Brain default mode network mediates the association between negative perfectionism and exercise dependence

HONGSHENG XIE[1,2†] ⦿, FEIFEI ZHANG[2,3†], YUAN CAO[1,2,4], XIPENG LONG[1,2], BAOLIN WU[2,5], QIYONG GONG[2,6*] ⦿ and ZHIYUN JIA[1,4,5*] ⦿

[1] Department of Nuclear Medicine, West China Hospital of Sichuan University, Chengdu, 610041, China

[2] Huaxi MR Research Center (HMRRC), Department of Radiology, West China Hospital of Sichuan University, Chengdu, 610041, China

[3] Department of Radiology, First Hospital of Shanxi Medical University, Taiyuan, 030001, Shanxi Province, China

[4] Research Unit of Psychoradiology, Chinese Academy of Medical Sciences, Chengdu, 610041, China

[5] Functional and Molecular Imaging Key Laboratory of Sichuan University, West China Hospital of Sichuan University, Chengdu, 610041, China

[6] Department of Radiology, West China Xiamen Hospital of Sichuan University, Xiamen, 361021, Fujian Province, China

ABSTRACT

Background and aims: Perfectionism is correlated with the occurrence of exercise dependence. We aim to reveal the role of functional connectivity (FC) between gray matter (GM) and white matter (WM) networks in the association between perfectionism and exercise dependence. *Methods:* In this cross-sectional study, one hundred ten participants with exercise dependence underwent behavioral evaluation and resting-state functional magnetic resonance imaging. Perfectionism and exercise dependence were quantified using the Frost Multidimensional Perfectionism Scale (FMPS) and Exercise Dependence Scale (EDS). We used a K-means clustering algorithm to identify functional GM and WM networks and obtained the FCs of the GM-GM, GM-WM, and WM-WM networks. Partial correlation and mediation analyses were performed to explore the relationships among FCs, FMPS, and EDS. *Results:* We identified ten stable GM networks and nine WM networks. Of these, FCs existed between the corona radiata network (WM1) and default mode network (DMN, GM8), WM1 network and WM DMN (WM4), WM1 network and midbrain WM network (WM7), and WM4 network and inferior longitudinal fasciculus network (WM9). The WM1-GM8 and WM1-WM4 FCs were positively correlated with the EDS and negative FMPS. The mediating effects of the WM1-GM8 and WM1-WM4 FCs were established in the association between the negative dimensional FMPS and EDS. *Discussion and Conclusions:* The WM1 network anatomically linked the subregions within the GM8 and WM4 networks, and WM1-GM8 and WM1-WM4 FCs mediated the association between negative dimensional FMPS and EDS. These findings indicated that DMN function might be involved in the increased risks of exercise dependence promoted by negative perfectionism.

KEYWORDS

†Hongsheng Xie and Feifei Zhang contributed equally to this work.

*Corresponding authors.
E-mail: qiyonggong@hmrrc.org.cn, zhiyunjia@hotmail.com

INTRODUCTION

Exercise dependence refers to compulsive and excessive engagement in exercise, which is now considered a behavioral addiction for exhibiting various well-defined addictive features,

such as inducing feelings of euphoria, persistence to continue, and withdrawal symptoms (Landolfi, 2013). Currently, the definition of exercise dependence is still an actively debated topic party because of its subtle relationship with eating disorders. While exercise dependence is often viewed as secondary to eating disorders, existing literature suggests the existence of primary exercise dependence that highlights the intrinsic motivation of physical activity itself (Cunningham, Pearman, & Brewerton, 2016; Grandi, Clementi, Guidi, Benassi, & Tossani, 2011). At present, the Exercise Dependence Scale (EDS) is the most commonly used tool for identifying individuals with exercise dependence (Downs, Hausenblas, & Nigg, 2004). Although EDS is not capable of a clinical diagnosis, it provides an adequate indication for research purposes (Alcaraz-Ibáñez, Paterna, Sicilia, & Griffiths, 2022). A recent systematic review reported that the prevalence of the risk for exercise dependence was between 3 and 7% in regular exercisers and between 6 and 9% in athletes (Marques et al., 2019). Individuals with high risks of exercise dependence continue exercising despite pain or discomfort, resulting in physical injury and poor recovery (Heather A. Hausenblas & Danielle Symons Downs, 2002b; Kardefelt-Winther et al., 2017; Strand, Gammon, Eng, & Ruland, 2017). Additionally, exercise dependence greatly influences social life and creates conflicts with study, work, and interpersonal relationships (Kolnes, 2016; Timulak, 2009). However, the mechanisms of exercise dependence are still unclear, which inevitably hampers the accurate identification of the target population and limits the development of an appropriate behavioral intervention.

Perfectionism is a personality trait characterized by the tendency to pursue high standards of performance and critical self-evaluations. It is considered to be closely associated with the occurrence of general mental disorders (Sutović, 2021). According to the Frost Multidimensional Perfectionism Scale (FMPS), negative perfectionism refers to concern over mistakes, personal standards, parental expectations, parental criticism, and doubts about actions, while positive perfectionism emphasizes the organization in daily life (Frost, Marten, Lahart, & Rosenblate, 1990). Early in the process of development and validation of the EDS, it was found that individuals with high risks of exercise dependence reported more perfectionism than the nondependent groups (Heather A. Hausenblas & Danielle Symons Downs, 2002a, 2002b). Subsequently, the negative dimensional FMPS was found to be positively correlated with the total EDS score and all seven subdomains in 169 general exercisers (Costa, Coppolino, & Oliva, 2016). Recently, a systematic review reported that perfectionism (or its subdomains) was positively correlated with exercise dependence in 21 included studies using correlation or regression analyses (Çakın, Juwono, Potenza, & Szabo, 2021). More importantly, three months after the cognitive-behavioral treatment for perfectionism, both negative dimensional FMPS and Compulsive Exercise Test scores were decreased in 29 regular exercisers (Valentine et al., 2018). These findings suggested that negative perfectionism might be a personal factor increasing the exercise dependence risk. Notably, all these findings are based on behavioral and psychological assessments, and the neurobiological mechanisms underlying the correlation remain unknown.

Functional magnetic resonance imaging (fMRI) studies have revealed that the altered function of the default mode network (DMN) is associated with behavioral addictions. The DMN is a set of brain areas that are activated during the resting state and considered to be closely related to self-directed thought, introspection, emotional processing, and decision-making (Moreno-López et al., 2012; Raichle, 2015). In patients with gambling disorder, symptomatic severity was negatively correlated with functional connectivity (FC) between the posterior cingulate cortex (PCC) and precuneus (Jung et al., 2014). In patients with internet gaming disorder, the DMN showed more engagement when making risky decisions (Wang et al., 2016). In individuals with phone addiction, FC within the DMN increased despite no correlation with addiction severity (Lou et al., 2019). These findings suggested that the abnormal function of the DMN might be a shared neural mechanism of behavioral addictions. Recently, the blood oxygenation level-dependent (BOLD) signal of white matter (WM) has been demonstrated to represent tract-specific responses to neural activity rather than noise (Gore et al., 2019). Specifically, it exhibits similar resting-state and stimulus-evoked fluctuations to those in the gray matter (GM), suggesting that it might carry important neural information (M. Li, Newton, Anderson, Ding, & Gore, 2019). Peer, Nitzan, Bick, Levin, and Arzy (2017) proposed that WM was intrinsically organized as interacting networks of functional modules, and each WM functional network could be separated by clustering analyses. These findings make it possible for us to investigate the FC of GM-GM, GM-WM, and WM-WM networks, and thereby, we can evaluate the whole-brain functional changes in people with exercise dependence.

In the present study, we aimed to investigate whether FCs existed between brain networks involving the association between perfectionism and primary exercise dependence by using resting-state fMRI. We hypothesized that DMN-related FC is associated with both EDS and FMPS, and it may play a mediating role in the relationship between these three factors. This study will provide a comprehensive understanding of the neural mechanism of exercise dependence from the perspective of FC between GM-GM, GM-WM, and WM-WM networks.

METHODS

Study participants

We distributed electronic posters in universities, gymnasiums, and communities to contact the athletic population from September 2018 to March 2021. The inclusion criteria were as follows: 1) Age 18–30 years; 2) Right-handed based on the Edinburgh handedness inventory (Oldfield, 1971); 3) Native Chinese speakers; and 4) Regular exercise ≥30 min each time and at least once a week for more than 3 months (O'Donovan, Lee, Hamer, & Stamatakis, 2017).
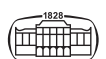
5) At-risk or symptomatic exercise dependence based on the EDS evaluation. The exclusion criteria were as follows: 1) Neurological disease, head injury, and other serious medical illness; 2) Participants were screened with the Structured Clinical Interview for DSM-5 to rule out the presence of a psychiatric disorder (Association, 2013). 3) Eating disorders, such as anorexia nervosa or bulimia nervosa; 4) Elite athletes; 5) Claustrophobia or other contraindications to MRI.

We used G-Power software to calculate the proper sample size and found that a minimum number of 84 participants were required to detect medium-sized effects ($r = 0.3$, $\alpha = 0.05$, $1-\beta = 0.80$) (Faul, Erdfelder, Lang, & Buchner, 2007; King, 2019; Kong, Zhao, You, & Xiang, 2019). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed (Table S1) (von Elm et al., 2007).

Behavioral measurements

Participants completed behavioral measurements on the same day of MRI scanning, and a psychologist expert would assist if they proposed any questions during the whole process. They were required to estimate the exercise frequency and average duration in the last three months. More importantly, the EDS was used to identify and quantify the exercise dependence risk because of its high reliability and validity (Yang et al., 2021). It has 21 items with a scale from 1 (never) to 6 (always), which involves the withdrawal effects, continuance, tolerance, lack of control, reduction in other activities, time, and intention effects components (Cronbach's $\alpha = 0.81$). By using a syntax file in SPSS, we calculated the total and subscale scores of each participant and classified them as "asymptomatic", "symptomatic", and "at-risk" exercise dependence (Hausenblas & Downs, 2002a). The total EDS score was recorded for correlation and mediation analyses.

Perfectionist traits were quantified using the 27-item FMPS, and each item was scored on a scale from 1 (strongly disagree) to 5 (strongly agree) (Cheng, Chong, & Wong, 1999). FMPS has shown good cross-cultural reliability and been widely used in Chinese residents (Wu et al., 2017; M. Zhao, Li, Lin, Zhang, & Shi, 2022). In this study, negative perfectionism (Cronbach's $\alpha = 0.79$) referred to the sum of personal standards, concern over mistakes, parental expectations, and doubts about actions, while positive perfectionism (Cronbach's $\alpha = 0.86$) referred to the organization. In addition to the total FMPS score, both negative and positive dimensional FMPS were also used for exploring the relationship among perfectionism, function connectivity, and exercise dependence.

In this study, personality traits, general intelligence, and economic status were included as covariates in the correlation and mediation analyses. Previous studies reported that personality traits were associated with brain functions, exercise dependence, and perfectionism (Burcaş & Creţu, 2021; Kern, 2010; Toschi, Riccelli, Indovina, Terracciano, & Passamonti, 2018). Therefore, personality traits were viewed as potentially confounding covariates, and they were quantified

using the 44-item Neuroticism Extraversion Openness Five-Factor Inventory (NEO-FFI) (McCrae & John, 1992; Palomo, Beninger, Kostrzewa, & Archer, 2008). NEO-FFI has shown good validity and reliability in Chinese people (Chou, Ko, Wu, Chang, & Tung, 2015). It assesses 5 personality domains including extraversion, agreeableness, conscientiousness, neuroticism, and openness with a scale from 1 (strongly disagree) to 5 (strongly agree) and shows good internal consistency (Cronbach's $\alpha = 0.74$). In addition, as general intelligence is associated with brain functions, the 12-item brief Raven's Advanced Progressive Matrix was used to acquire intelligence data (Bathelt, Scerif, Nobre, & Astle, 2019; Catani et al., 2016). Participants were required to select the proper pictures to fill in the missing parts in 15 min. The total number of correct answers was used as the general intelligence score for each participant (Cronbach's $\alpha = 0.78$). Like other neuroimaging studies, it was used to exclude the potential influence on brain functions (Filbey et al., 2014). Last, considering the potential effects of economic status on brain structures, the family Socioeconomic status (SES) scale was used for the evaluation (Adler, Epel, Castellazzo, & Ickovics, 2000; Ursache, Noble, the Pediatric Imaging, & Genetics, 2016). Increasing evidence has shown that the SES scale is a better predictor of health-related outcomes than objective measures, and is widely used in Chinese people (Cundiff & Matthews, 2017; Tian, Fang, & Li, 2018). Participants were required to mark in a 10-step ladder chart (bottom to top = 1 to 10 grade) to represent their SES in the local society.

Image acquisition

Each included participant underwent MRI scanning 30 min after the behavioral measurements. In West China Hospital of Sichuan University, a whole-brain MRI scan was performed using a Siemens 3.0 T system (Tim Trio, Siemens Healthineers, Erlangen, Germany) with a standard 8-channel head coil as the radiofrequency receiver. High-resolution 3D T1-weighted anatomical images (rapid gradient-echo planar imaging sequence) were collected using the parameters repetition time = 1.96 s, echo time = 2.26 ms, flip angle = 90°, contiguous slices = 176 with a thickness of 1 mm each, matrix = 256×256, and field of view = 240×240 mm. Second, participants were required to stay still, keep their eyes closed, avoid thinking about anything, and remain awake during resting-state functional MRI scanning. The functional data were obtained using the same sequence with parameters of repetition time = 2 s, echo time = 30 ms, flip angle = 90°, slice thickness = 5 mm, matrix = 64×64, and field of view = 240×240 mm. Eventually, clinical T2-weighted images were acquired to determine the absence of any significant pathological brain changes.

MRI preprocessing

MRI preprocessing was performed using SPM12 (https://www.fil.ion.ucl.ac.uk/spm) and DPARSFA (http://rfmri.org/DPARSF) based on MATLAB (R2013b; MathWorks Natick, Massachusetts). For T1-weighted data, the coordinate system

was manually reoriented at the anterior commissure. Then, the structural images were segmented into GM, WM, and cerebrospinal fluid (CSF) using the new segment algorithm (Ashburner, 2007). Image registration and normalization were applied with the diffeomorphic image registration algorithm template (MNI152, $1.0 \times 1.0 \times 1.0$ mm). Last, the modulated and spatially normalized images were smoothed using a Gaussian kernel at 4 mm full-width at half-maximum (Peer et al., 2017).

For functional MRI data, the first 10-time frames were discarded to ensure the reach of signal equilibrium, followed by slice time correction and head-motion correction (excluding participants with head motion >2.0 mm translation or >2.0° rotation). Then, the corrected functional images were co-registered with the segmented structural images, followed by detrending (removing linear drift) and bandpass filtering (0.01–0.10 Hz). After that, Friston 24 motion parameters, framewise displacement (FD), and CSF signal were regressed (Friston, Williams, Howard, Frackowiak, & Turner, 1996; Jiang et al., 2019). Notably, WM and whole-brain signals were not regressed to retain the signals of interest. Eventually, gray and white matter images were smoothed at 4 mm full-width at half-maximum and were spatially normalized to the Montreal Neurological Institute (MNI) template and resampled to a 3-mm cubic voxel.

Clustering WM and GM networks

First, we created group WM and GM masks. For the segmentation results of each participant, we identified each voxel as WM, GM, or CSF based on the maximum probability. Then, we averaged these masks to obtain for each voxel the percentage of subjects in which it was identified as WM or GM. For WM, the maximum probability method was used to ensure that WM voxels were identified in more than 60% of participants (Peer et al., 2017). For GM, a threshold of 20% was used to define the GM mask without any voxels contained in the WM mask (Y. Zhao et al., 2021). Subcortical structures were removed from the WM masks using the Harvard-Oxford atlas brain template and redefined as GM masks, including the thalamus, caudate nucleus, putamen, globus pallidus, and nucleus accumbens (Desikan et al., 2006). Eventually, we obtained the group-level WM mask with 19,926 voxels and GM mask with 42,279 voxels and co-registered them to the standard MNI echo-planar imaging template.

Second, we established the individual- and group-averaged connectivity matrices. We first calculated Pearson's correlation coefficients between each pair of WM voxels. Notably, we subsampled the WM mask by using an interchanging grid to decrease the complexity of the subsequent clustering. For each WM voxel, we calculated the Pearson correlation with subsampled nodes and averaged them across 110 participants, obtaining a $19,926 \times 4,950$ matrix. Notably, this process was adapted to only two WM voxels that originated from the segment of the structural template, therefore excluding GM signals. By the same procedure, the individual- and group-level GM matrix ($42,279 \times 4,706$) was acquired.

Third, we adopted K-means clustering (distance metric-correlation, 10 replicates) on the group-level functional matrices and obtained the most stable clustering networks. Each group-level matrix was randomly divided into 4 folds ($19,926 \times 1,237$ matrix/fold). Then, K-means clustering was performed on each fold separately (K ranged from 2 to 22) (Yeo et al., 2011). We calculated each adjacency matrix to assess the similarity of the clustering solutions and compared them based on Dice's coefficient. Eventually, we obtained the average Dice's coefficient from 4 adjacency matrices to plot the scatter diagram. Previous studies demonstrated that the clustering results were stable if the average Dice's coefficient >0.85 (Lange, Roth, Braun, & Buhmann, 2004; Zhang et al., 2021). In summary, this clustering method has been widely performed in previous studies and has been proven to be robust and stable (Peer et al., 2017). BrainNet Viewer (www.nitrc.org/projects/bnv/) was used to visualize the results (Xia, Wang, & He, 2013).

Construction of functional networks

Pearson's correlation coefficient between BOLD signals of two functional networks was calculated to construct individual WM networks ($K_{White} \times K_{White}$), GM networks ($K_{Gray} \times K_{Gray}$), and WM-GM networks ($K_{White} \times K_{Gray}$). The FC value was transformed into the Fisher z score.

Statistical analysis

Demographic and behavioral characteristics. All demographic and behavioral data were assessed for normality using the Shapiro–Wilk test and viewing qq-plots (Shapiro & Wilk, 1965). They were expressed as mean and standard deviation with skewness and kurtosis. The correlation between EDS and FMPS was determined by computing Pearson correlation coefficients.

FC-behavior correlation analyses. By referring to previous studies, the FCs between brain networks were detected using the one-sample t-test, and all obtained FCs were corrected using the false discovery rate (FDR) method with the threshold of FDR <0.05 (Zhang et al., 2021). Then, partial correlation analyses were conducted to explore the correlations between significant FCs and FMPS/EDS in SPSS (IBM SPSS 26.0, SPSS Inc). All correlation analyses used a threshold of $\alpha < 0.05$ and were corrected for age, sex, body mass index (BMI, kg m^{-2}), general intelligence, SES, FD, and Big Five personality traits.

Mediation analyses. Mediation analyses were conducted to further explore the role of FCs in the association between FMPS and EDS. First, we corrected the FCs that were correlated with either FMPS or EDS for age, sex, BMI, general intelligence, SES, FD, and Big Five personality traits in SPSS (IBM SPSS 26.0, SPSS Inc.). FMPS and EDS scores were also corrected using the above data except for FD. Then, SPSS macro PROCESS 3.2 was used with the parameters of the number 4 model, showing the total effect

model and effect size (Bolin & Hayes, 2014, 2013). The corrected EDS score was preset as the dependent variable (Y), and the roles of corrected FCs and perfectionism scores were determined by whether the mediation model could hold. Concretely, the estimation of indirect effect was considered statistically significant when the bootstrapped 95% CIs (5,000 iterations) did not contain zero. Eventually, the corrected perfectionism score was identified as the independent variable (X), and the corrected FCs were identified as the mediator variable (M). Four paths consisted of a) the relationship between X and M; b) the relationship between M and Y; c') the direct effect of X on Y; c - c') the indirect effect of X on Y (c - c' = a ^ b).

Ethics

This cross-sectional study was approved by the Ethics Committee of the West China Hospital of Sichuan University, and voluntary informed consent was obtained from each participant before enrolment.

RESULTS

Participant characteristics

The participant flowchart was shown in Figure S1, and eventually, 110 general exercisers (57 males and 53 females) were included in the study. Of these, 96 participants were symptomatic exercise dependence, and 14 participants were at-risk for exercise dependence according to the EDS. All female participants were free-cyclers and took no birth control pills. The detailed characteristics of demography, exercise, and disposition were shown in Table 1. The EDS was positively correlated with the total FMPS ($r = 0.23$, $P = 0.02$) and negative dimensional FMPS ($r = 0.25$,

Table 1. Demographic characteristics of 110 EXA participants

Characteristics	Mean ± SD	Skewness	Kurtosis
Age (years)	21.93 ± 2.69	1.40	1.54
BMI	21.84 ± 2.67	0.26	−0.09
General intelligence	6.89 ± 2.60	−0.43	−0.44
SES	4.65 ± 1.71	0.10	−0.27
Exercise frequency (times/week)	4.77 ± 2.31	1.25	1.17
Exercise duration (h/time)	1.50 ± 0.66	0.31	−0.46
EDS	58.30 ± 9.09	0.71	0.35
Extraversion	27.24 ± 4.68	−0.01	−0.94
Agreeableness	33.39 ± 4.22	−0.37	0.78
Conscientiousness	29.41 ± 4.15	−0.19	−0.04
Neuroticism	21.86 ± 3.80	0.09	0.20
Openness	34.36 ± 5.32	0.07	1.08
FMPS positive dimension	11.75 ± 2.44	−0.39	0.17
FMPS negative dimension	70.58 ± 10.52	0.22	0.78

Abbreviations: BMI, body mass index; EDS, Exercise Dependence Scale; FMPS, Frost Multidimensional Perfectionism Scale; SES, Socio-economic status.

$P = 0.01$). There was no correlation between EDS and positive dimensional FMPS ($r = -0.01$, $P = 0.93$; Figure S2).

GM networks and WM networks

The K-means clustering analysis identified 10 stable GM networks (maximum cluster number with Dice's coefficient >0.85). According to the anatomical location, they were defined as the supplementary motor area (SMA) network (GM1), frontal-parietal network (GM2), frontal-temporal network (GM3), occipital-superior cerebellar network (GM4), superior temporal network (GM5), midbrain-cerebellar network (GM6), salience network (GM7), DMN (GM8), temporoparietal network (GM9), and executive control network (GM10) (Table 2, Fig. 1).

The same K-means clustering approach revealed 9 WM networks defined as the corona radiata network (WM1), frontal-parietal WM network (WM2), SMA WM network (WM3), anterior DMN WM network (WM4), cerebellar-brainstem WM network (WM5), occipital WM network (WM6), midbrain WM network (WM7), DMN WM network (WM8), and inferior longitudinal fasciculus WM network (WM9) (Table 2, Fig. 1).

Functional connectivity between brain networks

Participants with exercise dependence showed FC in clustered GM-WM networks and WM-WM networks rather than GM-GM networks (Fig. 3a, $P < 0.05$, FDR-corrected). FC existed between WM1 and GM8, WM1 and WM4, WM1 and WM7, and WM4 and WM9.

Functional connectivity linking EDS and negative dimensional FMPS

The total EDS score was positively correlated with WM1-GM8 FC ($r = 0.23$, $P = 0.03$), WM1-WM4 FC ($r = 0.21$, $P = 0.04$), and WM1-WM7 FC ($r = 0.27$, $P = 0.01$; Fig. 2a). The negative dimensional FMPS score was positively correlated with WM1-GM8 FC ($r = 0.37$, $P < 0.01$) and WM1-WM4 FC ($r = 0.29$, $P = 0.01$; Fig. 2b).

The mediating effects of FCs were established when setting the negative dimensional FMPS as the independent variable (Fig. 3b). WM1-GM8 FC played a mediating role in the relationship between the negative dimensional FMPS and EDS score (indirect effect = 0.078; 95% CI = [0.005, 0.176]). WM1-WM4 FC played a mediating role in the relationship between the negative dimensional FMPS and EDS score (indirect effect = 0.059; 95% CI = [0.002, 0.135]). GM8-WM1-WM4 FC played a mediating role in the relationship between the negative dimensional FMPS and EDS score (indirect effect = 0.073; 95% CI = [0.006, 0.153]).

DISCUSSION

In the present study, we found a positive correlation between EDS and the total-score/negative dimensional FMPS and revealed that the DMN might be an important neural

Table 2. Gray matter and white matter functional networks

Number	Network name	Main region
GM1	SMA network	Paracentral lobule, precentral gyrus, postcentral gyrus
GM2	Frontal-parietal network	Inferior parietal lobule, superior frontal gyrus, dorsolateral frontal cortex
GM3	Frontal-temporal network	Inferior temporal gyrus, gyrus rectus
GM4	Occipital-superior cerebellar network	Superior cerebellar hemisphere, occipital lobe
GM5	Superior temporal network	Superior and middle temporal gyrus, inferior frontal gyrus
GM6	Midbrain-cerebellar network	Caudate nucleus, dorsal thalamus, vermis and hemisphere of cerebellum
GM7	Salience network	Insular, anterior cingulate cortex, putamen
GM8	DMN	Medial prefrontal cortex, angular gyrus, posterior cingulate cortex, superior temporal gyrus
GM9	Temporoparietal network	Superior parietal lobule, inferior temporal gyrus, precuneus
GM10	Executive control network	Prefrontal gyrus, inferior parietal lobule, anterior cingulate cortex, inferior temporal gyrus, cerebellar hemisphere
WM1	Corona radiata network	Corona radiata white matter
WM2	Frontal-parietal WM network	White matter within the superior parietal lobule
WM3	SMA WM network	White matter within precentral gyrus and postcentral gyrus
WM4	Anterior DMN WM network	White matter within the medial prefrontal lobe, angular gyrus, posterior cingulate gyrus, and medial temporal lobe
WM5	Cerebellar-brainstem WM network	White matter within brainstem and cerebellum
WM6	Occipital WM network	Occipital white matter
WM7	Midbrain WM network	White matter within internal capsule, thalamus and middle radial crown
WM8	DMN WM network	White matter within angular and middle frontal area
WM9	ILF WM network	White matter within the occipital and temporal cortex

Abbreviations: DMN, default mode network; ILF, inferior longitudinal fasciculus; SMA, supplementary motor area; WM, white matter.

substrate underlying this correlation. Above all, we identified 10 GM networks and 9 WM networks with high stability in the participants with exercise dependence by performing the K-means clustering algorithm. More importantly, the GM8 network and WM4 network well represented the function of the DMN and exhibited a high degree of anatomical overlap. They were both functionally connected with the WM1 network (corona radiata) and thereby realized information exchange among the subregions of the DMN. Interestingly, the FCs of the WM1-GM8 networks and WM1-WM4 networks were positively correlated with the total-score/negative dimensional FMPS and EDS and showed mediating effects in the relationship between the total-score/negative dimensional FMPS and EDS. These observations emphasized that the DMN might be a neurobiological substrate underlying exercise dependence and that the DMN was involved in the link between perfectionism and exercise dependence.

It has been repeatedly reported that general exercise is associated with both structural and functional improvement in key DMN regions. The DMN can be functionally divided into three subsystems: 1) the midline core subsystem, consisting of the PCC, precuneus, and medial prefrontal cortex (mPFC), is involved in introspection; 2) the dorsal mPFC subsystem, consisting of the dorsal mPFC, temporoparietal area, and lateral temporal cortex, is involved in mentalizing; and 3) the medial temporal lobe subsystem, consisting of the ventral mPFC, inferior parietal lobule, and parahippocampal cortex, is associated with episodic decisions (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Ochsner et al., 2004). A multimodal neuroimaging study revealed that both current and

10-years accumulation of physical activities were related to the larger gray-matter volume and stronger perfusion in the midline core DMN (Boraxbekk, Salami, Wåhlin, & Nyberg, 2016). Further, using the conditional Granger causality analysis, aerobic exercise was found to predict causal influence from the hippocampus to midline core and medial temporal DMN (Kronman et al., 2020). A meta-analysis including 14 randomized controlled trials found that the intervention of aerobic exercise increased both GM volume of medial temporal DMN and functional connectivity between the parahippocampal cortex and other brain regions (M. Y. Li et al., 2017).

At present, although the alterations of DMN are associated with exercise duration and intensity, the specific neurobiological pathway underlying exercise training and expertise remains not very clear. An fMRI study found that the activity of mPFC and PCC was increased in young adults during the Serial Interception Sequence Learning task, suggesting that the DMN was involved in motor skill acquisition (Gobel, Parrish, & Reber, 2011). Besides, based on graph theory, a diffusion-tensor imaging study found that the nodal parameters of the default mode and attention networks were higher in young athletes compared with healthy controls, suggesting that exercise training and expertise were beneficial for efficient communication between brain regions (Pi et al., 2019). Inconsistently, using the increased parietal lobe, insula, and cerebellum as seeds, a stepwise functional connectivity analysis revealed that the optimal connectivity distance between these areas and DMN was larger in athletes (Gao et al., 2019). This might be associated with regulation of the switching between internal and external attention and acceleration of the reaction time
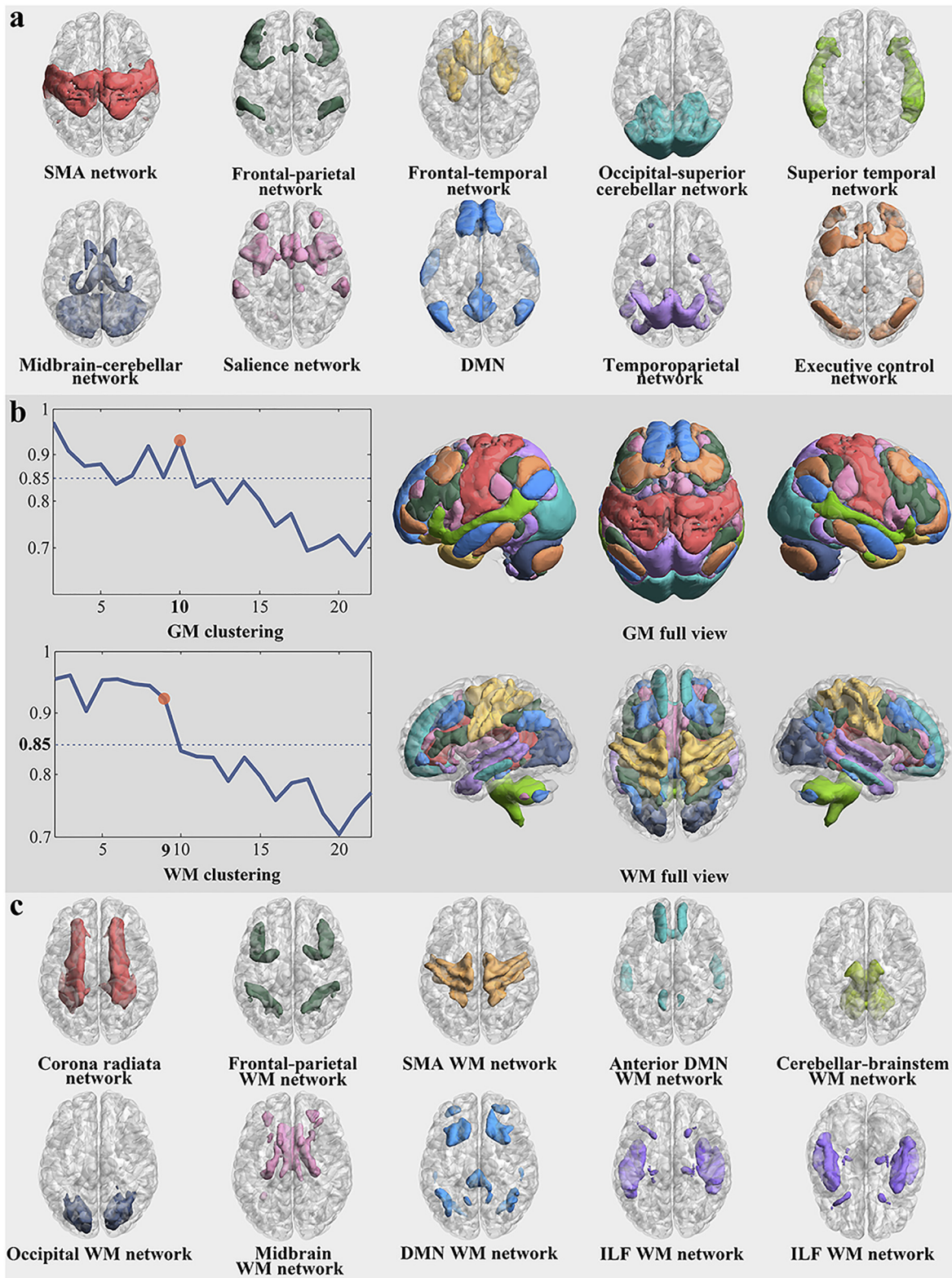
Fig. 1. **Brain networks with stability measured by Dice's coefficient in the K-means clustering analysis.** **(a)** Ten defined gray matter networks. **(b)** Clustering results with different cluster numbers and full views of GM networks and WM networks. Red dots represent maximum cluster numbers when Dice's coefficient >0.85. **(c)** Nine defined white matter networks
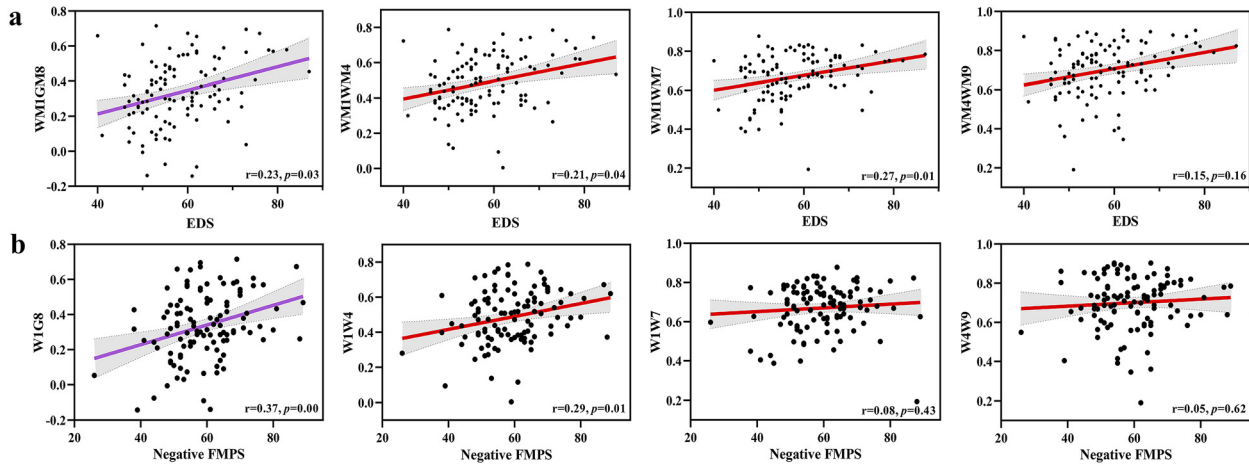
Fig. 2. **Linear correlations between functional connectivity and behavioral characteristics. (a)** Correlations between functional connectivity and Exercise Dependence Scale scores. **(b)** Correlations between functional connectivity and negative Frost Multidimensional Perfectionism Scale scores
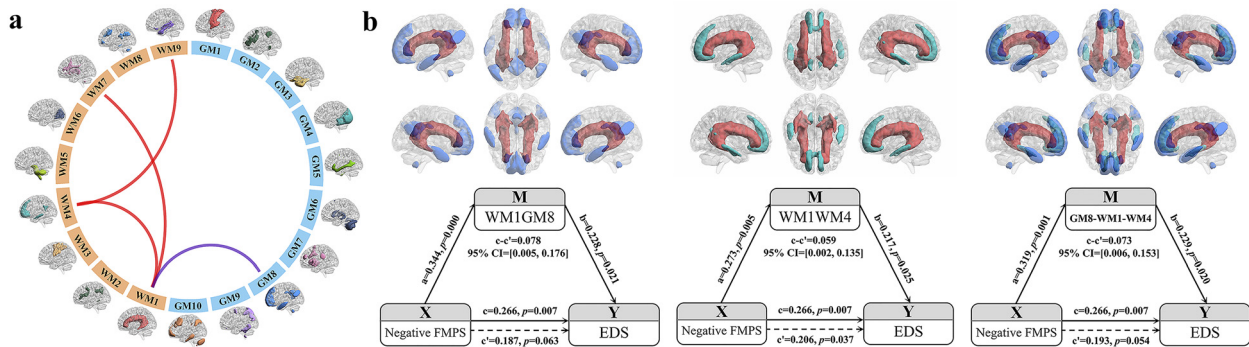

Fig. 3. **Functional connectivity linking EDS and negative dimensional FMPS. (a)** The purple link indicates the functional connectivity between clustered gray and white matter networks, and the red links indicate the functional connectivity between clustered white matter networks. **(b)** Mediating effect models of WM1-GM8/WM1-WM4/GM8-WM1-WM4 network functional connectivity between the negative dimensional FMPS score and EDS

in athletes. Notably and importantly, a recent neuroimaging meta-analysis reported that short-term exercise/physical training could induce activation in default mode and frontoparietal networks, whereas long-term training was associated with the frontoparietal and dorsal attention networks in young adults (Yu et al., 2021). These findings might suggest that the effects of exercise training and expertise on neuroplasticity be a continuous process from DMN to wider brain networks.

Exercise dependence is now an active topic, and we believe that it should be considered differently from healthy and moderate physical activity. From a psychobehavioral perspective, individuals with exercise dependence tend to lose control of their strong exercise motivations and are eager for excessive participation in exercise. This inevitably brings a great burden on the human body and social life. Based on the neuroimaging studies, our previous work revealed that EDS was negatively correlated with the regional GM volume of the inferior parietal lobe, orbitofrontal cortex, and cingulate gyrus, suggesting that exercise dependence might override the

beneficial effects of physical activity on DMN and other brain regions (Feifei et al., 2021). Similarly, a meta-analysis included 20 voxel-based morphometry studies of internet gaming and gambling disorders and found decreased GM volume in the key DMN and striatal areas (Qin et al., 2020). Additionally, in 20 endurance runners with exercise dependence, a task-based fMRI study found that the dorsal mPFC and anterior cingulate cortex were activated when they were allowed to exercise as usual compared to the prohibited-exercise condition, suggesting that the participants demonstrated greater recruitment of cognitive control regions when making decisions involving exercise and reward (Martin et al., 2017). Similarly, a review reported that fMRI studies consistently identified dysregulation in the mPFC and striatum in gambling disorders (Clark, Boileau, & Zack, 2019). These findings indicated that the structural and functional alterations in DMN seem to be a common phenomenon in exercise dependence and other behavioral addictions.

In the present study, negative dimensional FMPS was positively correlated with EDS and played a role as the

independent variable in the mediation model, suggesting that negative perfectionism might be a risk factor for exercise dependence. In line with our results, a study found that negative perfectionism was a unique predictor of exercise dependence in 248 gym members, and it was positively correlated with four aspects of symptoms (withdrawal, continuance, diminished control, and reduced time for other activities) (Hill, Robson, & Stamp, 2015). Consistently, EDS and its subdomains were found to be positively correlated with the negative dimensional FMPS in 340 exercisers (Costa, Hausenblas, Oliva, Cuzzocrea, & Larcan, 2016). More importantly, negative perfectionism was positively correlated with the degree of compulsiveness and obsessiveness in 172 exercisers (Gulker, Laskis, & Kuba, 2001). These findings indicated that negative perfectionism might facilitate and maintain the behaviors of excessive and additional exercise.

In the present study, we did not find any association between positive dimensional FMPS and EDS, indicating that organization might not be one personality trait associated with exercise dependence. In fact, contrary to the organization, impulsivity is considered to be a central feature in the etiology of behavioral addiction (Billieux & Van der Linden, 2012). Impulsivity is defined as a personality and behavior trait characterized by insufficient response inhibition and contemplation for potential negative consequences (MacKillop et al., 2011). A study found that the EDS was positively correlated with the lack of premeditation and sensation-seeking domains of the UPPS Impulsive Behavior Scale in 684 exercisers with exercise dependence, suggesting that exercise might be an unplanned choice to obtain the internal reward (Kotbagi, Morvan, Romo, & Kern, 2017). In addition, higher scores on the Barratt Impulsiveness Scale were also identified in 100 individuals with exercise dependence compared to healthy controls, indicating that multidimensional impulsivity might exist in people with exercise dependence (Ioannidis et al., 2021). Consistent with these findings, our previous work revealed a mediating effect of the orbitofrontal cortex in the association between the Depression Anxiety Stress Scales and EDS, suggesting that impulsivity might be the central link encouraging the engagement of exercise (Feifei et al., 2021). In summary, instead of positive dimensional perfectionism, impulsivity might be a crucial risk factor in the development of exercise dependence.

In the present study, we found that the FC between corona radiata and DMN was positively correlated with the negative FMPS. Individuals with negative perfectionism tend to set unrealistically high personal standards and be concerned over mistakes, which is often involved in the DMN activities of self-directed thought, introspection, and decision-making (Alaloğlu & Bahtiyar, 2020; Ji et al., 2017). A study found that negative perfectionism was negatively correlated with body satisfaction in 580 university students, and self-judgment/self-compassion showed a mediating effect between this correlation (Barnett & Sharp, 2016). Besides, an fMRI study found increased FC in the precuneus of individuals with obsessive-compulsive personality disorder,

which might indirectly suggest that posterior DMN might be the neural substrate of perfectionism (Coutinho, Goncalves, Soares, Marques, & Sampaio, 2016). Overall, the association between perfectionism and DMN is currently not very clear, so our results should be interpreted with great caution.

Limitations

First, mediation analysis cannot determine causality, and our results only emphasized that the DMN might be involved in the relationship between perfectionism and exercise dependence. Second, we did not consider the intensity and type of exercise as a potential confounding factor because most individuals with exercise dependence participated in over two types of sports. In addition, self-assessment exercise frequency and duration might differ from the actual situation, and future studies should consider using an objective instrument. Besides, the competitive status of participants was ignored in this study, which might exaggerate the degree of exercise dependence. Thus, our results require careful interpretation, and future studies might need to consider the repeated-measures designs. Last, our study had a relatively small sample size, and the findings need to be replicated in future prospective cohorts with large sample sizes.

CONCLUSION

The present analysis of resting-state fMRI data revealed an integrative role of negative perfectionism in increasing the risk for exercise dependence and emphasized that DMN function might be the neural substrate underlying the correlation between negative perfectionism and exercise dependence. These findings provide preliminary evidence that FCs between GM and WM networks could serve as a new potential marker for recognizing brain functional changes in people with exercise dependence. More importantly, our study laid the foundation for developing a specific cognitive behavioral therapy to intervene in those at high risk of exercise dependence by targeting negative perfectionism. In the future, exploring how negative perfectionism causes adverse effects on mental health and helping individuals maintain an appropriate degree of perfectionism are necessary.

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writing (editing), funding acquisition. YC: data curation. XPL: validation. BLW: data curation. QYG: conceptualization, supervision, writing (revising), funding acquisition. ZYJ: supervision, writing (revising), funding acquisition.

Conflict of interest: The authors declare no financial or other conflicts of interest.

Data availability: The data and code that support the findings of this study are available from the corresponding author upon reasonable request.

SUPPLEMENTARY MATERIAL

Supplementary data to this article can be found online at https://doi.org/10.1556/2006.2022.00067.

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