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Association between abnormal default mode network homogeneity and sleep disturbances in major depressive disorder

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ABSTRACT

Background Sleep disturbance is a common comorbidity of major depressive disorder (MDD). However, network homogeneity (NH) changes of the default mode network (DMN) in MDD with sleep disturbances are unclear.

Aims The purpose of this study was to probe the abnormal NH in the DMN in MDD with sleep disturbances and to reveal the differences between MDD with or without sleep disturbances.

Methods Twenty-four patients with MDD and sleep disturbances (Pa_s), 33 patients with MDD without sleep disturbances (Pa_ns) and 32 healthy controls (HCs) were recruited in this study. Resting-state functional imaging data were analysed using NH.

Results Compared with Pa_ns and HCs, Pa_s showed decreased NH in the left superior medial prefrontal cortex and increased NH in the right precuneus. There was a negative correlation between NH in the left superior medial prefrontal cortex and sleep disturbances (r=−0.42, p=0.001) as well as a positive correlation between NH in the right precuneus and sleep disturbances (r=0.41, p=0.002) in patients with MDD.

Conclusions MDD with sleep disturbances is associated with abnormal NH in the DMN, which could differentiate pa_s from pa_ns. The DMN may play a crucial role in the neurobiological mechanisms of MDD with sleep disturbances.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Sleep disturbance is a common comorbidity of major depressive disorder (MDD), which may alter the network homogeneity (NH) of the default mode network (DMN).

⇒ Sleep regularity may be related to DMN function, and abnormal NH in the DMN has been found in first-episode and drug-naive patients with MDD.

WHAT THIS STUDY ADDS

⇒ In this study, NH was applied to determine the changes in the DMN between patients with MDD with (Pa_s) and without sleep disturbance symptoms (Pa_ns).

⇒ We hypothesised that abnormal NH may be associated with sleep disturbances in certain areas of the DMN, which would be applied to differentiate Pa_s from Pa_ns.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Abnormal DMN, especially aberrant NH of the left medial prefrontal cortex and right precuneus, has an association with sleep disturbance symptoms, which could differentiate pa_s from pa_ns.

⇒ The DMN may play a crucial role in the neurobiological mechanisms of MDD with sleep disturbances.

INTRODUCTION

Major depressive disorder (MDD) is a serious psychological and mental disorder that significantly impacts one in five individuals during their lifetime. MDD features longer, deeper depression, loss of insight and higher suicidal ideation, making it the primary contributor to global disability.

Sleep is indispensable for the maintenance of normal life activities of human body and sleep habits are important aspects of lifestyle. Abnormal sleep patterns are one of the clinical symptoms and signs of MDD. Sleep disturbances, such as early awakening and shortened sleep duration, are the most common symptoms accompanying patients with MDD, which significantly impact their quality of life. In addition, sleep deprivation deteriorates brain function and is thus supposed to be associated with cognitive decline, anxiety and depression. Although a strong link between sleep disturbances and MDD has been proposed,[1] the precise relationship between sleep duration and MDD is still largely understudied. Roenneberg *et al* reported that early bedtime preference was associated with circadian rhythm and sleep homeostasis balance,[2] which may be protective for the risk of MDD and has been studied in many observational studies.[3 4] Indeed, a positive relationship between early bedtime

preference and a lower incidence of MDD has been demonstrated in a follow-up study.[3]

In China, up to 64.6% of patients with MDD are estimated to have insomnia. Low mood is heavily influenced by evening orientation,[5] a type of sleep habit characterised by staying up late. Patients with MDD and sleep disturbances typically experience more pronounced anxiety symptoms and a higher burden of hyperarousal compared with those without sleep disturbance symptoms.[6] Additionally, sleep disturbances may arise alongside other symptoms during the early stages of MDD and are often considered a useful prodromal symptom. Many patients with MDD and sleep disturbances continue to experience insomnia even after mood symptoms have been adequately addressed. They are deemed to have a worse prognosis than those without sleep problems. In adolescents, sleep disturbances were associated with reduced connectivity in the intrinsic default mode network (DMN).[7] Furthermore, individuals experiencing sleep disturbances exhibit greater activation in key regions of the DMN during tasks involving self-referential processing compared with healthy controls (HCs).[8] Our previous study revealed altered local regional activity across multiple networks (including the DMN) in patients with MDD with sleep disturbances by using a regional homogeneity method.[9] These findings underscore the potential role of the DMN in the neuropathological mechanisms of sleep disturbances in MDD. However, it remains unclear whether there exist abnormalities in functional connectivity within the DMN.

DMN includes a cohort of brain regions covering the medial prefrontal cortex (MPFC), posterior cingulate cortex, adjacent precuneus (PCu) and lateral parietal cortex. Increasing evidence has shown that patients with MDD exhibit widespread brain structural alterations, especially in DMN. Volumetric reduction of MPFC is one of the most well-documented neural abnormalities in MDD which is pivotal for interoceptive stimuli and processing emotions.[10] PCu is involved in retrieving autobiographical memory and coding, and the connectivity between the right amygdala and right PCu is significantly correlated with physical and social trait anhedonia in MDD. Furthermore, a recent study has revealed altered spontaneous neural activities of the right PCu in subclinical depression.[11] The posterior cingulate cortex is associated with emotional regulation and a thinner cortical grey matter has been reported in adults with MDD. These data strongly suggest that MDD can reshape brain structure in a highly dynamic way. Intriguingly, sleep regularity may also be related to the DMN function.[12] The structural and functional differences in the DMN are linked to idiopathic hypersomnia. Participants with idiopathic hypersomnia had greater volume and cortical thickness in the PCu and lower functional connectivity within the anterior DMN, showing that disrupted DMN contributes to the drowsiness symptom in idiopathic hypersomnia.[13] Moreover, patients with MDD and sleep disturbances present increased connectivity in the DMN.[14]

The network homogeneity (NH) method is used to evaluate network integrity in clinical populations, allowing for the identification of brain regions with compromised network coherence correlating with a particular disorder or pathological process.[15] This voxel-wise measure assesses the correlation between a voxel and all other voxels within a specified network, representing the average correlation between the time series of a particular voxel and those of all other voxels in the network. Regional homogeneity calculates the synchronisation or similarity of the time series of the nearest neighbouring voxels (usually 26 voxels). This method is based on the assumption that a given voxel is temporally similar to its neighbours.[16] Compared with regional homogeneity, the NH method considers interactions between brain regions within a specific network, which may better reflect the dynamic processes. We can gain some insights into the dynamic nature of brain connectivity by assessing changes in network synchronisation across different states or tasks. It captures the variations in network interactions, revealing how brain networks adapt and reconfigure their connectivity in response to different stimuli.

Abnormal NH in the DMN has been found in first-episode and drug-naive patients with MDD. Specifically, patients with MDD exhibited significantly increased NH in the left MPFC and decreased NH in the right inferior temporal gyrus compared with HCs.[17] Importantly, first-episode and drug-naive patients with MDD may share brain regions with increased NH in the anterior DMN,[18] which highlights the close involvement of the DMN in the pathophysiology of MDD.

Sleep regularity may be related to DMN function,[12 19] although the association between abnormal DMN homogeneity and sleep disturbances in MDD remains unclear. Therefore, in this study, NH was applied to determine the changes in the DMN between patients with MDD and sleep disturbances (Pa_s) and patients with MDD without sleep disturbance symptoms (Pa_ns). We hypothesised that abnormal NH may be associated with sleep disturbances in certain areas of the DMN, which would be applied to differentiate Pa_s from Pa_ns.

MATERIALS AND METHODS

Participants

Twenty-four patients with MDD and chief complaint of sleep disturbance symptoms were enrolled as the Pa_s, and 33 patients with MDD without sleep disturbance symptoms were included as Pa_ns. All patients were recruited from the Second Xiangya Hospital of Central South University, China. Moreover, 32 HCs were recruited from the local community. The inclusion criteria for the patients were as follows: (1) first major depressive episode; (2) 17-item Hamilton Rating Scale for Depression (HAMD-17) total scores ≥18; (3) no other accompanying conditions that may result in sleep disturbances. The severity of depressive symptoms was assessed by the scores of HAMD-17. Anxiety/somatisation severity was

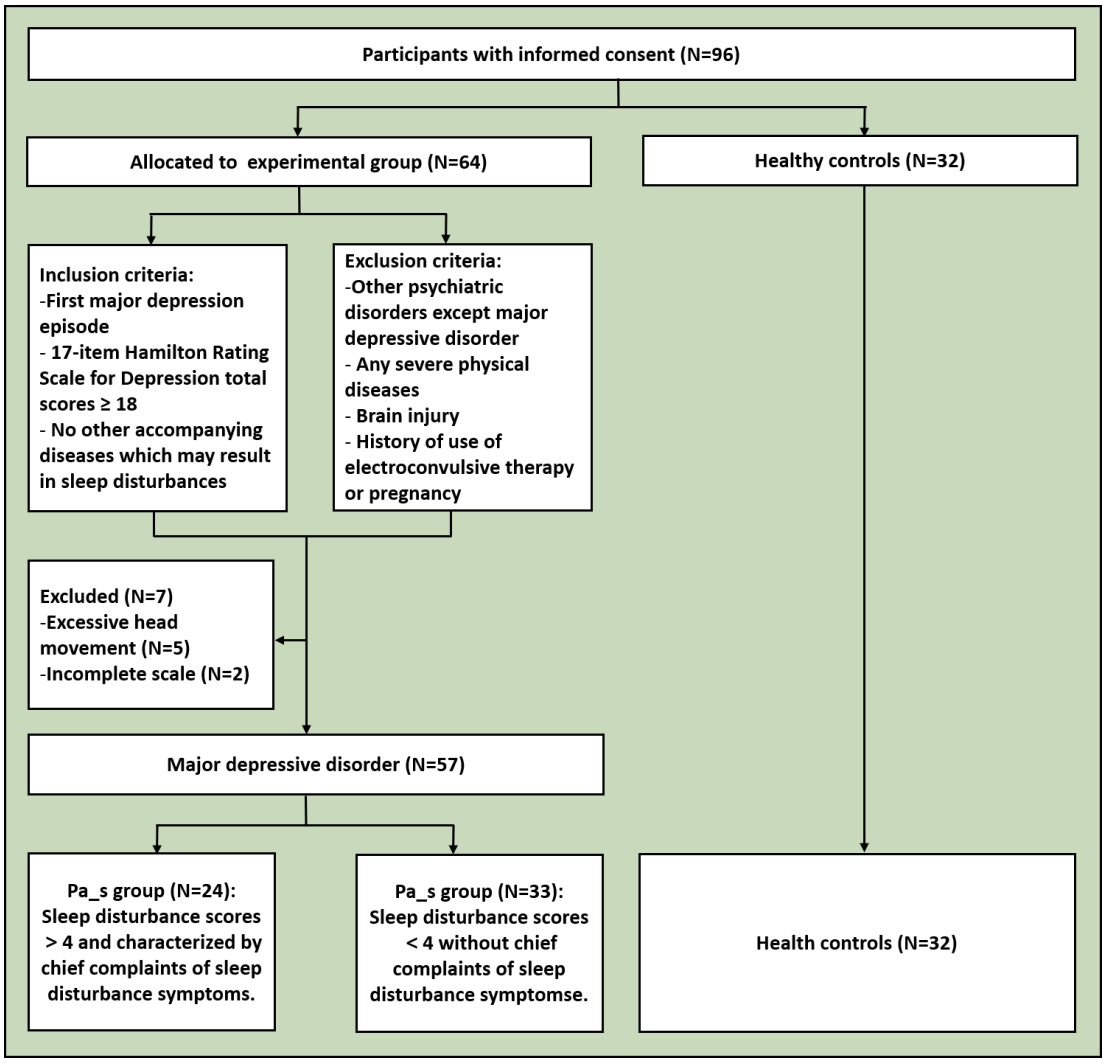

Figure 1 Flowchart for the enrolment and follow-up of subjects in the study.

evaluated by items 10–13, 15 and 17. Retardation symptoms were evaluated by items 1, 7, 8 and 14. The severity of cognitive disturbances was evaluated by items 2, 3 and 9. The severity of weight loss was evaluated by item 16. The anxiety state was assessed by the Beck Anxiety Inventory (BAI). Sleep disturbance scores were computed by summing the scores of items 4, 5 and 6 of HAMD-17. If sleep disturbance scores are greater than 4 and characterised by chief complaints of sleep disturbance symptoms, the patients with MDD would be assigned to the Pa_s group. If sleep disturbance scores are 4 or lower without chief complaints of sleep disturbance symptoms, the patients with MDD would be assigned to the Pa_ns group[20](figure 1).

All the participants were aged between 29 and 38 years, right-handed and educationally matched. Patients were diagnosed with MDD independently by two psychiatrists using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). The participants were excluded if they had other psychiatric disorders except MDD, any severe physical diseases, brain injury, a history of electroconvulsive therapy use or were pregnant. For HCs, they were excluded if they had a family history of mental illness, substance abuse or psychotic symptoms.

The study was conducted in accordance with the Helsinki Declaration. Each participant has submitted written informed consent before enrolment.

Image acquisition

All images were obtained using a 3.0 T GE scanner (General Electric, Fairfield Connecticut, USA). Participants were asked to close their eyes, remain awake and quiet during the scan. Parameters were as follows: repetition time/echo time=2000/30 ms, 30 slices, 64×64 matrix, 90° flip angle, 24 cm field of view (FOV), 4 mm slice thickness, 0.4 mm gap and 250 volumes (500 s).

Data preprocessing

Data were preprocessed by the data processing assistant for resting-state functional magnetic resonance imaging (fMRI) with MATLAB (MathWorks). To mitigate initial signal instability and early adaptation time of subjects, the first 10 original images were discarded. The primary processes included slice timing and normalisation.

Participants who had more than 2° of angular rotation in each axis and 2 mm of translation in the x, y or z direction were excluded. After normalisation, the imaging data were temporally band-pass filtered at 0.01–0.08 Hz and linearly detrended. Several covariates were removed, including Friston-24 head motion parameters acquired by rigid body correction, signals from a ventricular region of interest, and signals from a ventricular region centred in the white matter. The global signal was retained as indicated previously.[21] After data preprocessing, the DMN mask was constructed using Group Independent Component Analysis of fMRI toolbox (GIFT). The analysis processes were as follows: data reduction, independent component separation and back reconstruction. The DMN components were chosen based on the templates provided by GIFT. For each component, a statistical map was generated by voxel-wise one-sample t-tests (Gaussian random field (GRF) theory corrected at $p<0.05$ with voxel significance at $p<0.001$ and cluster significance at $p<0.05$), and masks were generated to apply in the following NH analysis.

The NH analysis was conducted using MATLAB, which calculated correlation coefficients between each voxel and other voxels within the DMN mask. The resulting NH maps were smoothed with a Gaussian kernel of 8 mm full width at half-maximum.

Statistical analyses

For the differences in the three groups, the χ^2 test was applied to describe qualitative variables. The analysis of variance was used to compare quantitative variables, such as age, years of education, HAMD-17 total score and the five-factor scores across the groups.

The NH analysis was performed by an analysis of covariance across the three groups, followed by post hoc t-tests. Age, sex, level of education and the average frame-wise displacement were used as covariates. The p value was set at 0.05 and corrected using the GRF (voxel significance at $p<0.001$ and cluster significance at $p<0.05$).

The correlation between NH abnormalities and clinical variables, such as HAMD-17 total scores, was analysed using partial correlation analysis.

The receiver operating characteristic (ROC) curve was employed to distinguish between Pa_s and Pa_ns. Subsequently, the optimal cut-off maximising the combined sensitivity and specificity was computed.

RESULTS

Demographic characteristics and clinical information

There were no group differences in age and years of education among the three groups. For the two patient groups, a significant difference was found in sex ratios but not for illness duration. Both patient groups showed higher HAMD-17 total and factor scores than HCs. Additionally, the Pa_s group showed higher BAI scores, HAMD-17 total scores and sleep disturbances than those of the Pa_ns group (table 1).

NH differences across groups

Intriguingly, the NH values showed notable differences in the DMN, mainly in the left superior MPFC and right Pcu across the three groups (figure 2). Compared with Pa_ns, Pa_s showed significantly decreased NH in the left superior MPFC ($T=-3.99$, $p<0.001$) and increased NH in the right PCu ($T=4.08$, $p<0.001$). Compared with HCs, Pa_s displayed decreased NH in the left superior MPFC ($T=-4.43$, $p<0.001$) and increased NH in the right PCu ($T=4.97$, $p<0.001$). Between the pa_ns and HCs groups,

Table 1 Demographic and clinical characteristics of participants

Variables	Pa_s group (n=24)	Pa_ns group (n=33)	HCs (n=32)	F/c^2/t	Post hoc t-tests or P values
Age (years)	31.38 (6.78)	29.48 (7.13)	29.59 (5.00)	1.07*	0.354
Sex (male/female)	12/12	6/27	15/17	8.09†	0.023
Education (years)	13.63 (3.73)	13.91 (3.06)	14.59 (2.82)	0.72*	0.494
Illness duration (months)	5.83 (4.12)	6.77 (4.65)	–	0.78‡	0.432
BAI scores	47.39 (13.11)	37.97 (7.58)	22.63 (2.28)	63.75*	Pa_s>Pa_ns>HCs
HAMD-17 scores	23.38 (3.70)	20.18 (2.64)	0.94 (0.95)	670.29*	Pa_s>Pa_ns>HCs
Sleep disturbances§	5.54 (0.51)	3.15 (0.94)	0.34 (0.60)	357.41*	Pa_s>Pa_ns>HCs
Anxiety/somatisation	7.38 (1.91)	6.76 (1.82)	0.44 (0.62)	190.43*	Pa_s, Pa_ns>HCs
Retardation symptoms	6.25 (1.51)	6.64 (1.32)	0.16 (0.37)	313.83*	Pa_s, Pa_ns>HCs
Weight loss	0.71 (0.81)	0.39 (0.70)	0	9.83*	Pa_s, Pa_ns>HCs
Cognitive disturbances	3.50 (2.04)	3.24 (1.70)	0	52.83*	Pa_s, Pa_ns>HCs

*Analysis of covariance.
†χ^2 test.
‡Two sample t-test.
§Sleep disturbance scores were computed by adding scores of items 4, 5 and 6 of the HAMD-17 scale.
BAI, Beck Anxiety Inventory; HAMD-17, the 17-Item Hamilton Rating Scale for Depression; HCs, healthy controls; Pa_ns, major depressive disorder without sleep disturbance; Pa_s, major depressive disorder with sleep disturbance.

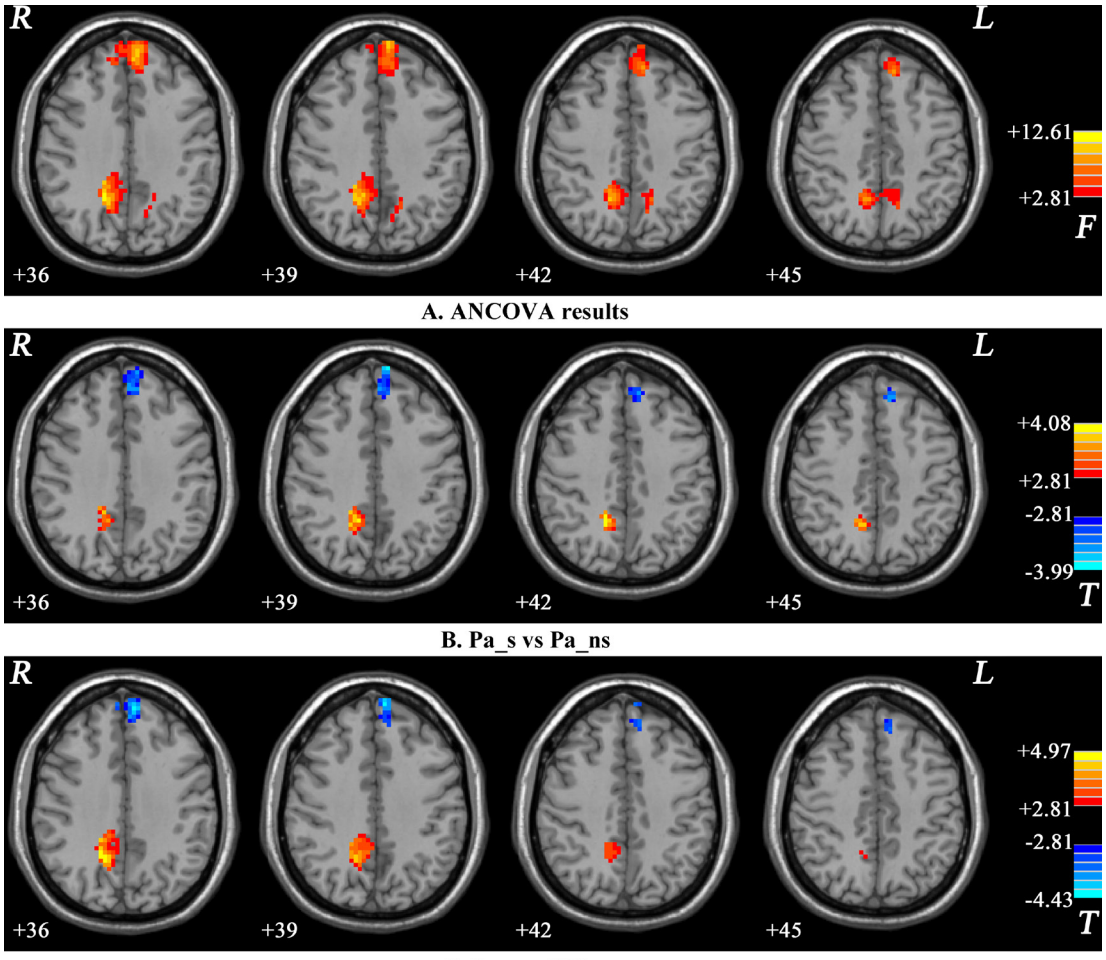

Figure 2 Brain regions within the DMN show group differences in NH values across the three groups. The colour bar indicates F values from ANCOVA (age, sex, years of education and frame-wise displacement as covariates). The statistical map depicts higher and lower NH of patients with MDD and sleep disturbance symptoms compared with patients with MDD without sleep disturbance symptoms. Blue denotes lower NH, and red denotes higher NH. The colour bar indicates T values from the two-sample t-test. ANCOVA, analysis of covariance; DMN, default mode network; HCs, healthy controls; MDD, major depressive disorder; NH, network homogeneity; Pa_ns, major depressive disorder without sleep disturbance; Pa_s, major depressive disorder with sleep disturbance.

no difference in NH values was found in the DMN (figure 2 and table 2).

Correlations between NH and clinical characteristics

For all patients, there was a negative correlation between the NH values of the left superior MPFC and BAI scores (r=−0.37, p=0.005), a positive correlation between the NH values of the left superior MPFC and retardation (r=0.28, p=0.038) and a negative correlation between the NH values of the left superior MPFC and sleep disturbances (r=−0.42, p=0.001). There was a positive correlation between the NH values of the right PCu and BAI scores (r=0.35, p=0.010), a positive correlation between the NH values of the right PCu and weight (r=0.36, p=0.005), a negative correlation between the NH values of the right PCu and retardation (r=−0.33, p=0.013) along with a positive correlation between the NH values of the right PCu and sleep disturbances (r=0.41, p=0.002). However, only the correlations between the NH values of the left superior MPFC and the right PCu and the sleep disturbances for all patients survived the Bonferroni correction (figure 3).

For Pa_ns, there was a positive correlation between the NH values of the right PCu and weight (r=0.37, p=0.035). However, this correlation could not survive the Bonferroni correction. For Pa_s, there was no significant correlation between abnormal NH and the HRSD-17 total scores as well as the five-factor scores.

ROC curves in MDD with and without sleep disturbances

We then used abnormal NH values in DMN to classify Pa_s from Pa_ns. We achieved 81.06% accuracy for the right PCu and 78.03% for the left superior MPFC. Sensitivity reached 83.33% for both the right PCu and the left superior MPFC. Specificity stood at 78.79% for the right PCu and 72.73% for the left superior MPFC. The ROC analysis yielded an area under the curve of 0.84 for the

Table 2 Abnormal network homogeneity of the default mode network across three groups

Cluster location	Peak (MNI) x	y	z	Voxels (n)	T value
Pa_s vs Pa_ns					
Right precuneus	15	−54	42	66	4.08
Left superior MPFC	−9	60	39	84	−3.99
Pa_s vs HCs					
Right precuneus	15	−57	36	122	4.97
Left superior MPFC	−6	57	39	88	−4.43
Pa_ns vs HCs					
None					

T values were conducted from an analysis of covariance across the three groups, followed by post hoc t-tests. The p value was set at 0.05 and corrected using the GRF (voxel significance at p<0.001 and cluster significance at p<0.05).
GRF, Gaussian random field; HCs, healthy controls; MNI, Montreal Neurological Institute; MPFC, medial prefrontal cortex; Pa_ns, major depressive disorder without sleep disturbance; Pa_s, major depressive disorder with sleep disturbance.

left superior MPFC and 0.83 for the right PCu (online supplemental figure 1).

DISCUSSION

Main findings

In this study, we demonstrated that the Pa_s group displayed more serious depressive and anxious symptoms than the Pa_ns group. Importantly, Pa_s showed decreased NH in the left superior MPFC and increased NH in the right PCu compared with Pa_ns and HCs. The NH values of the left superior MPFC were negatively correlated with sleep disturbances, while the NH values of the right PCu showed a positive correlation with sleep disturbances. Moreover, abnormal NH values in the DMN can successfully distinguish pa_s from pa_ns.

The superior MPFC is a core region of the DMN, which is important for sleep rhythm maintenance. It is also tightly linked with affective-limbic regions (such as the amygdala and the hippocampus), executive control, as well as emotional processing regions (such as the orbital frontal cortex and anterior cingulate cortex). Through these connections, MPFC may be involved in the modulation of emotional behaviour and self-referential processing.[22] Dysfunction of this region, such as decreased NH in the left superior MPFC, can affect the balance between the cognitive system and the ventral emotional system. Therefore, decreased NH in the left superior MPFC may reflect a decrease in emotional regulation capabilities and more severe MDD symptoms.

PCu is usually involved in awareness and conscious self-perception.[23] Based on the concept of 'default mode', it is the most active cortical region during silent rest.[24] PCu activity during conscious resting states contributes to the self-referential 'thought' processing, which has the highest metabolic activity in the baseline resting state and consumes about 35% more glucose than other areas of the cerebral cortex.[24] Recent functional imaging studies[23] also revealed an obvious inactivation of states of consciousness presented by the PCu and adjacent posteromedial cortical regions. Because PCu and prefrontal cortices were less active than the rest of the brain during different sleep cycles,[25 26] PCu dysfunction may be associated with sleep disturbances and contribute to abnormal NH in the right PCu.

Numerous studies have consistently demonstrated increased DMN activity in patients with MDD, which may be associated with the prevalent negative self-referential thinking, rumination and difficulties in emotion regulation. Notably, previous studies have indicated a close correlation between abnormal DMN activity and sleep

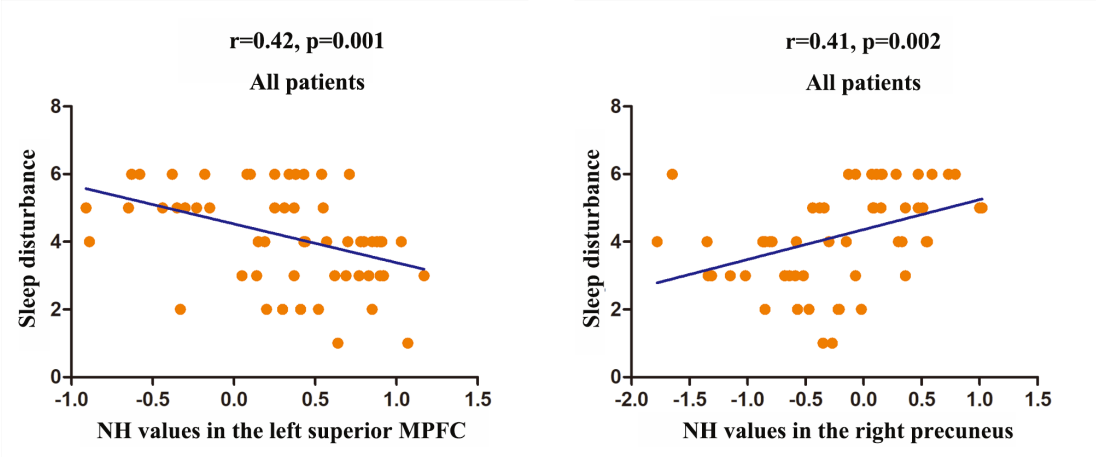

Figure 3 Partial correlations between NH values and clinical variables. Age, sex, level of education and the average frame-wise displacement were used as covariates. For all patients with MDD, there was a negative correlation between NH values of the left superior MPFC and sleep disturbances. A positive correlation was observed between NH values in the right precuneus and sleep disturbances. MDD, major depressive disorder; MPFC, medial prefrontal cortex; NH, network homogeneity.

disturbances in individuals with MDD.[27] Sleep disturbances may lead to enhanced DMN activity, thus forming a vicious cycle that exacerbates the severity of depressive symptoms. Moreover, excessive DMN activity may relate to decreased rapid eye movement sleep and altered deep sleep stages in patients with MDD.[8] These changes can cause poor sleep quality and disrupted sleep patterns. Additionally, the abnormal functional connectivity between the DMN and dorsal attention network may correlate with sleep duration in depression.[27] In line with these observations, we have found that patients with MDD and sleep disturbances exhibit abnormal DMN activity, which may contribute to more severe depressive symptoms compared with those without sleep disturbances.

Besides, the functional connectivity between Pcu and MPFC has been reported to significantly correlate with both sleep quality and circadian preference.[28] Patients with MDD showed increased activity in the right Pcu, which was associated with disease severity and poor social cognition. Additionally, patients with MDD had significantly altered regional homogeneity in the bilateral Pcu.[29] The above results collectively reflect the decreased neural activity in the Pcu of patients with MDD. Consistently, our study confirmed increased NH in the right PCu and decreased NH in the left superior MPFC in Pa_s compared with Pa_ns and HCs. Sleep restriction can inhibit MPFC activation and cause activation in the PCu for the most difficult task condition. The result demonstrated that the two brain regions would make compensatory functional responses. In this study, we found that higher NH values in the MPFC of patients with MDD corresponded to milder sleep disturbances, whereas higher NH values in the PCu indicated more severe sleep disturbances. This could suggest that the MPFC region is still in a functional compensation state, whereas the PCu region has lost this compensation. The increased functional connectivity between the MPFC and PCu within the DMN indirectly supports this possibility.[28] Besides, antidepressant treatment can improve the functional connectivity of DMN,[30] which suggests that the DMN itself may play a significant role in the pathology of MDD. Therefore, the DMN may play a crucial role in the neurobiological mechanisms of MDD with sleep disturbances.

Our study has several highlights. First, all recruited patients with MDD in this study were first-episode and drug-naive, avoiding the influence of medication and illness duration on NH values. Second, we compared the differences in brain functional connectivity using the NH method between patients with MDD with and without sleep disturbances to reveal NH differences within the DMN. Third, abnormal NH values in DMN successfully differentiated pa_s from pa_ns.

This study is not without its limitations. First, the sample size was relatively small. Second, the age range of the sample was relatively narrow. Third, our study only focused on the abnormal function of the DMN, which may overlook the functions of other brain regions. Finally, we have not analysed other specific factors for sleep problems, such as sleep deprivation and sleep duration, which could potentially bias our results.

CONCLUSIONS

Patients with MDD and sleep disturbances showed abnormal NH in the DMN, which can differentiate pa_s from pa_ns. The DMN may play a crucial role in the neurobiological mechanisms of MDD with sleep disturbances.

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Contributors WG and BL designed the research. YO carried out the experiments and analysed the date. YO and MH wrote the paper. JZ, HL, FL and PL contributed to the MRI date acquisition. All authors contributed to the article and approved the submitted version. WG and BL are responsible for the overall content as the guarantors.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the Medical Research Ethics Committee of the Second Xiangya Hospital of Central South University, China (approval code: 2013023; approval date: 20130304). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data has the potential to be shared with others upon request.

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REFERENCES

1 Huang J, Zuber V, Matthews PM, *et al*. Sleep, major depressive disorder, and Alzheimer disease: a Mendelian randomization study. *Neurology* 2020;95:e1963–70.
2 Roenneberg T, Pilz LK, Zerbini G, *et al*. Chronotype and social jetlag: a (self-) critical review. *Biology (Basel)* 2019;8:54.

3 Daghlas I, Lane JM, Saxena R, *et al*. Genetically proxied diurnal preference, sleep timing, and risk of major depressive disorder. *JAMA Psychiatry* 2021;78:903–10.
4 Basnet S, Merikanto I, Lahti T, *et al*. Associations of common noncommunicable medical conditions and chronic diseases with chronotype in a population-based health examination study. *Chronobiol Int* 2017;34:462–70.
5 Zhao D, Wu Z, Zhang H, *et al*. Somatic symptoms vary in major depressive disorder in China. *Compr Psychiatry* 2018;87:32–7.
6 Nyer M, Farabaugh A, Fehling K, *et al*. Relationship between sleep disturbance and depression, anxiety, and functioning in college students. *Depress Anxiety* 2013;30:873–80.
7 Tashjian SM, Goldenberg D, Monti MM, *et al*. Sleep quality and adolescent default mode network connectivity. *Soc Cogn Affect Neurosci* 2018;13:290–9.
8 Marques DR, Gomes AA, Caetano G, *et al*. Insomnia disorder and brain's default-mode network. *Curr Neurol Neurosci Rep* 2018;18:45.
9 Lv D, Ou Y, Xiao D, *et al*. Identifying major depressive disorder with associated sleep disturbances through fMRI regional homogeneity at rest. *BMC Psychiatry* 2023;23:809.
10 Belleau EL, Treadway MT, Pizzagalli DA. The impact of stress and major depressive disorder on hippocampal and medial prefrontal cortex morphology. *Biol Psychiatry* 2019;85:443–53.
11 Zhang B, Qi S, Liu S, *et al*. Altered spontaneous neural activity in the precuneus, middle and superior frontal gyri, and hippocampus in college students with subclinical depression. *BMC Psychiatry* 2021;21:280.
12 Lunsford-Avery JR, Damme KSF, Engelhard MM, *et al*. Sleep/wake regularity associated with default mode network structure among healthy adolescents and young adults. *Sci Rep* 2020;10:509.
13 Pomares FB, Boucetta S, Lachapelle F, *et al*. Beyond sleepy: structural and functional changes of the default-mode network in idiopathic hypersomnia. *Sleep* 2019;42:zsz156.
14 McKinnon AC, Hickie IB, Scott J, *et al*. Current sleep disturbance in older people with a lifetime history of depression is associated with increased connectivity in the default mode network. *J Affect Disord* 2018;229:85–94.
15 Yan M, Cui X, Liu F, *et al*. Abnormal default-mode network homogeneity in melancholic and nonmelancholic major depressive disorder at rest. *Neural Plast* 2021;2021:6653309.
16 Zang Y, Jiang T, Lu Y, *et al*. Regional homogeneity approach to fMRI data analysis. *Neuroimage* 2004;22:394–400.
17 Guo W, Liu F, Zhang J, *et al*. Abnormal default-mode network homogeneity in first-episode, drug-naive major depressive disorder. *PLoS ONE* 2014;9:e91102.
18 Guo W, Cui X, Liu F, *et al*. Increased anterior default-mode network homogeneity in first-episode, drug-naive major depressive disorder: a replication study. *J Affect Disord* 2018;225:767–72.
19 Gao Y, Zheng J, Li Y, *et al*. Abnormal default-mode network homogeneity in patients with temporal lobe epilepsy. *Medicine (Baltimore)* 2018;97:e11239.
20 Trivedi MH, Bandelow B, Demyttenaere K, *et al*. Evaluation of the effects of extended release quetiapine fumarate monotherapy on sleep disturbance in patients with major depressive disorder: a pooled analysis of four randomized acute studies. *Int J Neuropsychopharmacol* 2013;16:1733–44.
21 Hahamy A, Calhoun V, Pearlson G, *et al*. Save the global: global signal connectivity as a tool for studying clinical populations with functional magnetic resonance imaging. *Brain Connect* 2014;4:395–403.
22 Phillips ML, Drevets WC, Rauch SL, *et al*. Neurobiology of emotion perception II: implications for major psychiatric disorders. *Biol Psychiatry* 2003;54:515–28.
23 Cavanna AE, Trimble MR. The precuneus: a review of its functional anatomy and behavioural correlates. *Brain* 2006;129:564–83.
24 Cavanna AE. The precuneus and consciousness. *CNS Spectr* 2007;12:545–52.
25 Maquet P, Degueldre C, Delfiore G, *et al*. Functional neuroanatomy of human slow wave sleep. *J Neurosci* 1997;17:2807–12.
26 Maquet P, Péters J, Aerts J, *et al*. Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature* 1996;383:163–6.
27 Xu Z, Zhao W, Wang H, *et al*. Functional connectivity between dorsal attention and default mode networks mediates subjective sleep duration and depression in young females. *J Affect Disord* 2023;325:386–91.
28 Tian Y, Chen X, Xu D, *et al*. Connectivity within the default mode network mediates the association between chronotype and sleep quality. *J Sleep Res* 2020;29:e12948.
29 Lai CH. The regional homogeneity of cingulate-precuneus regions: the putative biomarker for depression and anxiety. *J Affect Disord* 2018;229:171–6.
30 Li B, Liu L, Friston KJ, *et al*. A treatment-resistant default mode subnetwork in major depression. *Biol Psychiatry* 2013;74:48–54.

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