choo WC. Functional imaging of working memory after 24 hours of total sleep deprivation. J Neurosci 2004;24:4560-7.
15. Drummond SP, Bischoff-Grethe A, Dinges DF, et al. The neural basis of the psychomotor vigilance task. Sleep 2005;28:1059-68.
16. Drummond SP, Meloy MJ, Yanagi MA, Orff HJ, Brown GG. Compensatory recruitment after sleep deprivation and the relationship with performance. Psychiatry Res: Neuroimaging 2005;140:211-23.
17. Knutson B, Adams CM, Fong GW, Hommer D. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. J Neurosci 2001;21:RC159.
18. Knutson B, Taylor J, Kaufman M, Peterson R, Glover G. Distributed neural representation of expected value. J Neurosci 2005;25:4806-12.
19. Delgado MR, Locke HM, Stenger VA, Fiez JA. Dorsal striatum responses to reward and punishment: effects of valence and magnitude manipulations. Cogn Affect Behav Neurosci 2003;3:27-38.
20. Bechara A, Damasio AR. The somatic marker hypothesis: a neural theory of economic decision. Games Econom Behav 2005;52:336-72.
21. Thomas M, Sing H, Belenky G, et al. Neural basis of alertness and cognitive performance impairments during sleepiness: effects of 24 hours of sleep deprivation on waking human regional brain activity. J Sleep Res 2000;9:335-52.
22. Coricelli G, Critchley HD, Joffily M, et al. Tegret and its avoidance: a neuroimaging study of choice behavior. Nat Neurosci 2005;8:1255-62.
23. Rogers RD, Ramnani N, Mackay C, et al. Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. Biol Psychiatry 2004;55:594-602.
24. Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 2003;26:117-26.
25. Ernst M, Nelson EE, McClure EB, et al. Choice selection and reward anticipation: an fMRI study. Neuropsychologia 2004;42:1585-97.
26. Huettel SA, Song AW, McCarthy G. Decisions under uncertainty: probabilistic context influences activation of prefrontal and parietal cortices. J Neurosci 2005;25:3304-11.
27. Drummond SP, Brown GG, Gillin JC, et al. Altered brain response to verbal learning following sleep deprivation. Nature 2000;403:655-7.
28. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. Annu Rev Neurosci 2001;24:167-202.
29. Chuah YML, Venkatraman V, Dinges DF, Chee MW. The neural basis of interindividual variability in inhibitory efficiency after sleep deprivation. J Neurosci 2006;26:7156-62.
30. Rushworth MF, Walton ME, Kennerley SW, Bannerman DM. Action sets and decisions in the medial frontal cortex. Trends Cogn Sci 2004;8:410-7.
31. Ullsperger M, von Cramon DY. Neuroimaging of performance monitoring: error detection and beyond. Cortex 2004;40:593-604.
32. Walton ME, Bannerman DM, Alterescu K, Rushworth MF. Functional specialization within medial frontal cortex of the anterior cingulate for evaluating effort-related decisions. J Neurosci 2003;23:6475-9.
33. Kuhnen CM, Knutson B. The neural basis of financial risk taking. Neuron 2005;47:763-70.
34. Ernst M, Paulus MP. Neurobiology of decision making: a selective review from a neurocognitive and clinical perspective. Biol Psychiatry 2005;58:597-604.
35. O'Doherty J, Critchley H, Deichmann R, Dolan RJ. Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices. J Neurosci 2003;23:7931-9.
36. Sanfey AG, Rilling JK, Aronson JA, Nystrom LE, Cohen JD. The neural basis of economic decision-making in the Ultimatum Game. Science 2003;300:1755-8.
37. Elliott R, Newman JL, Longe OA, Deakin JF. Differential response patterns in the striatum and orbitofrontal cortex to financial reward in humans: a parametric functional magnetic resonance imaging study. J Neurosci 2003;23:303-7.
38. O'Doherty J, Kringelbach ML, Rolls ET, Hornak J, Andrews C. Abstract reward and punishment representations in the human orbitofrontal cortex. Nat Neurosci 2001;4:95-102.
39. Rolls ET, Hornak J, Wade D, McGrath J. Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. J Neurol Neurosurg Psychiatry 1994;57:1518-24.