Article

睡眠障害とパーソナリティとの関連 ―fMRIを用いた研究―

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Effects of Sleep Deprivation on Risk Perceptional Function from Action Observation Network

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Abstract

This study is aimed to examine the neural correlates of effect of the total sleep deprivation on the risk-taking of the action observation network (AON) in humans using functional magnetic resonance imaging (fMRI). We also explored the influence of interindividual psychological differences on patterns of activation in the risk-taking of AON, which may mediate the relationship between the lack of sleep and the risk perceptional ability. We first demonstrated that viewing Risk-taking versus Safe actions recruited brain areas involved in the inferior/middle temporal gyrus, inferior/medial/middle frontal gyrus, precentral gyrus, inferior parietal lobule, anterior/posterior cingulate gyrus, precuneus, and insula, and areas thought to be associated with the AON of risk-taking. Next, within these networks, individuals under the well-slept state showed higher signal change in the right middle temporal gyrus, left middle frontal gyrus. In addition, individuals under sleep-deprived conditions showed higher signal change in the insula in the observation of risk-taking than well-slept conditions. The increase in insula activation showed a significant positive correlation with psychological anxiety scores (STAI state). Further, the another anxiety scores (STAI-trait) showed a positive correlation only with neural activity in the insula among the sleep deprivation group. Our findings suggested that the understanding of risk-taking actions that underlies AON is related to neural activation in AON and pain processing related areas, under conditions of both regular sleep and sleep deprivation. Importantly, we found that sleep deprivation was associated with increased neural responses to pain actions in insula. This pattern of activation changes suggests that sleep deprivation may induce hyperactivation for interpreting negative emotional states in AON.

Key Words: sleep deprivation, risk perception, mirror neuron system, action observation network, fMRI, anxiety

Introduction

People believe that adequate sleep is important for human health. Insufficient sleep is disruptive to a variety of cognitive processes. In particular, sleep deprivation leads to instability of normal cognitive functioning, which is often manifested as variability in performance and lapses of attention[1]. In conjunction with this state instability, sleep deprivation is associated with significant declines in alertness, vigilance and the speed of psychomotor responses and cognitive processing. In the domain of sleep

research, there has been recent interest in the large differences in behavior and neural activity displayed by lack of adequate sleeping hours[2]. Recent evidence suggests that sleep deprivation may also affect a number of higher-order cognitive processes and executive function capacities, such as cognitive control[3], planning and set shifting[4], fluency, creativity and mental flexibility[5] and inhibitory processes[3, 6]. A number of functional imaging studies have examined the neuroanatomical correlates of impaired performance during sleep deprivation, as well as possible underlying mechanisms of performance decline and their compensation. These productive studies have revealed both impairments and potential compensations in the individuals without adequate amount of sleep, by means of test of working memory, attention, monitoring, decision making, and memory encoding[7-9]. Moreover, this is not surprising considering the societal and medical ramifications of the deficits caused by sleep loss, which commonly include impaired attention together with deficits in learning and memory[1-4].

One aspect of higher-order processing that has been relatively understudied during sleep deprivation involves judgment, decision-making and risk-taking propensity. Available evidence suggests that the relationship between sleep deprivation and risk-taking is complex. Sleep deprived subjects do show a tendency to choose riskier alternatives when presented with a forced choice response among several alternatives[4] , especially when the outcome is framed in terms of potential gains rather than losses[10]. On the other hand, sleep-deprived subjects tend to perceive themselves as less risk prone and less motivated to engage in high-risk sensational activities[4]. In fact, when risky behavior requires the expenditure of additional energy, sleep-deprived subjects tend to show more conservative responses on effortful behavioral tasks[4,11]. Together, these findings suggest that the judgment and decision making processes associated with risk-taking may be impaired by sleep deprivation, along with the motivation to act upon these judgments.

Risk assessment is a pattern of activities involved in detection and analysis of threat stimuli and the situations in which the threat is encountered. While the cognitive impairment of risk perception due to sleep loss has been long discussed, the impact of sleep deprivation on the observation of risk-taking action have received considerably none research interest. Previous studies have demonstrated that when we observe somebody else executing an action many areas of our own motor systems are active. Functional magnetic resonance imaging (fMRI) studies have demonstrated such activations in ventral and dorsal premotor cortices, inferior parietal lobule, and primary motor cortex[12-16]. Whereas there is no doubt that the motor areas are active during action observation, there is uncertainty as to whether these activations are either in part or entirely due to mirror neurons. Mirror neurons have been found in areas F5 and PF of the macaque monkey and discharge when an action of the same type is either executed or observed[17, 18]. As some of the areas in humans that are active during action observation are believed to be the human homologues of areas of the macaque monkey where mirror neurons have been found, this network sometimes referred to as the mirror neuron system. However, given that the presence of mirror neurons in humans remains controversial, and that not all areas active have been shown to have mirror neurons, we will refer to this network as the action observation network (AON).

The vast majority of studies that have investigated the functional role of activity in the AON have used fMRI. As a result we know a lot about which areas of the human brain are active when we observe action, but very little about how this activity of risk-taking changes across sleep deprivation. This study is aimed to examine the neural correlates of effect of the total sleep deprivation on the risk-taking of the AON in humans using fMRI. We measured the hemodynamic response to observing others in painful situations, which potentially taps into

individual risk perceptual abilities through the AON. We compared this risk-taking activation related to the AON between participants under sleep deprived condition and those under regular sleeping controls. We hypothesized that the sleep deprived group show different neural response in AON- and pain- related affective regions demonstrated by previous neuroimaging studies about pain processing, for example, AON-related regions; ventral and dorsal premotor cortices, inferior parietal lobule, and primary motor cortex[12-16], pain-related regions; anterior cingulate cortex, insula, and prefrontal cortex[19, 20].

Because it is known that individual differences in affective style may influence reactivity to emotional stimuli[21], including physical pain[22], we examined relationships between activity in regions involved in perception of painful situation and scores on measures of general mental health (a 60-item version of the General Health Questionnaire, GHQ 60)[23], anxiety (the Spielberger State-Trait Anxiety Inventory, STAI state or trait)[24], depression (the Self-rating Depression Scale, SDS; the Center for Epidemiologic Studies Depression Scale, CES-D)[25, 26]. Here, we also explored the influence of interindividual psychological differences on patterns of activation in the risk-taking of AON, which may mediate the relationship between the lack of sleep and the risk perceptual ability.

Materials and methods

Participants

Fourteen healthy adults (9 men, five women, mean age ± SD = 24.8 ± 3.7 years) participated in the study. All participants were right-handed, as assessed by the Edinburgh inventory[27]. Wrist actigraphy (a small, light-weight, wrist-worn activity monitor) was used to monitor sleeping habits over the duration of the study (approximately two weeks). Volunteers were prescreened with actigraphy to ensure that they slept an average of 6.5 – 9 hours per night. The actigraphy data indicated that all participants exhibited habitually good sleep (i.e. they usually went to sleep no later than 1:00 a.m. and woke no later than 9:00 a.m.[28]. Subjects also kept a sleep diary in which all sleep episodes were recorded. Examination of sleep data showed that all subjects exhibited satisfactory sleep patterns and were compliant with the study rules during the data collection period. Participants refrained from smoking and did not ingest any medication, stimulants or alcohol for at least 24 hours prior to scans. Participants had no history of relevant medical, psychiatric, or neurological disorders based on family medical history (including self-reports), examined with a medical questionnaire. Informed consent was given before participation in the study, which was approved by the Institutional Review Board of the National Center of Neurology and Psychiatry, Japan.

Study procedure

Participants visited the laboratory three times (Figure 1A). First, a briefing session was conducted, which informed participants of the study protocol and requirements. At the end of this session, every participant was supplied with a wrist actigraphy (Actiwatch; Philips Respironics G. K., Netherlands) to wear throughout the study. The wrist actigraphy was worn on the non-dominant wrist to provide participants with information about when they were scheduled to sleep, when the lights would turn off, and other relevant events. The participants underwent scanning sessions twice; after regular sleeping (RS) or after one-night sleep deprivation (SD). The order of the two sessions was counterbalanced across all participants, and separated by one week. Thus the second visit to the laboratory was for the first scanning session which took place approximately one week after the first visit for the briefing. The third visit was for the second scanning session, two weeks after the second visit. This extra one-week gap between RS and SD was intended to minimize

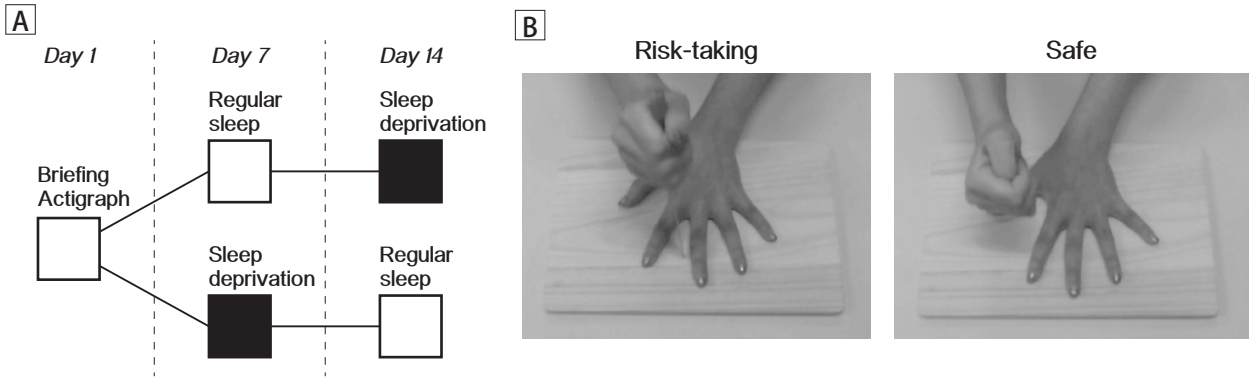

Figure 1. Experimental protocol and presentation task. (A) Participants visited the laboratory 3 times. They first attended a briefing session during which they were informed of the study protocol and requirements. The first scanning session took place approximately a week later. The order of the 2 sessions (RS and SD) was counterbalanced across all the participants and separated by 1 week. The scans at RS or SD took place between 17:00 and 21:00 on day 1 and 2. (B) Participants passively viewed 20 s movie clips (Risk-taking or Safe: playing hand stabbing trick with or without knife). All conditions were presented in a block design. The order of presentation of the stimuli was determined according to optimized random sequence for each block.

the possibility of residual effects of sleep deprivation on cognition for those participants whose sleep deprivation session preceded their regular sleep session[29, 30].

The scans in both conditions took place between 05:00 pm and 09:00 pm at the same time on each day, separated by two weeks (Figure 1A). In the RS session, participants slept at home during the night (from 11:00 p.m. to 07:00 a.m.). In the SD session, participants stayed awake in the laboratory overnight, and were monitored throughout the night to ensure they did not fall asleep. Subjects were maintained in dim light from 11:00 p.m. to 07:00 a.m. (< 5 lux). Their level of physical activity was kept as low as possible (e.g. limited to reading, homework, watching DVDs, conversing etc.), and followed a regular schedule. Every hour, participants were allowed to stand up and to eat a small, standardized snack. During the following day, participants were instructed to continue their usual activities. Prior to the fMRI session, participants completed the Pittsburgh Sleep Quality Index (PSQI)[31,32], the Morningness-Eveningness Questionnaire (MEQ)[33, 34], a 60-item version of the General Health Questionnaire (GHQ 60)[23, 35], the Spielberger State-Trait Anxiety Inventory (STAI state or trait)[24, 36], the Self-rating Depression Scale (SDS)[25, 37], and the Center for Epidemiologic Studies Depression Scale (CES-D)[26, 38].

Stimuli and task

Participants underwent two fMRI scans, each 5 min in length for one session (regular sleep: RS, or 35 hours of sleep deprivation: SD). For each run, participants passively viewed 20 s movie clips (safe or risk-taking: playing hand stabbing trick with or without knife) (Figure 1B). All conditions were presented in a block design. Each movie clip and picture was presented 5 times. The order of presentation of the stimuli was determined according to optimized random sequence for each block. The brightness of the screen, the intensity of contrast, the velocity of hand actions, and the representation of objects were equalized for the all video clips. The hand movements of participants were monitored by direct visual inspection and video-monitoring from the back of the fMRI tunnel. Participants were instructed to just observe the movie clips.

fMRI data acquisition

Images were acquired using a 1.5 T Magnetom Vision plus MRI scanner (Siemens, Erlangen, Germany) using a gradient-echo echo-planar imaging (EPI) sequence with the following parameters: gradient-echo, repetition time (TR) = 3,000 ms, echo time (TE) = 40 ms, field of view (FOV) = 192 mm, flip angle = 90°, 64 × 64 matrix. Thirty-six axial slices of thickness 3.5 mm approximately parallel to the anterior commissure-posterior commissure line were collected. To facilitate the appropriate registration of functional and anatomical images, we obtained a high-resolution T1-weighted anatomical image (3D MP-RAGE sequence, TR = 11.4 ms, TE = 4.4 ms, flip angle = 15°, 256 × 256 matrix, slice thickness 1.25 mm) after the functional runs. Stimuli were displayed on a screen positioned at the rear of the scanner, which the participant could comfortably see through a mirror mounted on the standard head coil. The Karolinska Sleepiness Scale (KSS) was administered immediately following completion of the task, while participants were still in the fMRI scanner[39, 40]. During acquisition sessions, eye movements were measured continuously using an infrared eye tracking system to monitor arousal state. Participant's movements were monitored by direct visual inspection and video-monitoring from the back of the fMRI tunnel. No visible movements were observed during the presentation of the experimental stimuli.

fMRI data analysis

Image processing was carried out using statistical parametric mapping software (SPM8, the Wellcome Trust Centre for Neuroimaging, London, UK). The EPI images were realigned and coregistered to the participants' T1-weighted MR images. The T1 images were then transformed to the anatomical space of a template brain, based on Montreal Neurological Institute (MNI) stereotactic space. The parameters of the transformation were applied to the coregistered EPI images. The normalized images were smoothed by an 8 mm full-width half-maximum (FWHM) Gaussian kernel.

A first level of analysis was performed using the general linear model. The hemodynamic response function was modeled as a boxcar function, and was matched in length to the video clips. The epoch model was generated with four blocked predictive regressors [RS (Safe), RS (Risk-taking), SD (Safe), and SD (Risk-taking)]. Second-level analysis utilized the individual contrast images from the first-level analysis. The main effect of the experimental task (Risk-taking as task condition versus Safe as control) was assessed separately for each group (RS and SD) with repeated measures ANOVA (full factorial model). Group differences between Safe and Risk-taking for both experimental conditions [RS (Risk-taking versus Safe) versus SD (Risk-taking versus Safe) and SD (Risk-taking versus Safe) versus RS (Risk-taking versus Safe)] were tested separately with repeated measures ANOVA.

The resulting set of voxel values constituted a statistical parametric map of the t statistic SPM(t). Anatomic localization was performed in MNI coordinates. Talairach coordinates (Talairach Daemon, www.talairach.org/daemon.html) were used for anatomical localization to be compared with Brodmann areas[41]. Significant activations were defined using a height threshold of $p < .001$, uncorrected, and then applying a subsequent cluster size threshold based on Monte Carlo simulations (AlphaSim), resulting in $k = 22$ (voxels) which is equivalent to a corrected threshold of $p < .05$.

To further clarify the characteristics of regions showing group differences for risk-taking to the AON, the correlation coefficients between the mean contrast values [RS (Risk-taking versus Safe) versus SD (Risk-taking versus Safe), and SD (Risk-taking versus Safe) versus RS (Risk-taking versus Safe)] and psychological measurement scores were also calculated to investigate the features of the regions that demonstrated between group differences.

Results

Behavioral measures

Table 1 presents means and standard deviations of the data from the behavioral measures. As shown in the table, subjects reported significantly higher level of sleepiness following the SD session than the RS session ($p < .0001$, paired t-test).

Neural response to Pain versus Safe actions

We compared neural activation elicited by observing Risk-taking versus Safe actions across whole-brain (Table 2). In well-slept states, the results revealed that Risk-taking actions elicited significantly stronger activation, in the bilateral middle temporal gyri (BA21/22), cingulate gyri (BA31/32), and anterior cingulate (BA32) compared with Safe actions. Additional areas of significant activation were also found in the left inferior temporal gyrus (BA21), medial/middle frontal gyrus (BA6/11), inferior parietal lobule (BA40), precent gyrus (BA6), inferior frontal gyrus (BA9), and insula (BA13). In the right hemisphere, we found significant activation in the precuneus (BA31). No regions exhibited greater activation while viewing Safe actions compared with Risk-taking actions in well-slept states. A contrast of the neural activity in sleep-deprived states in response to Risk-taking versus Safe actions revealed significantly increased responses in the right inferior frontal gyrus (BA47), and middle temporal gyrus (BA21). In the left hemisphere, we found significant activation in the inferior temporal gyrus (BA20/21), insula (BA13), middle frontal gyrus (BA6), and anterior cingulate (BA25). However, the reverse contrast did not reveal significant activation differences in any areas.

The results indicate that observing Risk-taking compared with Safe actions elicited neural activation in 1) AON-related regions; ventral and dorsal premotor cortices (inferior/middle frontal gyrus and precentral gyrus), and inferior parietal lobule[12-16]; 2) cingulate cortex (anterior/posterior cingulate gyrus) and insula in pain related region[19, 20, 42]; 3) inferring and representing mental states of self and other (precuneus, ventral medial prefrontal cortex; medial/middle frontal gyrus, and temporo-parietal junctions; inferior/middle temporal gyrus)[43, 44]; 4) decision making and emotion processing regions; orbitofrontal cortex (a part of inferior/medial/middle frontal gyrus)[45-47].

Neural response to regular sleep versus sleep deprivation

We compared the RS group with SD group, examining group effects on neuronal activity in response to Risk-taking actions controlled with Safe actions (Table 3). A contrast between the neural activity exhibited in response to painful AON in well-slept versus sleep deprived states (Risk-taking versus Safe) revealed significantly increased responses in the right middle temporal gyrus (BA21), left middle frontal gyrus (BA11). In addition, an SD versus RS (Risk-taking versus Safe) contrast of responses to to painful AON network revealed significantly increased activation in the left insula (BA13).

The results indicate that, under the well-slept state, the neural response in the middle frontal/ temporal gyrus elicited 1) inferring and representing mental states of self and other[43, 44], and 2) decision making and emotion processing regions; orbitofrontal cortex (middle frontal gyrus)[45-47]. Also, sleep-deprived state-related increase of neural activation elicited the pain network in the insula[19, 20, 42, 48].

Relationship between AON of risk-taking and psychological variables in each contrast of sleep condition

Correlation coefficients calculated between the hemodynamic activation in each neural activation

Table 1. Behavioral data.

N		14
Sex (M/F)		9/5
Pittsburgh Sleep Quality Index score	PSQI	4.4 ± 2.1
Morningness-Eveningness Questionnaire score	MEQ	46.5 ± 12.8
Karolinska Sleepiness Scale score*	KSS (RS)	4.1 ± 1.9
	KSS (SD)	7.6 ± 2.0
General Health Questionnaire 60-items score	GHQ60	11.1 ± 8.7
STAI-State score	STAI-state (RS)	37.6 ± 8.0
	STAI-state (SD)	39.2 ± 6.5
STAI-Trait score	STAI-trait	42.3 ± 11.6
Self-rating Depression Scale score	SDS	36.5 ± 8.2
Center for Epidemiologic Studies Depression Scale score	CES-D	11.4 ± 8.0

Data are presented as mean ± standard deviation *$p < .0001$

Table 2. Coordinates and z and t scores for brain areas differentially activated in response to Risk-taking versus Safe actions under each sleep condition (regular sleep or sleep deprivation).

		MNI						Cluster
Anatomical region	H	*x*	*y*	*z*	BA	*T*	*Z*	*k*
Regular sleep								
Risk-taking actions versus Safe actions								
Middle temporal gyrus	R	50	-6	-20	21	4.99	4.52	124
Inferior temporal gyrus	L	-58	-16	-22	21	4.91	4.46	135
Cingulate gyrus	L	-16	4	40	32	4.70	4.3	48
Medial frontal gyrus	L	-6	50	-16	11	4.52	4.16	152
Middle temporal gyrus	L	-46	-38	-4	22	4.22	3.92	51
Middle frontal gyrus	L	-30	42	-4	11	4.16	3.87	171
Cingulate gyrus	R	18	-50	28	31	4.13	3.84	74
Anterior cingulate	R	2	22	-8	32	4.12	3.83	41
Precuneus	R	8	-64	20	31	4.10	3.82	55
Anterior cingulate	L	-14	28	24	32	4.10	3.82	114
Inferior parietal lobule	L	-40	-36	35	40	3.84	3.6	28
Cingulate gyrus	L	-18	-26	44	31	3.83	3.60	30
Middle frontal gyrus	L	-36	10	58	6	3.83	3.59	24
Precentral gyrus	L	-42	-8	32	6	3.75	3.53	44
Inferior frontal gyrus	L	-44	8	32	9	3.71	3.49	25
Insula	L	-38	-24	14	13	3.42	3.25	26
Safe actions versus Risk-taking actions								
NA								
Sleep deprivation								
Risk-taking actions versus Safe actions								
Inferior frontal gyrus	R	36	34	-20	47	4.31	3.99	34
Inferior temporal gyrus	L	-58	-22	-22	20	4.01	3.74	24
Insula	L	-42	-8	-8	13	3.81	3.58	45
Middle frontal gyrus	L	-32	6	50	6	3.75	3.53	30
Anterior cingulate	L	-4	20	-4	25	3.68	3.47	30
Middle temporal gyrus	R	58	6	-14	21	3.55	3.35	22
Inferior temporal gyrus	L	-60	-6	-18	21	3.60	3.40	28
Safe actions versus Risk-taking actions								
NA								

MNI refers to montreal neurological institute coordinates; BA refers to putative Brodmann Area; L and R refer to left and right hemispheres.

Table 3. Coordinates and z and t scores for brain areas differentially activated by the risk-taking AON between the regular sleep and sleep deprivation groups.

Anatomical region	H	MNI *x*	*y*	*z*	BA	*T*	*Z*	Cluster *k*
Risk-taking actions versus Safe actions								
and Regular sleep versus Sleep deprivation								
Middle temporal gyrus	R	48	-6	-18	21	3.79	3.56	32
Middle frontal gyrus	L	-30	38	0	11	3.78	3.55	25
and Sleep deprivation versus Regular sleep								
Insula	L	-40	-8	-6	13	3.60	3.40	28

MNI refers to montreal neurological institute coordinates; BA refers to putative Brodmann Area; L and R refer to left and right hemispheres.

Table 4. Correlation coefficients between the mean neural activity found in group comparison for each psychological measurement.

	RS *versus* SD		SD *versus* RS
	Middle temporal gyrus	Middle frontal gyrus	Insula
Center MNI coordinate	R	L	L
(*x*, *y*, *z*) mm	48, -6, -18	-30, 38, 0	-40, -8, -6
GHQ60	0.027	0.093	0.093
STAI-trait	0.066	0.243	**0.545***
SDS	-0.505	0.145	0.113
CES-D	-0.149	-0.088	0.312

Spearman's rho. Bold type*: $p<0.05$. L and R refer to left and right hemispheres.

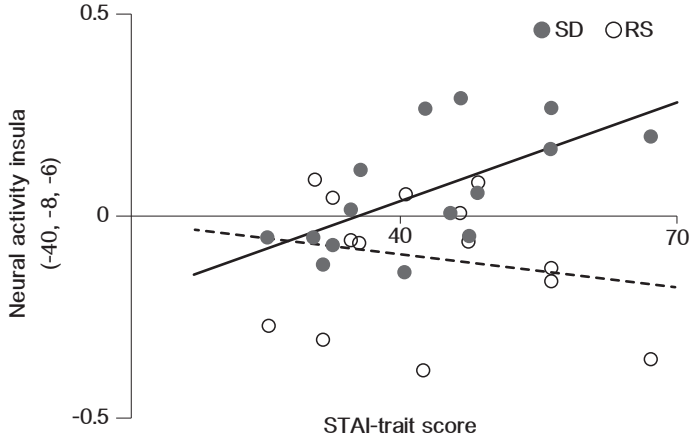

Figure 2. A correlation coefficient between the mean contrast values and STAI state scores. In insula activation, the STAI state score was positively correlated with SD elicited by risk-taking AON.

(see Table 3) and the psychological measurement scores are shown in Table 4 for the risk-taking AON. The insula was positively correlated with STAI-trait (Spearman's rho = .545, p = .036).

Further, we conducted correlation analyses separately for the RS group and SD group. The STAI-trait scores showed a positive correlation only with neural activity in the insula (Spearman's rho = .667, p = .007) in the SD group, but not in the RS group (Spearman's rho = -.193, p = .490) (Figure 2).

Discussion

The present study was aimed at investigating whether sleep loss affects neural circuits for key components of action observation network during risk-taking. Using fMRI, we first demonstrated that viewing Risk-taking versus Safe actions recruited brain areas involved in the inferior/middle temporal gyrus, inferior/medial/middle frontal gyrus, precentral gyrus, inferior parietal lobule, anterior/posterior cingulate gyrus, precuneus, and insula, and areas thought to be associated with the AON of risk-taking. Next, within these networks, individuals under the well-slept state showed higher signal change in the right middle temporal gyrus, left middle frontal gyrus. In addition, individuals under sleep-deprived conditions showed higher signal change in the insula in the observation of risk-taking than well-slept conditions. Here, we found that only one-night (35 hours) of sleep deprivation modulated neural systems (in the insula) associated with AON of risk-taking.

Differential contribution of AON to the neural processing of risk-taking action in sleep deprived or regular slept participants

Our results show that observation of others' risk-taking action activates the brain regions associated with painful AON, such as the anterior cingulate, middle temporal gyrus, middle frontal gyrus, and cingulate gyrus among well-slept participants. We also found that the insula exhibit increased activation during the observation of risk-taking action when participants were in a sleep-deprived state, compared with when they were viewing safe actions.

The cingulate cortices (anterior/posterior cingulate) were consistently activated across previous neuroimaging studies during pain processing, visuospatial processing, and memory retrieval[49-53]. Activation in the cingulate cortex has been repeatedly associated with the affective-motivational component of nociception[19, 42]. The robust neural response when empathizing with the pain of others is in line with the shared representations for understanding others, which proposes that neural circuits involved in the personal experience of an emotion underpin the understanding and sharing of the same emotion perceived in others[54-56]. The overlap of empathy-related activation in cingulate cortex with activation triggered by painful stimulation of the self, in the same participants, provides the most explicit support for this account[51-53]. Moreover, the cingulate cortex has been explicitly related to viscera-motor functions in homeostatic regulation[57], and it has been proposed that the cingulate cortex may play a crucial role in preparing appropriate motor responses to painful and aversive events in general[58]. Notably, intracerebral recordings in medial cingulate cortex in humans indicate that there might be a special class of neurons that show increased firing both when receiving painful stimulation, and when observing it in someone else[59].

We found greater responses in the joint activation of inferior parietal lobule and inferior frontal gyrus during well-slept. This joint activation is a hallmark feature of studies on action observation[44], and it has been suggested that action understanding is the core function of this cortical network[60]. A number of recent models of pain processing propose that our capacity to understand the affective and cognitive states of others is enabled by different mechanisms or "routes"[51, 61, 62]. Our results support such as they indicate the preferential recruitment of two separate neural networks, in addition to the common core

network of pain processing. On the other hand, pictures of body parts in painful situations activated neural structures such as the anterior inferior parietal cortex (supramarginal gyrus, intraparietal sulcus), and ventral premotor areas (inferior frontal gyrus, pars opercularis). However, we found no greater responses in the joint activation during sleep-deprived. Behavioral studies have shown that sleep deprivation can impair cognitive performance[63-70]. Sleep deprivation has also been found to impair a range of bodily functions, including immune regulation and metabolic control, as well as neurocognitive processes such as learning and memory[71]. Sleep deprivation can influence action observation/ understanding responses, that is, these changes portend to less circumspect behavior in the setting of sleep deprivation, but more research with different tasks is encouraged.

Moreover, we found greater responses in the middle/medial frontal gyrus, middle temporal gyrus, and precuneus during viewing risk-taking actions. On the other hand, there are recruited areas associated with "Theory of Mind" or "mentalizing" to a stronger extent; such as the precuneus, ventral parts of medial prefrontal cortex, posterior superior parietal cortex, temporo-parietal junction, and the temporal poles[43,44]. Accumulating evidence links the same network not only to the attribution of intentions and beliefs to others, but also to self-referential thought ("default mode function")[72-74]. A similar network is also activated during episodic memory recall and reflecting about both one's own and others' future events[75]. Hence, it has been suggested that the core function of this network is to draw inference on self- as well as other-related social information in the past, present, and future. This simulation enables sharing the other's state based upon one's own previous experiences and knowledge[76], and it might be partivularly important in situations in which externally provided sensory information about the other's mental state is lacking.

How can we explain the higher activation of risk-taking perception among sleep deprived participants?

We found that, under sleep deprived condition, observed Risk-taking movie led to increased activation in the insula. Meanwhile, under well-slept condition, we found greater activation in the middle frontal/ temporal gyrus.The possible functions of insula have recently received considerable attention. One influential view holds that insula is a part of tightly connected neural network engaged in interoceptive awareness and meta-representations of global emotional moments[77,78]. This idea has been extended by a conceptual framework suggesting that insula might be employed for current and prospective representations of both self- and other-related affective states, and that these representations play an important role in adaptive behavior, guiding decision making, and homeostatic regulation[79].

We propose that the increase we observed in insula responses to Risk-taking actions following a lack of sleep was due to sleep-related impairments in the function of inhibitory cognitive control regions, which might normally suppress emotion-related activity in conditions of regular sleep. A number of executive functions relying on inhibition are reported to be affected by sleep deprivation, resulting in cognitive inflexibility, impaired decision making[64, 68, 80], deficient error detection[68, 69], and impairments in various aspects of executive attention[67, 81, 82].

Sleep deprivation can also influence emotional responses and emotional memory. The first functional imaging study to evaluate the relationship between sleep deprivation and emotion found that sleep-deprived participants exhibited an increased amygdala response to emotionally charged scenes, accompanied by increased brainstem limbic connectivity and reduced amygdala-medial prefrontal connectivity[83]. Moreover, a study examining the relationship between neural stimuli and sleep deprivation reported that emotional responses and memory consolidation

elicited by pleasant images were reduced under conditions of sleep deprivation, but that sleep status did not affect amygdala activity or memory consoliation in response to aversive images[84]. The finding that sleep deprivation impairs memory for positive images while not affecting memory for images with a negative valence highlights the importance of sleep in the consolidation of positive emotional memories specifically. In accord with these previous studies, our results showed that activity in AON areas in response to risk-taking actions (negative valence) was significantly higher under conditions of sleep deprivation.

Sleep deprivation affects psychological anxiety states in insula activation

Finally, we examined data from questionnaires involving subjective behavioral and psychological measures, and analyzed the relationship between questionnaire scores, sleep and mood states, and neural activity. The results revealed that the increase in insula activation showed a significant positive correlation with STAI state score between-group comparison (SD versus RS and Risk-taking versus Safe). Further, the STAI-trait scores showed a positive correlation only with neural activity in the insula among the SD group, but not in the RS group. In other words, higher levels of anxiety (reflected by STAI state and trait score) were associated with higher insula responses to risk-taking actions under sleep-deprived conditions. Our findings suggest that individual differences in mental health (and levels of anxiety in particular) in healthy individuals can impact on the effects of sleep deprivation on risk-taking AON processing. A study of Simmons et al. (2006) suggested that greater insula activation during visual anticipation is associated with the visual processing of aversive stimuli in anxiety-prone individuals. Insula hyperactivity might be a common feature in persons with elevated anxiety and, as such, may function as a neuroimaging maker for anxiety proneness[85]. Our current results revealed that the insula, an area involved in risk-taking AON processing, showed a heightened response to risk-taking actions after sleep deprivation. This indicates an influence of not only the negative valence of risk-taking actions, but overall mental health state on activity in insula. In the future, extensive studies using a wider range of subjective measures of mental health and behavior might be useful to clarify the influence of interindividual factors on the effects of sleep deprivation on risk-taking processing.

Conclusion

The current results provide novel evidence indicating that the risk-taking AON are differentially modulated by sleep deprivation. Our findings suggested that the understanding of risk-taking actions that underlies AON is related to neural activation in AON and pain processing related areas, under conditions of both regular sleep and sleep deprivation. Importantly, we found that sleep deprivation was associated with increased neural responses to pain actions in insula. This pattern of activation changes suggests that sleep deprivation may induce hyperactivation for interpreting negative emotional states in AON.

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