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Research paper

Functional connectivity between dorsal attention and default mode networks mediates subjective sleep duration and depression in young females

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A R T I C L E I N F O

Keywords:
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Depression
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Resting-state functional connectivity

A B S T R A C T

Background: Depression prevails throughout the world. Young females are more likely to suffer from depression because of lack of sleep.
Methods: We recruited 405 young female participants to assess their subjective sleep duration and self-rating depression. The resting-state magnetic resonance imaging (rs-fMRI) data were collected to identify the brain regions related to sleep duration and depression, and a mediating model was established among sleep duration, depression and functional connectivity (FC) of rs-fMRI.
Results: Correlation analysis indicated that subjective sleep duration was negatively associated with self-rating depression in young females ($r = -0.22$, $p < .001$). The network connectivity between dorsal attention network (DAN) and default mode network (DMN) positively correlated with self-rating depression ($r = 0.13$, $p < .05$), and negatively correlated with subjective sleep duration ($r = -0.14$, $p < .01$). Furthermore, the mediation analysis revealed that the FC of DAN-DMN significantly mediated the effect of sleep duration on depression.
Limitations: The study was a cross-section design and the sleep duration of the participants was subjectively reported. Future studies should consider to track the participants longitudinally and to measure the objective sleep duration by actigraph or polysomnography.
Conclusions: The participants with less sleep duration are more prone to develop depression feelings. The FC of DAN-DMN mediated the effect of sleep duration on depression. Thus, the FC of DAN-DMN could be consider as a neural target to relieve depression by increasing sleep duration in young females.

1. Introduction

Depression has become the most common mental disorder: statistics have shown at least 350 million people worldwide suffering from depression (Chatterjee et al., 2021). Among the depression-susceptible population, women are almost twice more likely to be diagnosed with depression than men (Eid et al., 2019; Labaka et al., 2018), and the difference in prevalence of depression between men and women is thought to be linked to different kinds of psychophysiological and environmental factors (Salk et al., 2017; Stickel et al., 2019). In addition, a peak in prevalence for the first onset of major depression extends from the age of 20 to 40, and almost 40 % of people experience their first episode of depression before the age of 20 (Malhi and Mann, 2018). Therefore, studies designed to uncover potential risk factors for depression in young women remain imperative.

The bi-directional relationship between sleep duration and depression has been reported by numerous studies (Berk, 2009; Riemann et al., 2001). As a typical symptom of most depressed patients, insufficient sleep or short sleep duration has been demonstrated to be a risk factor for both onset and recurrent depression (Sun et al., 2018). However, the

Abbreviations: BOLD, blood oxygen level-dependent; DAN, dorsal attention network; DLPFC, dorsolateral prefrontal cortex; DMPFC, dorsal medial prefrontal cortex; DMN, default mode network; FC, functional connectivity; FEF, frontal eye field; IPS, intraparietal sulcus; PCC, posterior cingulate; PSQI, Pittsburgh Sleep Quality Index; ROI, region of interest; rs-fMRI, resting-state magnetic resonance imaging; Rsp, retosplenial cortex; SDS, Self-rating Depression Scale; VMPFC, ventral medial prefrontal cortex.

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underlying neuro-mechanism about the relationship between sleep duration and depression remains to be determined. Moreover, although sleep duration can be measured both in the objective and subjective way, it has been demonstrated that subjective sleep duration, obtained from questionnaires, bear a strong resemblance to objective sleep duration obtained from polysomnography in both participants with depression and healthy controls (Armitage et al., 1997). Thus, in our study we retrieved the subjective sleep duration from the Pittsburgh Sleep Quality Index (PSQI) and then this subjective estimation was used to investigate the underlying neural correlation with depression.

Large-scale brain network analysis has been widely used to understand the neurocognitive and brain dysfunction across psychiatric disorders (Sha et al., 2019). Among the large-scale brain networks, dorsal attention network (DAN) and default mode network (DMN) have been a focal research topic over the past several decades (Yang et al., 2021). DAN consists of the frontal eye field (FEF) and intraparietal sulcus (IPS), and is involved in goal-directed top-down attention (Fox et al., 2006). Sometimes it was also grouped together with dorsolateral prefrontal cortex (DLPFC) of the frontal-parietal area (Qian et al., 2020; Siddiqi et al., 2019). DMN comprises a set of interacting brain regions centered on posterior cingulate/retosplenial cortex (PCC/Rsp), ventral medial prefrontal cortex (VMPFC), dorsal medial prefrontal cortex (DMPFC), and medial temporal and inferior parietal regions (Buckner et al., 2008). It's typically activated during spontaneous cognition of the resting-state and internally oriented focused tasks like autobiographical memory retrieval. Attempts were made to explore the relationship of DAN and DMN and the researchers concluded that the two networks shown a negative temporal correlation during resting-state and they termed this phenomenon as "anti-correlation" (Fox et al., 2005; Greicius et al., 2003). Moreover, the temporal anti-correlation of DAN and DMN has been found to be a feature of healthy functional connectivity of brain system and the reduced anti-correlation (i.e., reduced negative correlation between the two networks) may correlate with numerous psychophysiological disorders such as major depression (Chin Fatt et al., 2021), post-traumatic stress disorder (Patriat et al., 2016), and insomnia disorder (Dong et al., 2018).

Indeed, the recent burgeoning research on brain networks is indicative of a growing conviction that functional connectivity (FC) of DAN-DMN has the potential to serve as a factor that influences the relationship between sleep duration and depression. First, short sleep duration is found to be associated with the reduced DAN-DMN anti-correlation. For the sleep-deprived participants, evidence shown that short sleep duration induced increased sleep pressure before bedtime, which reduced anti-correlation of DAN-DMN (Kaufmann et al., 2016; Sun et al., 2022). For participants in preadolescence, the results were quite similar: both sleep disturbance and mental problems were associated with the FC strength of DAN-DMN (Yang et al., 2022). Second, depression is found to be associated with the decreased anti-correlation of DAN-DMN. DAN and DMN were essential networks in the neurocognitive network model of depression (Yu et al., 2019). In addition, by using the graph theory, recent study shown a significant correlation between the antidepressant response and global network characteristics in the FC of DAN-DMN (Uykur et al., 2021). However, among these relevant studies (Kaufmann et al., 2016; Sun et al., 2022; Yang et al., 2022), either the topics of the research focused only one of them or the sample size was limited. Therefore, the relationship among the FC of DAN-DMN, sleep duration and depression in young females still needs to be explored.

To investigate and better delineate the effect of the FC of DAN-DMN on the relationship between sleep duration and depression, we analyzed the data with larger sample size in young females. Our aim was to understand the neural-psychological basis between subjective sleep duration and depression. We hypothesized a significant correlation between sleep duration and depression, and this relationship may be mediated by the FC of DAN-DMN.

2. Materials and methods

2.1. Participants and psychological assessment

All young female participants were included as they completed demographic information in Brain Behavior Project (BBP, a project initiated at Southwest University, Chongqing, China) (Wang et al., 2022), and there were 471 young female participants in the current study. We used G*power (https://www.gpower.hhu.de) to calculate the needed sample size of current study. According to the previous literature (Raniti et al., 2017), the correlation between sleep duration and depression is −0.33, the standard deviation (SD) of sleep duration is 1.31 and the SD of depression score is 10.79. We input the bias (α error probability) = 0.05 and the statistical power (1-β) = 0.95. The needed sample size for our study is 109.

They were asked to complete the psychometric-related questionnaires, functional and structure MRI scanning. Fourteen participants were excluded because of invalid and incomplete questionnaires. Fifty-two participants were excluded because of lower signal-to-noise ratio of MRI data. Finally, 405 participants were included in our study for further analysis, and this number is larger than the needed sample size estimated by G*power. All participants provided written informed consent prior experiments, and the experimental procedures were approved by the ethical committee at the Southwest University.

The Chinese version of 19-items Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) was used to assess participants' global sleep quality during the past month. The item 4 of PSQI was used to obtain their subjective sleep duration. The Chinese version of Self-rating Depression Scale (SDS), an established 20-item self-report questionnaire was used to assess participants' depression levels (Zung, 1965). The standard score of SDS was computed for further analysis.

2.2. Image data acquisition and preprocessing

The MRI images of all participants were collected on a 3T Siemens Prisma scanner (Siemens, Erlangen, Germany) with 64-channels head coils. High-resolution T1 weighted anatomical images were firstly acquired by a three-dimensional gradient sequence (3D-SPGR) with the following scanning parameters: repetition time 2530 ms, echo time 30 ms, flip angle 7°, matrix size 512 × 512, field of view 256 × 256 mm^2, voxel size 1 × 0.5 × 0.5 mm^3, number of slices 192, thickness 1 mm. An echo-planar imaging sequence was used to acquire functional blood oxygen level-dependent (BOLD) images. Parameters were as follows: repetition time 2000 ms, echo time 30 ms, flip angle 90°, field of view 224 × 224 mm^2, thickness 2 mm, matrix size 112 × 112, number of axial slices 62, number of multiband acceleration factor 2. During the process of scanning, participants were instructed to stare at the white fixation with black background without thinking intentionally in the mind and keep as motionless as possible.

SPM12 (a toolbox of Matlab, https://www.fil.ion.ucl.ac.uk/spm/) was used to preprocess the rs-fMRI data with 4 stages: slice timing, field map-based deformation correction and motion correction, spatial standardization and smoothing. In the spatial standardization stage, we first aligned the individual's high-resolution anatomical image to the functional image, and then segmented it into gray matter, white matter, cerebrospinal fluid, and other parts. After through Dartel's standardization method, the images were standardized to the Montreal Neurological Institute (MNI) space. For the smooth stage, the parameter of full width at half maximal (FWHM) was selected as 6 mm.

In addition, the resting-state images were denoised with 5 steps: regression of the head movement parameters, regression of the signal in the white matter and cerebrospinal fluid regions, detection of the abnormal points, delinear drift and band-pass filtering. In the process of regressing head movement parameters, we regressed 6 head movement parameters and 6 first derivatives of head movement. In order to remove physiological noises such as breathing and heartbeat and further reduce the interference of head movement artifacts, we used aCompCor algorithm for denoising. aCompCor used the principal component analysis (PCA) method to extract the first five principal components of the signal in the individual's white matter and cerebrospinal fluid regions and added them as noise variables to the regression model. At the same time, we used the Artifact Detection Tools (ART) program (http://web.mit.edu/swg/software.htm) to monitor the outliers in the BOLD signal. If the whole brain signal changed >5 standard deviations, or the head moves >0.9 mm frame by frame, it was considered as abnormal. Each abnormal time point obtained by ART and a subsequent time point were established as a separate regressor (box function) for scrubbing to eliminate the influence of the signal at the abnormal time point. Taking the influence of scrub on the integrity/degree of freedom into account, the subjects whose time points were scrubbed out for >1 min (30 time points) were excluded. Then, we set the band-pass filter parameter as 0.008–0.09 Hz. Finally, we performed quality checks on rs-fMRI data with removing abnormal brain structures, incomplete images, excessive ART scrubbing (loss of data for >1 min). We also eliminated the participants with absolute head movement >2 mm or 2°, average frame-by-frame displacement (FD) >0.2 mm, the maximum frame-by-frame displacement >5 mm.

After the data were preprocessed and the BOLD signal of each region of interest (ROI) in DAN and DMN were extracted, the coordinates of ROIs based on the Power-264 template (Power et al., 2011) were selected and the mean correlation coefficient of each pair between the DAN (11 nodes) and DMN (58 nodes) were normalized to z-scores with Fisher's r-to-z transformation for further statistical analysis as the functional connectivity of DAN and DMN (Fig. 1).

2.3. Statistical analysis

To further investigate the relationships among depression, sleep duration, and the FC of DAN-DMN, the bivariate correlations were calculated among the three variables. The calculations were performed in SPSS (SPSS Inc., Chicago, IL, USA) and R (version 3.5.0). In addition, to investigate whether the FC of DAN-DMN could mediate the relationship between subjective sleep duration and depression, mediation analysis was performed by PROCESS (a toolbox of SPSS, www.processmacro.org/index.html), with age as the covariate. In the process of establishing the mediating model, X is the subjective sleep duration, Y is the depression score, and M is the mean FC of all ROI pairs between DAN and DMN. 5000 bootstrap samples and the bias-corrected confidence interval were reported.

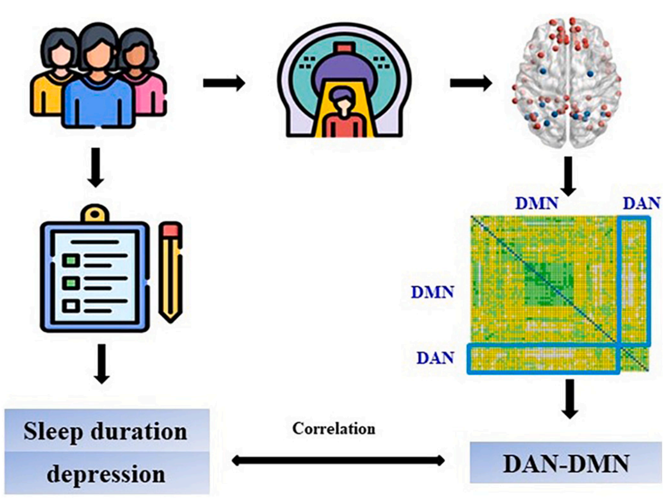

Fig. 1. The schematic flow diagram of our study. Participants completed the self-reported questionnaires (middle-left panel), and their rs-fMRI data were then acquired when they lied in the MRI scanner (top-middle panel). Second, the BOLD signals of the regions in DMN (the red dots in the top-right panel) and DAN (the blue dots) were extracted, and the mean correlation coefficient was calculated for each ROI pair between the two networks (the blue bordered region in the middle-right panel). Finally, the mediation analysis was performed among sleep duration, depression and the FC of DAN-DMN. (Note: DAN: dorsal attention network; DMN: default mode network). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3. Results

3.1. Descriptive statistics and the correlations between subjective sleep duration, depression and the FC of DAN-DMN

As shown in Table 1, the correlation analysis revealed that the self-reported sleep duration was negatively associated with the score of SDS ($r = -0.22$, $p < .001$), which meant participants who slept less with lower quality were more likely to be depressed. To evaluate the possibility of establishing a mediating model, the correlations between subjective sleep duration, depression and FC of DAN-DMN were performed. As shown in Fig. 2 and Table 1, the FC of DAN-DMN showed positive correlation with SDS ($r = 0.13$, $p = .012$), while a negative correlation was found between the FC of DAN-DMN and subjective sleep duration ($r = -0.14$, $p = .006$).

3.2. Mediation analysis

As described above, sleep duration, depression and the FC of DAN-DMN are significantly correlated with each other. Therefore, the self-reported sleep duration was entered in the mediating model as the predictor variable, the SDS score as the dependent variable, and the FC of DAN-DMN as the mediating variable with the age as the covariate. As shown in Fig. 3, after the age was regressed out in the model, the relationship between subjective sleep duration and self-rating depression ($c' = -0.190$, $p = .001$, 95%CI [−0.190, −0.093]) was mediated by the FC of DAN-DMN ($a = -0.138$, $p = .006$, 95%CI [−0.236, −0.040]; $b = 0.097$, $p = .046$, 95%CI [0.002, 0.193]). The statistical results revealed that the indirect effect was significant ($ab = -0.013$, 95%CI [−0.034, −0.0004]) between subjective sleep duration and self-rating depression via the FC of DAN-DMN.

4. Discussion

In the current study, we aimed to investigate the mediation effect of the FC of DAN-DMN on the relationship between subjective sleep duration and depression in young females. First, we found the significant negative correlation between subjective sleep duration and self-rating depression. Second, the FC of DAN-DMN was positively correlated with self-rating depression, and negatively correlated with subjective sleep duration. Then the mediation analysis revealed that the FC of DAN-

Table 1
The descriptive statistics of the demographic measures and the correlations between subjective sleep duration, depression and the functional connectivity of DAN-DMN (Note: PSQI, Pittsburgh Sleep Quality Index; SDS: Self-Rating Depression Scale).

	M	SD	Correlation with SDS	Correlation with sleep duration
Age (years)	20.16	0.96	–	–
Sleep duration (hours)	6.77	0.89	−0.22***	–
PSQI	5.24	2.53	0.41***	−0.55***
SDS	45.15	8.67	–	−0.22***
DAN-DMN	−0.04	0.04	0.13*	−0.14**

* $p < .05$.
** $p < .01$.
*** $p < .001$.

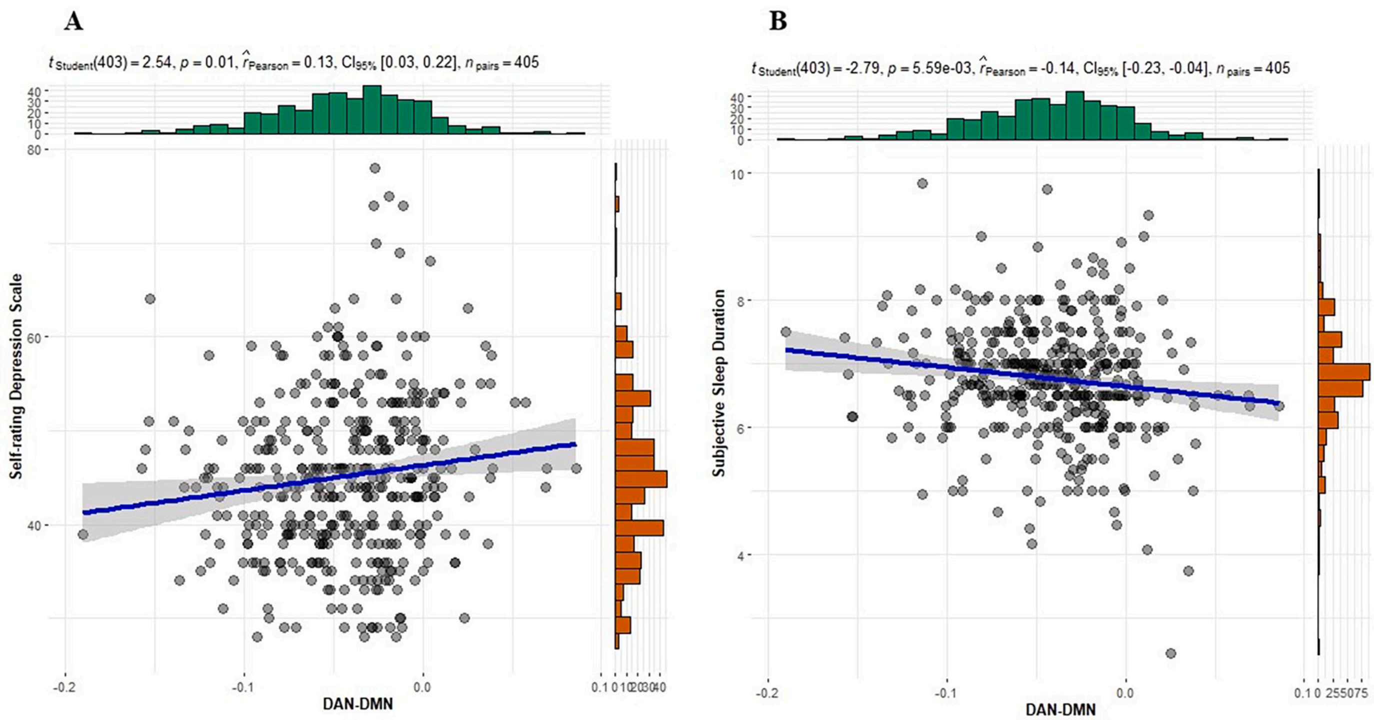

Fig. 2. Relationships between the FC of DAN-DMN and self-relating depression (A), and between the FC of DAN-DMN and subjective sleep duration (B). The gray dots represent the data of each female participant and the blue line refers to the fitting line (the shadow refers to the 95 % confidence interval). The green bars in (A) and (B) illustrate the distribution of DAN-DMN. The orange bars in (A) illustrate the distribution of depression score of SDS and the orange bars in (B) illustrate the distribution of subjective sleep duration. (Note: FC: functional connectivity; DAN: dorsal attention network; DMN: default mode network.) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

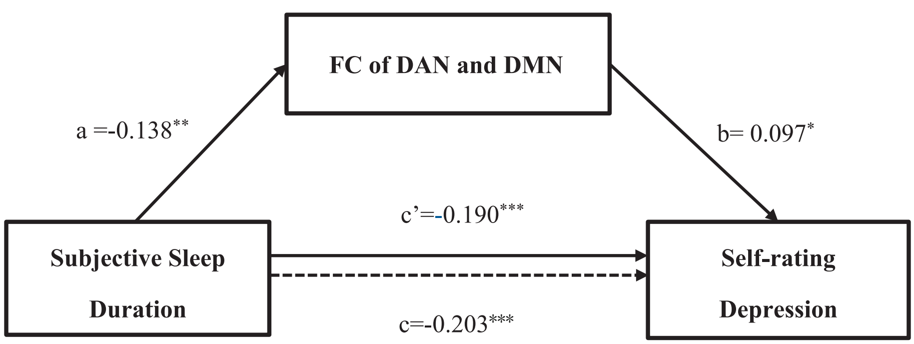

Fig. 3. The functional connectivity of DAN-DMN mediated the effect of subjective sleep duration on self-rating depression (Note: FC: functional connectivity; DAN: dorsal attention network; DMN: default mode network; $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$).

DMN mediated the effect of subjective sleep duration on self-rating depression. Taken together, our results highlight that the brain functional connectivity between DAN and DMN plays a mediating role in the relationship between sleep duration and depression.

4.1. The negative correlation between sleep duration and depression

In line with previous research (Sun et al., 2018), we also found a significant negative correlation between subjective sleep duration and depression. There are several points that can account for this result. First, systematic inflammation may be responsible for the negative correlation (Prather et al., 2015). People who were observed with limited sleep duration were found to coexist with an increase of inflammation level, and this syndrome was a potential risking factor of depression (Miller and Raison, 2016; Prather et al., 2015). Second, sleepiness and fatigue were the pathways both linking to short sleep duration and depression. Through impairing the arousal mechanism, limited sleep caused sleepiness and fatigue the next day (Shen et al., 2006) and these two consequences were predictive of depression (Baldwin and Papakostas, 2006; Schönberger et al., 2014) Third, both depression and short sleep duration can be the comorbidities of other physiological and psychological diseases such as hypertension and anxiety (Gangwisch, 2014; van Mill et al., 2010). In summary, the reduction of sleep duration is a potential signal of depression. Through increasing the sleep duration of young female, we have the possibility to prevent the onset and recurrence of depression.

4.2. The correlations among the FC of DAN-DMN, sleep duration and depression

In the current study, bivariate correlation was performed to test the relationship between the FC of DAN-DMN and sleep duration. Consistent with the previous literature related to sleep deprivation and sleep disturbance (Sun et al., 2022; Yang et al., 2022), our study also indicated the FC of DAN-DMN becomes less segregated in young female short sleepers. Because of the opposite function of these two networks (Fox et al., 2006), a popular explanation of the decreased DAN-DMN is the lower ability of changing from rest to task and task to rest, which has been proved as the decreased cognitive flexibility in cognitive performance (Dai et al., 2020; Yang et al., 2022) and these are also afflictions to people with short sleep duration (Yaffe et al., 2014).

We further performed the bivariate correlation between the FC of DAN-DMN and depression. Similar to the related literature in children depression (Schirmer et al., 2023; Yu et al., 2019), our study clarified the FC of DAN-DMN becomes less segregated in young females with more depressive feelings. The less segregated DAN-DMN is always associated with attention (Amer et al., 2016) and memory problems (Franzmeier et al., 2017), which are also problems in depressive people (Burt et al., 1995; Keller et al., 2019).

4.3. The Mediating role of the DAN-DMN FC in the relationship between sleep duration and depression

The mediation analysis showed the FC of DAN-DMN significantly mediated the effect of subjective sleep duration on depression. In most cases, it was ideal for just one of these two networks to be activated and the other one was inhibited (Owens et al., 2020). For example, in a cognitive task, DMN should be inhibited, and DAN should be activated to ensure more optimal allocation of mental resources; while in resting state, DMN should be activated and DAN should be inhibited (Fox et al., 2006; Marques et al., 2015). This is because that DMN functions as internal attention and self-referential (Sheline et al., 2009) and DAN functions as external attention and cognition (Spreng et al., 2013). Therefore, antagonism of DMN and DAN was thought as a helpful and beneficial property of the brain. For people with sleep deprivation or sleep disturbance, short sleep duration may lead to the neural fragility with reduced antagonism of DAN-DMN, and this reduction can predict their depression status.

4.4. Limitations

There are several limitations to our study which merit further discussion. First, caution should be taken in explaining the mediating role of DAN-DMN FC in the relationship between objective sleep duration and depression. Although subjective sleep duration bears a strong resemblance to objective sleep duration in both participants with depression and healthy controls (Armitage et al., 1997), it remains unclear whether we can observe the similar mediating role between objective sleep duration and depression. In addition, the mediation effect of DAN-DMN is relatively small, which explains only about 6 % of the total effect, so it should be careful when our neuroimaging results need to be extended in other studies. Second, no clinical evaluation was performed in all the included participants, thus our study may include both healthy ones and others who met the clinical diagnosis of insomnia disorder or major depression. Future studies should further validate our results in clinical depression and insomnia groups. Third, we used a cross-sectional design and did not track the participants longitudinally. Finally, our participants were primarily young female students. Future studies could further validate our current results in middle-aged and older adults.

5. Conclusion

The current study primarily investigated the relationship between subjective sleep duration, self-rating depression and the FC of DAN-DMN. We found these three variables were significantly correlated with each other. Mediation analysis showed the functional connectivity of DAN-DMN significantly mediated the effect of subjective sleep duration on depression. The participants with short sleep duration presented decreased anti-correlation between DAN and DMN, which induced more depressive feelings. Our results emphasized the important contribution of the antagonism between brain large-scale networks, i.e., the DAN and DMN, in the relationship between subjective sleep duration and depression. Future studies could consider the functional connectivity between DAN and DMN as a potential biomarker for the efficiency of brain stimulation and behavioral therapy targeting for relieving depression by increase sleep duration.

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Credit authorship contribution statement

Ziye Xu: Conceptualization, Data Analysis and Writing - Original Draft.
WenRui Zhao: Data Analysis, Writing - Original Draft and Writing - Review & Editing.
Haien Wang: Writing - Review & Editing.
Yun Tian: Data Analysis.
Xu Lei: Supervision, Funding Acquisition and Writing - Review & Editing.

Declaration of competing interest

Competing financial interests: The authors declare no competing financial interests.

Data availability

The fMRI data sharing is not applicable to this article, because the project of the fMRI data source of this article is still in progress and it is held jointly by the corresponding author and the other project leaders. Before the data for the entire project is made public, an agreement with the corresponding author and other project leaders is required if it is necessary to obtain the fMRI data. Data of other variables are available upon request.

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