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ORIGINAL RESEARCH

Altered Structure-Function Coupling Associated with Attention Decline in Shift Work Disorder

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Introduction: Previous studies on shift work disorder (SWD) have revealed altered functional and structural brain networks underlying attention decline. However, changes in structure-function coupling (SFC) and their relationship with attention decline remain unknown. This study aimed to examine the role of changed SFC in abnormal attentional network function in SWD.

Methods: Thirty-four patients with SWD and thirty-two healthy controls were recruited. All participants underwent resting-state functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) scans. All participants underwent an attentional network test to evaluate their functions. Finally, Pearson's correlation analysis was conducted to analyze the association between aberrant attentional network function and altered structural and functional connectivity (SC-FC) coupling in patients with SWD.

Results: Compared to healthy subjects, decreased alerting and executive functions were found in patients with SWD. In addition, we observed decreased SC-FC coupling in patients with SWD, specifically in the left anterior cingulate gyrus ($T = -3.6449$, $P = 0.0003$), central opercular cortex ($T = -3.7187$, $P = 0.0002$), middle frontal gyrus ($T = -3.8342$, $P = 0.0001$), and parietal operculum cortex ($T = -3.6121$, $P = 0.0003$), compared with healthy subjects. Better altering performance was significantly associated with lower SC-FC coupling in the anterior cingulate gyrus of patients with SWD ($r = -0.51$, $P = 0.002$).

Discussion: Our findings unravel that the decreased SC-FC coupling in the anterior cingulate gyrus may contribute to the impaired altering network function in SWD, which can further understand the neural mechanisms of impaired attention in SWD and inform a potentially therapeutic intervention for SWD patients.

Keywords: shift work disorder, fMRI, attentional network function, structure-function coupling

Introduction

Shift work disorder (SWD) is a condition that arises from the misalignment of circadian rhythms due to irregular work schedules, leading to significant impairments in overall health.[1] It has been suggested that SWD impacts on various cognitive areas, including memory, attention, and response inhibition.[2] Attention is fundamental to cognitive process and critical for optimal performance in both work and daily life.[3] Convergent evidence has suggested that SWD impairs both sustained attention and the reorientation of attention.[4] Posner and Petersen have developed a neurocognitive model of attention with three networks: the alerting network, the orienting network, and the executive network.[5] The Attentional Networks Test (ANT), which concurrently and rapidly, evaluates the efficacy of the three attentional networks.[6] The alerting network pertains to a person's capacity to attain and sustain heightened sensitivity to incoming information. The orientation network regulates the selection and concentration of relevant stimuli. The executive network regulates behavior to achieve desired goals and resolve conflicts among conflicting reactions.[7] Prior studies have demonstrated reduced alerting function and executive function in patients with SWD assessed by ANT.[8] And the executive effect of attention network significantly correlates with global network efficiency of structural networks of patients with SWD.[8]

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Notably, functional magnetic resonance imaging (fMRI) is prominently utilized to examine the underlying neural mechanisms of SWD.[9] And the structural changes associated with SWD have been linked to prolonged exposure to irregular work hours, which can lead to neuroanatomical alterations.[10] Furthermore, the patients with SWD exhibit abnormal functional connections between extensive brain networks.[9] Increasing evidence has pointed out the robust correlation between structural and functional brain connection metrics across several spatiotemporal scales, such as neuronal populations and cortical areas.[11–13] Characterizing the functional specialization of cortical regions according to the connection patterns has proven crucial in comprehending the hierarchies of brain organization.[14] Different from single functional or structural brain imaging analysis, structure-function coupling (SFC) integrates special anatomical structures and functional activities of the brain to understand of how the brain utilizes its physical architecture to support complex cognitive functions.[15] Recent studies have demonstrated that the decreased SFC relates to increased age and reduced cognitive level of normal aging subjects, supporting functional connection within specific functional networks, such as default mode network.[16,17] Specifically, abnormalities in SFC can result in various cognitive dysfunctions and enhance the risk for neurodevelopmental disorders, such as attention deficit hyperactivity disorder.[18] And disrupted sleep rhythm causes aberrant pattern of SFC, involving occipital areas and the precentral gyrus.[19] Hence, investigation of SFC is beneficial to understanding the neural mechanisms of abnormal attentional network function of patients with SWD. However, the role of SFC in the abnormal attentional network function in patients with SWD remains unclear.

In the current study, we hypothesized that altered SFC might be related to impaired attentional network function in patients with SWD. Here, we enrolled patients with SWD and matched healthy controls (HCs) undergoing diffusion tensor imaging (DTI), resting-state fMRI, and ANT. We also compared the attentional network function and regional SFC between patients with SWD and HCs. Finally, we performed a correlation analysis between attentional network function and altered SFC in patients with SWD. We aimed to explore whether SFC contributes to abnormal attentional network function in patients with SWD and whether it could be used as a potential neuromarker.

Materials and Methods

Participants

Thirty-four right-handed participants (31 females) were diagnosed with SWD, according to the International Classification of Sleep Disorders (3rd Edition, ICSD-3). According to the ICSD-3 criteria, we utilized three items from the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) to assess insomnia symptoms. Furthermore, the question "Have you had this sleep or sleepiness problem relate to the work schedule for at least one year? (yes/no)" was added to meet the criteria for screening the patients with SWD. Patients with SWD who were recruited (January 2022 to June 2022, shown in Figure 1) and employed at Beijing Anding Hospital who met the following criteria: (i) aged from 20 to 40 years; (ii) working regular night shift at least two shifts per week in the last one year; (iii) Pittsburgh Sleep Quality Index (PSQI) > 5;[20] (iv) with no history of prophylactic or therapeutic medicine in the past 3 months. The participants in SWD group should be excluded as following criteria: (i) being pregnant or breastfeeding; (ii) with history of neurologic or psychiatric disorders; (iii) participating in cognitive experiments within one year; (iv) with history of alcohol or drug abuse; (v) any MRI contraindications.

And we recruited thirty-two right-handed HCs (29 females) as day workers and exhibited regular sleep patterns according to the Horne-Ostberg Morningness-Eveningness Questionnaire,[21] which assessed individuals' chronotype (morningness-eveningness preference). And PSQI score of each individual in HCs group was less than 5.

To calculate the required sample size for the study on shift worker disorder and its neuroimaging correlates, we performed a statistical power analysis using by G*Power software (version 3.1). The two-sample t test (Difference between two independent means, two-tails) is used to determine the sample size of two groups. The parameters for the power analysis were set as follows: the effect size $d = 0.8$, α err prob = 0.05, power (1-β err prob) = 0.90. Thirty-four participants per group (SWD group and HCs group) would be required to detect the hypothesized neuroimaging differences with sufficient statistical power.

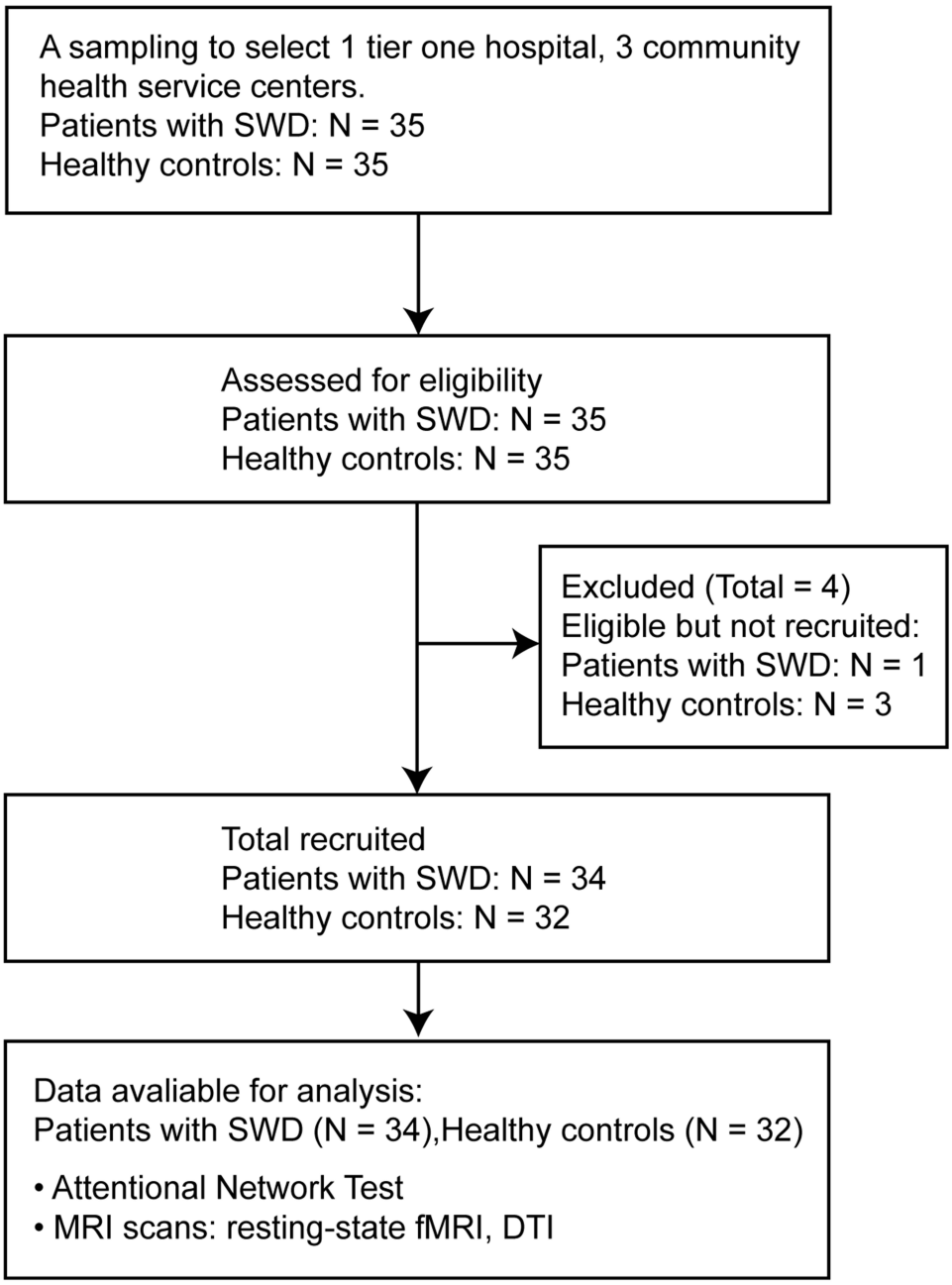

Figure 1 The flowchart of the participants inclusion in SWD group and healthy controls group.
Abbreviations: DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; N, number; SWD, shift worker disorders.

And this study was performed in compliance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of the Beijing Anding Hospital (Scientific Research 2021–93). All recruited participants provided informed consent before their participation in the study.

Study Procedure

All recruited participants were needed to visit our laboratory twice. An introduction of the study protocol was presented, and the informed consent was signed at the first visit. During the second visit after one day, the participants returned to the laboratory for two hours from 8:00 am to 10:00 am. All participants were required to complete ANT testing and MRI

scanning. At the MRI scanning, we performed the 8 min 10 s resting-state fMRI, 4 min 10 s T1 scan, and 12 min 30 s DTI scan.

Attentional Network Test

ANT was employed and programmed using E-Prime software to evaluate the attention network function of all participants (shown in Figure 2).[22] A total of 336 trails were completed, consisting of 312 testing trials and 24 practice trials. The task assigned to the recruited participants was to locate the target or arrow in the center and push the left or right key accordingly. The specific steps were as follows: cueing time (100 ms) after a varied fixation period (400–1600 ms). The cue presentation included four flavors: no cue (25%), center cue (25%), double cue (25%), and spatial cue (25%). Additionally, a 400 ms fixation period was shown, which was followed by a target time of 1700 ms. The target vanished after the participants' responses, and a fixation period ensued for an erratic 400–1600 ms. For each participant, the median reaction times (RT) under each of the four cue conditions and the three congruency conditions mentioned above were determined. RT differences were used to characterize the effects of conflict, orientation, and alert networks. Finally, we examined the task factors, which included accuracy, RT, altering effect, orienting effect, and control conflict. The following variables were computed: mean reaction time (RT), alerting RT (RT no cue minus RT center cue), orienting RT (RT center cue minus RT spatial cue) and executive control RT (RT incongruent flanker minus RT congruent flanker) as previously instructed. Incorrect responses and omissions were excluded as well as outliers defined as greater than the mean for each subject plus or minus two standard deviations.

MRI Acquisition

MRI scans were conducted using a Siemens 3.0 Tesla Prisma at Beijing Anding Hospital (Beijing, China). All subjects were required to remain motionless with their eyes closed and fight the urge to doze out during the scan. To further

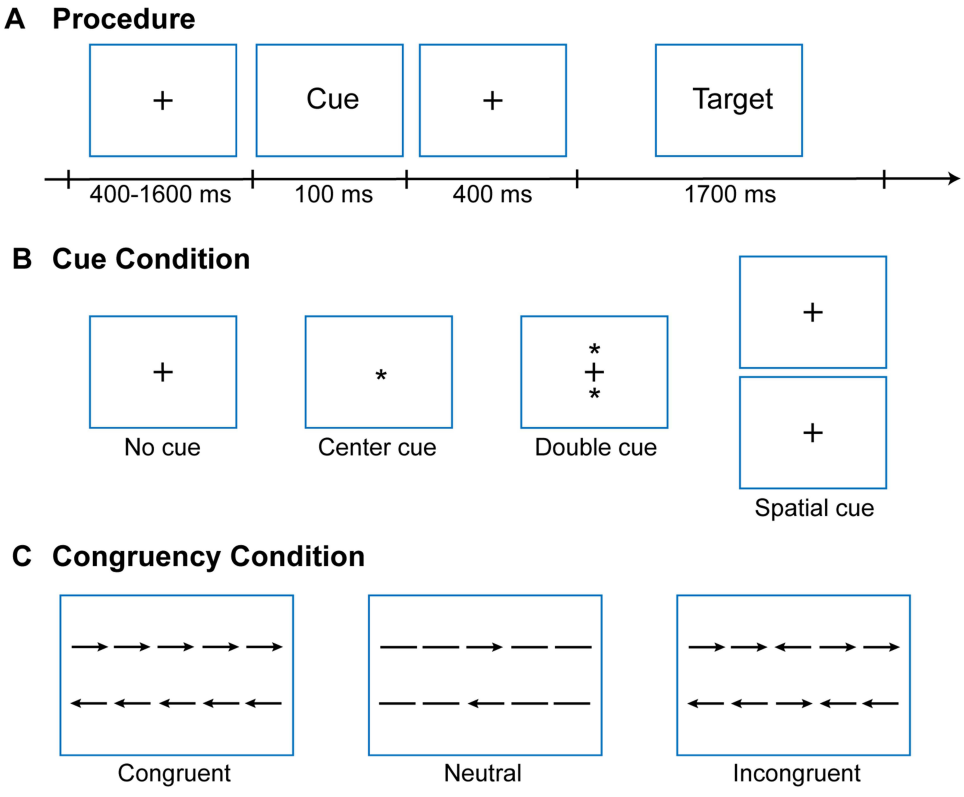

Figure 2 An illustration of the experimental procedure of the Attentional Network Test alongside with all potential stimuli linked to each event. (**A**) Sequence of each trial incident. In the "Cue display", one of the four cues was exhibited. During the "Target" phase, one of the stimuli was displayed either above or below the fixation cross. (**B**) The four cue conditions. (**C**) The three stimulation conditions. The arrow of each stimulus was the target. Note: the asterisk (*) indicates the cue.

reduce noise during the MRI scan, earplugs were worn. The resting-state fMRI data was acquired utilizing a single-shot, gradient-recalled echo-planar imaging technique with the subsequent parameters: 180 volumes, 32 interleaved axial slices, 90° flip angle, 64 × 64 matrix, 1 mm gap, 225 mm × 225 mm field of view, and 3.5 mm slice thickness, echotime = 30 ms, and repetition time = 2000 ms.

Before DTI scanning, a conventional 3D T1-weight higher solution structural image was obtained with the following parameters: 1 mm^3 voxel size, 2,530 ms TR, 3.39 ms TE, 90° flip angle, 256 × 256 matrix, 256 mm× 256 mm field of view, 1 mm slice thickness. A single-shot echo-planar imaging scan provided DTI data for 12 minutes and 30 s of DTI data. Diffusion-sensitizing gradients were applied in 64 noncollinear directions (b = 1,000 mm2) with an acquisition without diffusion weighting (b = 0 s/mm2). Additionally, these parameters were 11,000 ms TR, 98 ms TE, 128 × 128 matrix, 256 × 256 field of view, 2.0 mm slice thickness, and no gap.

Image Preprocessing

The DTI pre-processing was conducted using the diffusion toolbox of the Functional Magnetic Resonance Imaging of the Brain software library (FSL, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). Initially, we rectified distortion caused by eddy currents and head motions. Subsequently, we striped the brain skull and extracted the cerebral tissue, yielding improved alignment outcomes and diminishing computational time by excluding non-cerebral tissue. The eddy current distortions and motion artifacts were corrected by using a rigid body transformation from each diffusion-weighted image to the b0 image. The diffusion tensor matrix was determined using the Stejskal and Tanner equation. By diagonalization of the tensor matrix, three eigenvalues and eigenvectors were gained. Furthermore, fractional anisotropy maps were calculated. Each DTI image was aligned with the T1-weighted image and subsequently registered to the MNI-152 space. Three-dimensional fiber tract reconstruction was performed using the DiffusionKit toolkit (http://diffusion.brainnetome.org/). Whole-brain tractography was acquired with the Fiber Assignment by Continuous Tracking technique. Fiber tracking processes were discontinued upon encountering a voxel with a fractional anisotropy <0.2 or when the minimum angle exceeded 50°.

The fMRIprep procedure was used to preprocess the data from the functional images. First, FreeSurfer was used to apply skull stripping, segmentation into cerebrospinal fluid, white matter, and gray matter, and surface reconstruction of the cortical regions. Second, the segmented structural images were registered to the MNI152 standard space using a nonlinear approach for spatial normalization. Third, the first time points of the functional images were excluded to minimize any initial noise or instability in the data. The functional images were then normalized to a 2 mm resolution to match the standard template. Head motion correction was applied to the functional data to correct for any movement that occurred during scanning. And spatial normalization of the preprocessed structural images was also performed to ensure consistent alignment with the MNI template. Moreover, nuisance covariate regression was conducted to remove noise originating from non-brain sources such as white matter, CSF, and global brain signals.

Construction of Structural Brain Networks

All T1-weighted structural MRI images were preprocessed using FreeSurfer 7.0 (http://surfer.nmr.mgh.harvard.edu) with the recon-all function to remove non-brain structures through skull stripping. An image comprising five tissue types (cortical gray matter, subcortical gray matter, white matter, cerebrospinal fluid, and diseased tissues) was generated using MRtrix. The cortical ribbon was then divided into 400 distinct regions using the Schaefer 400 atlas.[23] The subcortical structure was segmented into 54 nodes based on the results from FreeSurfer, which provided detailed subcortical anatomical labels. The segmented cortical and subcortical regions were combined and converted into a set of 454 nodes. Furthermore, the 454 nodes were categorized into seven large functional brain networks based on the previous studies.[9] The original DTI data were denoised using the dwidenoise function of MRtrix, which employed random matrix theory to measure the noise level of the data and apply appropriate denoising.[24] Distortions due to susceptibility, motion, and eddy currents were corrected using the dwifslpreproc script from MRtrix. The N4 algorithm was used to correct the diffusion-weighted MRI data for any bias field.[25] The preprocessed T1-weighted structural images and the processed DTI data were registered using ANTs software, resulting in the acquisition of the alignment matrix. The fiber-constrained spherical deconvolution algorithm was applied to the DTI data to calculate the orientation distributions of the white matter fibers by estimating the multi-tissue response

function.[26] The generated fiber tracks were mapped to the 454 parcellated nodes to create a 454 × 454 connection matrix. The inverses of the node volumes and fiber lengths were included as covariates in the matrix to account for any potential confounding factors related to the size and fiber length of the brain regions.

Construction of Functional Brain Networks

Gaussian kernel smoothing with a full width at half maximum (FWHM) of 6 mm was applied to the functional data to improve the signal-to-noise ratio. At last, signal filtering was performed with a bandpass filter (0.01–0.1 hz) to remove high-frequency noise and low-frequency drifts, focusing on the frequency range typically associated with resting-state functional connectivity. Using the same network atlas as for the structural data, the time series for each parcellated region (node) was extracted from the preprocessed functional data. The correlation coefficients between the time series of different nodes were calculated, resulting in a 454 × 454 functional connectivity matrix that represents the temporal correlations between brain regions.

Structure-Function Coupling

To assess structure-function coupling (SFC), the connectivity from each row of the structural and functional matrices was extracted as vectors, representing the connection strength from a single node to all other nodes in the network. The relationship between the structural and functional connectivity profiles was evaluated using the Spearman rank correlation. This method was applied to the non-zero elements from the regional structural and functional connectivity profiles. The Spearman correlation allows for evaluating the strength and direction of monotonic relationships between the structural and functional connectivity of the brain regions. The results of the Spearman correlation were used to quantify the degree of coupling between structural and functional networks (shown in Figure 3). After calculating the structure-function coupling of each brain node, independent *t*-tests were performed on the coupling between the two groups of subjects. To estimate p-values, 5,000 permutations were generated, and the false discovery rate (FDR) was used to make multiple comparisons.

Statistical Analysis

To examine the altered SFC in SWD, independent *t*-tests were performed between the two groups of subjects after calculating the structure-function coupling of each brain node. To estimate *P*-values, 5,000 permutations were generated, and the false discovery rate (FDR) was used to make multiple comparisons. Gender, age, and head motion were included as covariates in the statistical analysis. And the Friston 24 head motion parameter model was used to regress out the head motion effects. Images with exhibiting a maximum framewise displacement of 1.5 mm or 1.5° were excluded from subsequent analysis. Furthermore, the similarity between all SFC matrices of SWD and HCs was assessed by the coefficient of variation (equal to standard deviation of matrix/mean of matrix). More than 75% of the points with similarity greater than 75% were considered to be more stable coupling matrices within the group. Besides, five points with positive results have a similarity greater than 80% and were considered to indicate good reliability. The data of demographic information and the ANT were presented as the range of mean ± standard deviation (SD) and median (interquartile range) depending on the normal distribution. And the *P* values were measured by two-sample *t*-test if the data are normally distributed (two-tailed, $P < 0.05$ indicated statistically significant difference between SWD and HC). Mann–Whitney *U*-test was performed if the data were not normally distributed. We then investigated the associations between the attentional network function and the changed structural and functional connectivity (SC-FC coupling) in SWD. The altered coupling locations between structural and functional connectivity (SC-FC coupling) in participants with SWD were associated with ANT scores by Spearman correlation analysis, with a significance threshold of $P < 0.05$.

Results

The Demographic Characteristics and ANT Performance

Two healthy participants had not completed the MRI scans and were free from this study. A total of 34 patients with SWD and 32 healthy subjects completed the ANT assessments and fMRI scanning in this study. There were no statistically significant

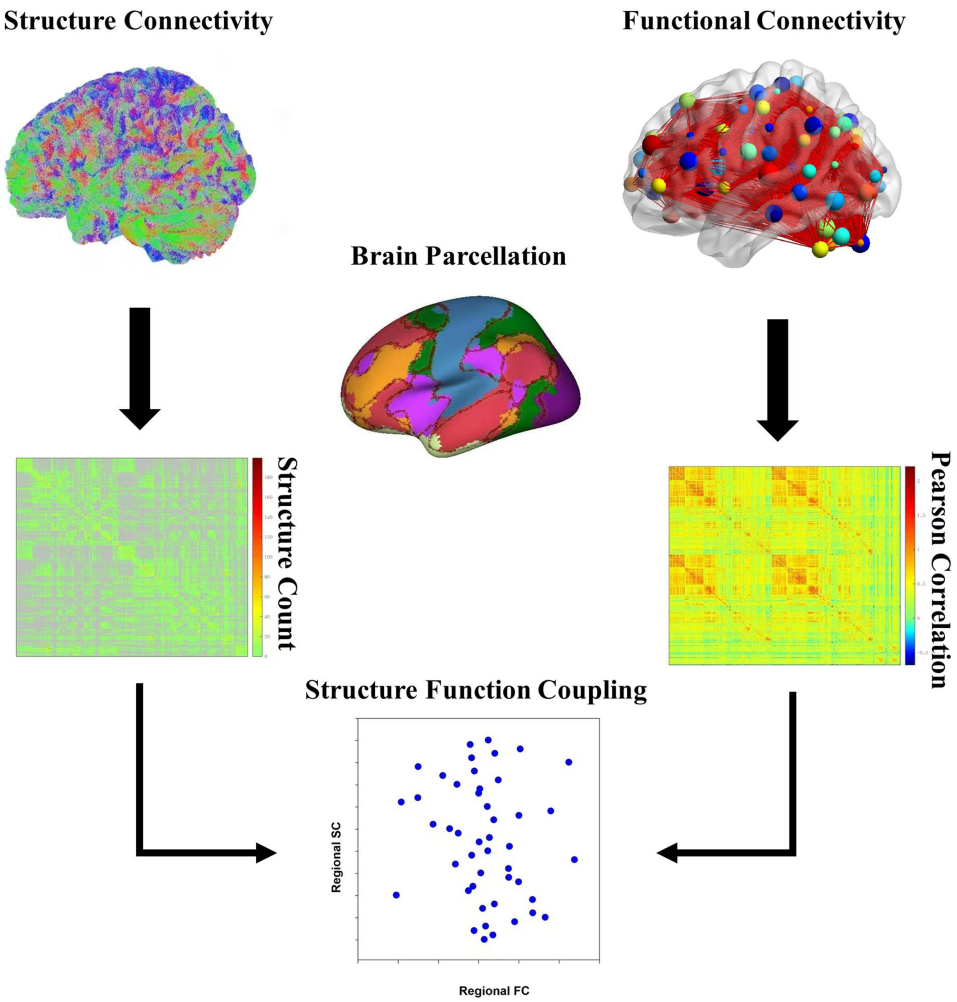

Figure 3 The flow diagram of structure-function coupling in patients with SWD and healthy controls.
Abbreviations: FC, functional connectivity; SC, structural connectivity.

differences in sex or age between the SWD group and HCs group ($P > 0.05$, shown in Table 1). And the sleep quality of patients with SWD was significantly poorer than HCs ($P < 0.001$). For ANT assessments, patients with SWD exhibited the reduced alerting effect ($P = 0.027$, Cohen's d = −0.51) and executive effect ($P = 0.018$, Cohen's d = 0.44) compared to HCs group. However, we did not observe the significant differences in orienting effect, overall mean RT, and accuracy between patients with SWD and HCs ($P > 0.05$).

Abnormal SC-FC Coupling Sites

For assessing the SC-FC coupling, we found the decreased SC-FC coupling in patients with SWD involving the left middle frontal gyrus (T = −3.8342, $P = 0.0001$), left anterior cingulate gyrus (T = −3.6449, $P = 0.0003$), left central opercular cortex (T = −3.7187, $P = 0.0002$), and left parietal operculum cortex (T = −3.6121, $P = 0.0003$) compared to HCs group (shown in Figure 4 and Table 2). Moreover, we performed the reliability of our methods for assessing SFC of SWD and HCs. Seventy-five percent of the SC-FC coupling with similarity among the SFC metrics of SWD and HCs was greater than 75% of the matrix. Furthermore, five points among the SFC matrices of SWD and HCs have a similarity greater than 80% and were considered to indicate good reliability (shown in Supplementary Materials, Figures S1–S4).

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Table 1 The Demographic Information and ANT Between Two Groups

Item	SWD N = 34	HC N = 32	χ^2/t/z	P
Gender (male/female)	3/31	3/29	0.006(χ2)	0.94
Age range (min, max)/years	23,33	24,33	/	/
Age [M(IQR)]/years	27.5(4.75)	26(2)	−1.57(z)	0.12
PSQI scores	10(4.25)	1(1)	−7.03(z)	<0.001
Alerting effect [Mean (SD)]/ms	40.34(22.61)	50.63(17.41)	−2.26(t)	0.027
Orienting effect [M (IQR)]/ms	42.5(22)	44.5(20.75)	−0.39(z)	0.7
Executive conflict effect [M (IQR)]/ms	125(46.5)	110(13)	−2.36(z)	0.018
Overall mean RT [M (IQR)]/ms	615.5(90.5)	593(78.25)	−1.67(z)	0.095
Accuracy [M (IQR)]/%	97(3)	98(1)	−1.75(z)	0.08

Notes: Mann–Whitney *U*-test was performed if the data were not normally distributed. χ^2 indicates the assessment the relationship between two categorical variables; *t* indicates that the data are normally distributed between SWD group and HC group; *z* indicates that the data are not normally distributed between SWD group and HC group.
Abbreviations: HC, healthy control; IQR, interquartile range; M, median; RT, reaction time; SD, standard deviation; SWD, shift work disorder.

Correlation Analysis

To detect the relationship between abnormal SC-FC coupling sites and ANT scores in subjects with SWD, we performed Pearson correlation analysis. Better altering performance was correlated with lower SC-FC coupling in the anterior cingulate gyrus in SWD (r = −0.51, P = 0.002, shown in Figure 5).

Discussion

In the current study, our results displayed abnormal attentional network function and decreased SC-FC coupling in SWD. Additionally, the alerting network function of subjects in the SWD group was significantly associated with decreased SC-

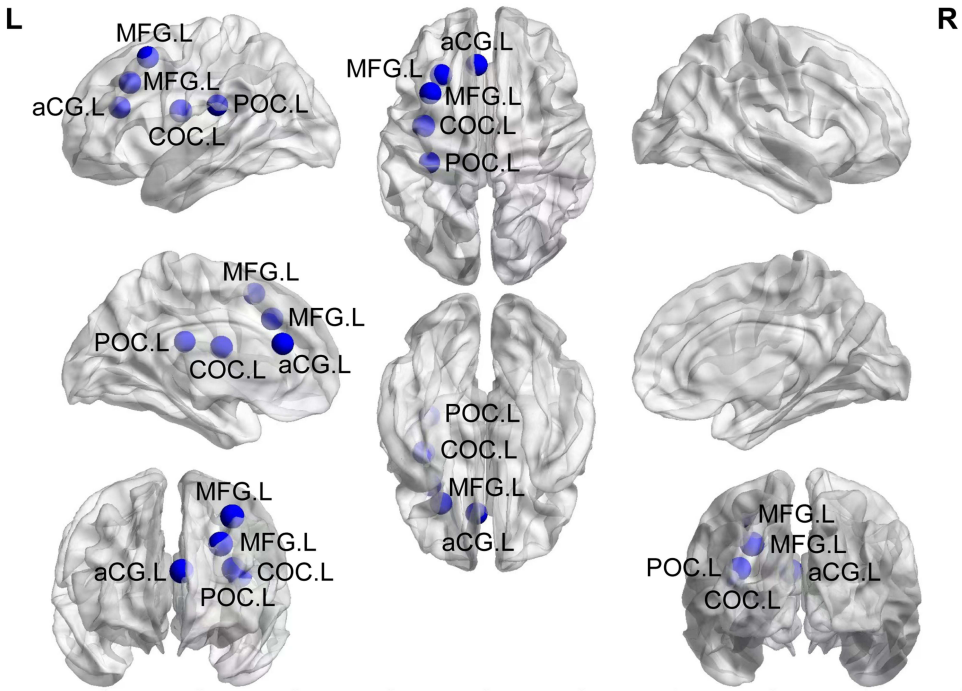

Figure 4 The altered structure-function coupling of brain areas in patients with SWD compared to healthy controls. L indicates the left cerebral hemisphere; R indicates the right cerebral hemisphere; blue sphere indicates the location of brain regions.
Abbreviations: aCG.L, the left cingulate gyrus (anterior division); COC.L, the left central opercular cortex; MFG.L, the left middle frontal gyrus; POC.L, the left parietal operculum cortex.

Table 2 The Abnormal SC-FC Coupling Sites Between the Two Groups

Node	Brain Area	Hemisphere	MNI			T	*P*
			x	y	z		
DMN-PFC-21	Middle Frontal Gyrus	Left	−34	13	49	−3.83415	0.000144
DMN-PFC-16	Middle Frontal Gyrus	Left	−26	24	34	−3.47075	0.000464
DMN-PFC-12	Anterior Cingulate Gyrus	Left	−5	30	19	−3.64487	0.000266
SMN-4	Central Opercular Cortex	Left	−37	−6	17	−3.71869	0.00021
SMN-5	Parietal Operculum Cortex	Left	−33	−28	20	−3.61209	0.000296

Abbreviations: DMN, default mode network; MNI, Montreal Neurological Institute; SMN, somatosensory network.

FC coupling in the anterior cingulate gyrus. These findings provide new evidence of the underlying mechanisms of aberrant attentional network function in SWD.

Increasing evidences have demonstrated that SWD leads to impaired executive function, information processing, visual-motor performance, and attention.[27] In the present study, we focused on the patients with SWD aged 20–40 years, minimizing age-related variability in the brain structure and FC. Prior researches have indicated older adults may exhibit age-related declines in neural plasticity and circadian disruption, potentially impacting on the attentional performance and the underlying mechanisms in SWD.[28] Additionally, shift work involves a sleep-wake schedule that consistently disrupts the natural circadian cycle of sleep and wakefulness.[29] And abnormal circadian cycle of sleep and wakefulness initiates a cascade of physiological events, which alter brain neurochemistry, leading to reduced attention.[30] In the current study, we found the abnormal attentional network function in SWD, involving reduced alerting network function and executive network function. An alert network is concerned with people's ability to achieve and maintain hypersensitivity to incoming information. The executive network governs the regulation of behavior to accomplish desired objectives and reconcile conflicts among competing responses.[7] Moreover, executive network facilitates the allocation of attention,

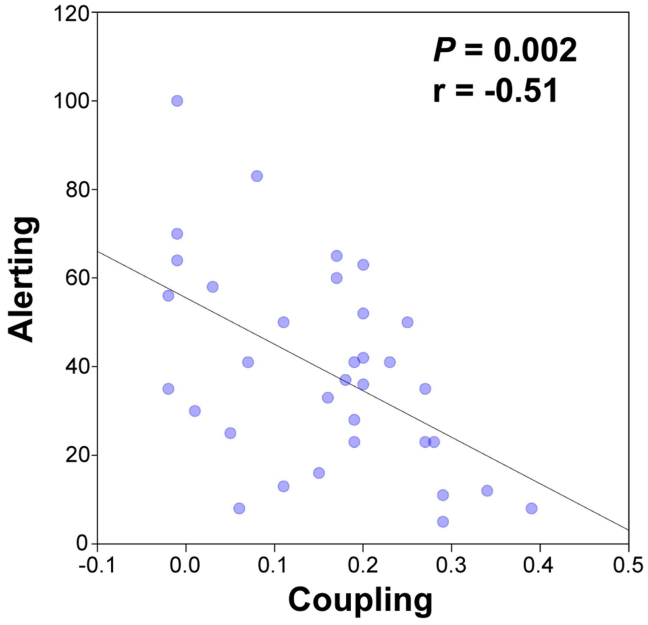

Figure 5 Correlation analysis between the altered structure-function coupling in the anterior cingulate gyrus and attentional network performance of patients with SWD.

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regulating the depth of processing and degree of awareness regarding the most pertinent and novel stimuli in the environment.[31] It is believed that the executive network is essential for planning or decision-making, error detection, novel or poorly learned responses, and in overcoming habitual behaviors.[32] Alertness can involve gradual alterations in mental state, such as those associated with the sleep-wake cycle or tiredness.[33] Prior clinical studies have demonstrated that alertness and performance were significantly diminished during night shifts,[34] which is consistent with our results in the current study.

Our previous researches have suggested that abnormal functional connectivity of large-scale brain networks contributes to cognitive dysfunction of individuals with SWD.[9] And the global network efficiency of structural networks significantly associates with executive function of patients with SWD.[8] Understanding the hierarchies of brain organization has been crucial by means of functional specialization of cortical regions depending on their patterns of connection.[14] Convergent findings highlight the strong association between SFC measurements at several spatiotemporal levels, such as cortical area and large-scale brain networks.[35] Furthermore, SC-FC coupling implies a bilateral interaction between structural and functional networks and has been used to investigate the progress of disorders.[36] Structure-function coupling is a phenomenon in which the intensity of interregional functional connectivity is predicted by the profile of interregional white-matter connectivity in a cortical region, thereby providing structural support for functional communication.[11] Patients with SWD showed in the current study the reduced SC-FC coupling in multiple brain areas, involving the left anterior cingulate gyrus, central opercular cortex, middle frontal gyrus, and parietal operculum cortex. Significantly, the SC-FC coupling was primarily found in the left hemisphere in patients with SWD, which related to goal-directed attention, verbal processing, and executive function.[37] Working memory and other cognitive functions have consistently been found to be correlated with the activation of the left middle frontal gyrus, social information processing and perception, memory retrieval, emotional regulation, and the processing of emotional stimuli.[38] Additionally, this region has been proposed as the cortical focus for both the storage and processing components of working memory in the human brain.[39] We hypothesized that cognitive dysfunction of patients with SWD might be caused in the left middle frontal gyrus by a reduced SC-FC coupling.[9] In terms of cognitive function, the anterior cingulate gyrus is regarded as a critical element of a variety of executive functions, including motivation, attention, working memory, learning, decision-making, and awareness and insight.[40] Our findings further suggested weakened integration between structural and functional brain networks in SWD, particularly in regions involved in attention regulation, cognitive control, and vigilance of individuals. Besides, disrupted SFC might impair the efficient allocation of attentional resources, leading to difficulty in maintaining focus and impaired executive function in patients with SWD. Our findings suggest that SFC metrics could serve as neuroimaging biomarkers for monitoring the progression of cognitive deficits in patients with SWD. Regular assessments of SFC could help identify patients at risk of developing severe attentional impairments, enabling early intervention. And attention deficits of patients with SWD might be mitigated by adopting telemedicine and personalized care strategies, as well as tailored rehabilitation and family-centered approaches.[41,42]

However, this study had certain limitations. First, this study aimed to investigate the effects of disrupted circadian rhythm on shift workers' attentional network function. Therefore, we recruited healthy adults with normal sleep habits as controls for the patients with SWD. Compared to shift workers without SWD, these shift workers with SWD are more susceptible on breaks.[43] Further research is required to determine the underlying mechanism in SWD that warrants care and therapy compared to shift workers without SWD. Second, this was a cross-sectional investigation, allowing for speculative interpretations based on observed relationships. Further research is needed to determine whether interventions for individuals with SWD can improve attentional network function. Thirdly, we did not consider the impact of several potential confounding factors on attentional function in SWD, such as shift duration, chronotype, sleep parameters, sleep duration, and mood swings. Mood disorders, such as depression and anxiety, are known to influence cognitive function, including attention.[44] While our study excluded participants with a history of psychiatric disorders, it is important to acknowledge that mood symptoms may still be present in some SWD patients and could contribute to attentional deficits. The longitudinal studies are needed to investigate whether the potential confounding factors impact on the attentional function in patients with SWD in the future. Fourthly, a larger number of females than males were recruited in this study. Gender differences in sleep duration variability, circadian rhythms, and hormonal fluctuations may

affect the attentional performance and neural alterations in patients with SWD. Future researches are needed to assess whether gender differences impact on the neural mechanisms of impaired attention in SWD.

Conclusions

In conclusion, our findings revealed that SWD was associated with abnormal attentional network function and decreased SC-FC coupling in key brain regions. Specifically, the altering network function in patients with SWD was significantly related to reduced SC-FC coupling in the anterior cingulate gyrus, which was critical for attention regulation. These results provide new evidence for the neural mechanisms underlying attentional deficits in SWD, highlighting the disrupted SC-FC coupling as a potential contributor to attentional processes. Furthermore, our findings advanced the understanding of SWD by SC-FC coupling measurement, shedding new light on the neurobiological basis of cognitive dysfunction in SWD.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author.

Ethics Approval and Consent to Participate

This study was performed in compliance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of the Beijing Anding Hospital. All recruited participants provided informed consent before their participation in the study.

Author Contributions

Dongqing Yin – Conceptualization, Writing – Review and Editing, Supervision; Yanzhe Ning – Conceptualization, Writing – Review and Editing, Supervision; Ziyao Wu – Investigation, Writing – Original draft; Sitong Feng – Investigation, Writing – Original draft; Kuangshi Li – Formal analysis, Writing –Original draft; Linrui Dong – Investigation, Writing – Review and Editing; Liang Zhang – Investigation, Writing – Review and Editing; All authors contributed to manuscript revision, read and approved the submitted version. And all authors agreed on the journal to which the article will be submitted and agreed to take responsibility and be accountable for the contents of the article.

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Disclosure

The authors declare that there was no conflict of interest.

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