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Extraversion and Neuroticism Related to Topological Efficiency in White Matter Network: An Exploratory Study Using Diffusion Tensor Imaging Tractography

Yajing Pang[1,2] · Heng Chen[1,2] · Yuyan Chen[1,2] · Qian Cui[3] · Yifeng Wang[1,2] · Zhiqiang Zhang[4] · Guangming Lu[4] · Huafu Chen[1,2]

Abstract

White matter (WM) fibers underpin individual differences in extraversion and neuroticism. These personality traits are associated with integration of emotion, cognition, and behavior, which rely on a large-scale brain network. Thus, research at network level is needed to characterize neural underpinnings of extraversion and neuroticism. We performed diffusion tensor imaging on 68 healthy individuals and combined a WM network with graph theory analysis to investigate the connectivity of the whole-brain network and individual regions associated with extraversion and neuroticism. Extraversion was negatively associated with local efficiency in the medial prefrontal cortex (MPFC), and neuroticism was positively associated with local and global efficiencies mainly in the hippocampus and MPFC regions, respectively. These identified regions demonstrated connectivity with other cortical and subcortical regions. No reliable associations were found between the network local and global efficiencies and extraversion, as well as neuroticism. These findings indicated the association between specific personality dimensions and information transfer in the prefrontal–limbic regions, which provided further insight into the neural mechanism to characterize extraversion and neuroticism.

Keywords Extraversion · Neuroticism · White matter network · Graph theory analysis

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✉ Qian Cui
  qiancui26@gmail.com

✉ Huafu Chen
  chenhf@uestc.edu.cn

1 The Clinical Hospital of Chengdu Brain Science Institute, MOE Key Lab for Neuroinformation, University of Electronic Science and Technology of China, Chengdu, China

2 School of Life Science and Technology, Center for Information in Medicine, University of Electronic Science and Technology of China, Chengdu, China

3 School of Public Administration, University of Electronic Science and Technology of China, Chengdu, China

4 Department of Medical Imaging, Jinling Hospital, Nanjing University School of Medicine, Nanjing, China

Introduction

Extraversion and neuroticism are two central and frequently studied dimensions of human personality (Eysenck 1991; Kennis et al. 2013). These dimensions are related to socio-emotional functioning and psychopathology (Canli 2004; Eysenck 1991). Extraversion is linked to the tendency to experience positive emotions, engage in social interactions, and sensitivity to reward cues (Clark and Watson 2008; Costa and McCrae 1992); such behavior is considered to stem from the tendency to give a positive response to socio-emotional stimuli (Fishman et al. 2011). Neuroticism is susceptible to the experience of negative thoughts, emotional dysregulation (Larsen and Ketelaar 1991; Robinson et al. 2007), which is thought to originate from self-generated thoughts (Perkins et al. 2015). Understanding these individual differences in the brain is crucial to identify the neurophysiological basis of personality from a neurophysiological view.

White matter (WM) fiber bundles provide a scaffold for functional integration on the spatial distribution of cognitive

processes in the brain (Burzynska et al. 2013; Johansen-Berg 2010). The WM integrity has been implicated in personality traits (Bjørnebekk et al. 2012, 2013; Xu and Potenza 2012). The brain is a network, and the integration of emotion, cognition, and behavior relies on a large-scale network rather than individual connections (Achard and Bullmore 2007; Barrett and Satpute 2013; Bressler and Menon 2010). The neuroanatomical structure of large-scale brain networks provides a framework of connected brain areas to facilitate information along preferred pathways for specific cognitive functions (Bressler and Menon 2010). Accordingly, a network analysis for assessing WM connectivity on a whole-brain basis is needed to characterize structural network organization in extraversion and neuroticism.

A structural brain network consists of anatomical locations in the gray matter (nodes) and WM fibers connecting the nodes (edges). The properties of the network or individual regions can be evaluated using graph theory analysis. The mathematical representations of the structural network have revealed that the brain is organized according to a highly efficient small-world topology, with high levels of segregation (related to efficient local information processing, local efficiency) and integration (related to global communication efficiency across the network, global efficiency) (Achard and Bullmore 2007; Mp et al. 2009). Variations in the efficiency of the brain structural network are related to a range of individual difference variables, including intelligence, processing speed, visuospatial and executive functions (Koenis et al. 2015; Wen et al. 2011; Zhong et al. 2015). Moreover, the network efficiency is sensitivity to psychiatric disorders (Lewis et al. 2013). Studies on the functional network organization of healthy adults have explored the relationship between connectivity of the whole-brain network and human personality from the perspective of topological properties (Gao et al. 2013; Servaas et al. 2015). However, no research has related the WM network to personality; determining their associations is vital to understand how the organization of communication in the brain network and individual regions relates to extraversion and neuroticism.

In this study, we first constructed structural brain network through diffusion tensor imaging (DTI) tractography on 68 healthy individuals. Second, graph theory analysis was employed to assess the efficiency of information transfer among connected regions. Lastly, correlation analysis was performed to evaluate the relation of brain region connectivity to extraversion and neuroticism, and the association of communication efficiency with personality. Basing on previous studies, we predicted the association of efficient information communication within the WM network with personality traits. Moreover, the prefrontal cortex (PFC) and limbic regions, which subserve emotion and cognitive control function, function as hub regions and

are mostly related to human personality traits (Mitchell and Kumari 2016; Pang et al. 2015, 2016; Wright et al. 2006). We further predicted that efficient information transfer between these regions and other brain regions is correlated with extraversion and neuroticism.

Methods

Subjects

Seventy young, healthy, and right-handed volunteers were recruited in this study. None of the participants had a history of alcohol or drug abuse, neurological or psychiatric disorders, head injuries, or receipt of any medication in the past 2 weeks. The participants were screened using the Structure Clinical Interview for DSM-IV, Non-patient Edition, which was administered by an experienced psychiatrist. This study was approved by the local medical ethics committee of Jinling Hospital, Nanjing University School of Medicine, and the methods and procedures were carried out in accordance with the approved guidelines. Informed written consent was obtained from all individual participants prior to any study procedure. The data were published in our previous studies (Pang et al. 2015, 2016) that used resting-state functional magnetic resonance imaging data, which investigated functional connectivity pattern underlying personality.

Personality Questionnaires

Personality dimensions were assessed using the Chinese version of the Eysenck Personality Questionnaire (Eysenck 1967; Gong 1984). This questionnaire is self-report that consists of four dimensions, namely, extraversion, neuroticism, psychoticism, and lie. The participants are required to respond with "true" or "false" to each of the 88 statements [extraversion (21), neuroticism (24), psychoticism (23), and lie (20)], with each dichotomous item scored 1 or 0. As two basic and significant dimensions, extraversion and neuroticism were used to measure the correlations with topological parameters. The raw scores of the two dimensions were converted into T scores by using the following formula (Gong 1984):

$$T = 50 + 10 \times \frac{raw\ score - mean}{SD},$$

where the mean represents the mean value of the personality scores over the normative sample, and SD is the standard deviation of the personality scores over the normative sample.

Image Acquisition

All subjects were scanned using a 3T Siemens Trio scanner (Siemens-Trio, Erlangen, Germany) at the Jinling Hospital, Nanjing, China. Foam pads and headphones were used to minimize head movement and scanner noise.

DTI Scans

A spin echo-based echo planar imaging sequence was used for scanning. Diffusion-sensitizing gradients were applied along 30 non-collinear directions ($b = 1000$ s/mm^2), together with a non-diffusion-weighted acquisition ($b = 0$ s/mm^2). For each DTI scan, 45 contiguous axial slices were acquired with the following parameters: repetition time (TR) = 6100 ms, echo time (TE) = 93 ms, flip angle = 90°, slice thickness = 3 mm, field of view (FOV) = 240 mm × 240 mm, matrix size = 256 × 256, and voxel size = 0.94 mm × 0.94 mm × 3 mm. The entire sequence was repeated four times to improve the signal-to-noise ratio.

3D T1-Weighted Structural Scans

The main parameters for 3D T1-weighted structural magnetic resonance imaging were set as follows: TR = 2300 ms, TE = 2.98 ms, flip angle = 9°, slice thickness = 1 mm, slices = 176, FOV = 256 mm × 256 mm, matrix size = 512 × 512, and voxel size = 0.5 mm × 0.5 mm × 1 mm. DTI and T1-weighted data were visually inspected for apparent artifacts caused by subject head motion and instrument malfunction. Two subjects were excluded from the study because of damaged DTI data. A total of 68 subjects (33 males; age range 19–26 years, mean ± standard deviation: 22.31 ± 1.52) remained for subsequent analysis. A significantly negative correlation was found between extroversion (54.82 ± 8.37) and neuroticism (44.56 ± 12.13) by Pearson's correlation ($r = -0.44$, $p < 0.001$), and this result is consistent with previous reports (Wright et al. 2006).

Construction of Structural Networks

WM Tractography

DTI data were first realigned to assess for head motion. No participant was excluded under the head motion criterion of ± 3 mm and ± 3°. Mean framewise displacement (FD) (Power et al. 2012) was calculated to measure instantaneous head motion by using a threshold of 0.5 mm. The mean ± SD of the mean FD over the subjects was 0.32 ± 0.05 mm. Analysis showed no significant correlation between extraversion and mean FD ($r = 0.0001$, $p = 0.99$) and between neuroticism and mean FD ($r = 0.02$, $p = 0.89$).

EDDY(Yamada et al. 2014), a new tool to correct for eddy current distortions and subject movements, was used with FMRIB Software Library v5.0.10 (http://www.fmrib.ox.ac.uk/fsl). Subsequently, the Diffusion Toolkit was employed to estimate diffusion tensor models through the linear least-squares fitting method at each voxel(Wang et al. 2007). For each subject, whole-brain fiber tracking was conducted in native diffusion space by using the Fiber Assignment by Continuous Tracking algorithm. Path tracing proceeded until either the fractional anisotropy (FA) was less than 0.2 or the angle between the current and previous path segment was larger than 45°.

Defining Network Nodes

Regions of interest (ROIs) were defined in native diffusion space to determine the nodes of structural network. The T1-weighted images of each participant were first co-registered to the non-diffusion-weighted B0 images ($b = 0$ s/mm^2) in the native diffusion space through a linear transformation. The co-registered T1 images were then mapped to the ICBM152 T1-template in the Montreal Neurological Institute space through an affine transformation with 12 degrees of freedom together with a series of nonlinear warps. Inverse transformations were used to warp the 90 automated anatomical labeling (AAL) ROIs (Tzourio-Mazoyer et al. 2002) (Supplementary Table S1) from the Montreal Neurological Institute space to the DTI native space (Shu et al. 2009; Zhang et al. 2011). These warped cortical and subcortical regions (45 regions for each hemisphere; the cerebellum has already been removed) corresponded to individual space and served as 90 nodes in the network of each individual. Finally, the ROIs were dilated by 3 mm into the WM to ensure that they were in contact with the WM fibers (Liao et al. 2011).

Defining Network Edges

In the native diffusion space, an edge between two nodes was considered to exist if at least ten fibers exist across node i and node j simultaneously (Chen et al. 2013; van den Heuvel et al. 2012). This step reduced the influence from artificial connections, which may occur due to the sensitivity of the fiber assignment by continuous tracking algorithm to image resolution and noise (Long et al. 2013). The edge was then weighted by the mean FA values of fibers that connected the two nodes to describe the strength of the connectivity of ROIs i and j. Thus, a symmetric 90 × 90 matrix was found for each participant.

Threshold

Each connectivity matrix was converted into an undirected binary network by using a connection sparsity (S), which is the ratio of the number of existing edges to all possible edges, to construct a graph network (Achard and Bullmore 2007). Thresholding each connectivity matrix, rather than setting a static sparsity value, was performed repeatedly over a wide range ($0.10 \leq S \leq 0.34$ with an interval of 0.01), thereby increasing the significance of the interpretation of topological property comparisons. The minimum threshold was determined to guarantee that the average degree over all the nodes of each network is larger than $2 \times \log (N)$, where N is the number of nodes and the degree of a node is the number of connections that links it to the rest of the network (Achard and Bullmore 2007; Lei et al. 2015). The maximum threshold was determined by selecting the minimum S value without thresholding across the subjects (Long et al. 2013). The generated threshold range of 0.10–0.34 guaranteed that the threshold connectivity network achieved a quantifiable small-world behavior and minimal spurious edges.

Graph Theoretical Analysis

In this study, the network properties computed included local and global efficiencies (Latora and Marchiori 2001) to quantify the small-world behavior of the WM structural network in extraversion/neuroticism by using the Gretna toolbox (https://www.nitrc.org/projects/gretna/). Network global efficiency E_{glob}, network local efficiency E_{loc}, nodal global efficiency $E_{glob,i}$ and nodal local efficiency $E_{loc,i}$ were mathematically defined as follows.

Network global efficiency:

$$E_{glob} = \frac{1}{N(N-1)} \sum_{i \neq j \in G} \frac{1}{L_{ij}}$$

Network local efficiency:

$$E_{loc} = \frac{1}{N} \sum_{i \in G} E_{glob}(G_i)$$

where N is the node of a network (graph) G, G_i denotes the subgraph containing the nearest neighbors of node i, and L_{ij} is the shortest path length between nodes i and j in G. The path length represents the number of edges included in the path connecting nodes i and j (Rubinov and Sporns 2010). The shortest path length L_{ij} is the length of the path with the shortest length between nodes i and j. E_{glob} quantifies how easy information can be exchanged over the network, thus providing information on the communication efficiency of a

network as a whole, E_{loc} measures the ability of information propagation of a subnetwork.

Nodal global efficiency:

$$E_{glob,i} = \frac{1}{N-1} \sum_{i \neq j \in G} \frac{1}{L_{ij}}$$

Nodal local efficiency:

$$E_{loc,i} = \frac{1}{N_{G_i}(N_{G_i}-1)} \sum_{j \neq k \in G_i} \frac{1}{L_{jk}}$$

where N represents the nodes of a network (graph) G, and G_i is the subgraph of G containing all the directly connected neighboring nodes of node i. N_{G_i} represents the nodes of G_i. L_{ij} is the shortest path length between nodes i and j in G. L_{jk} is the shortest path length between nodes j and k in G_i. $E_{glob,i}$ measures the ability of information propagation between a given node i with the rest of the nodes in G, $E_{loc,i}$ reflects how well information can travel in the direct neighborhood of node i.

Statistical Analysis

All the network measures (E_{glob}, E_{loc}, $E_{glob,i}$, and $E_{loc,i}$) were thresholded repeatedly over the range of $0.10 \leq S \leq 0.34$ with an interval of 0.01. The area under the curve (AUC) across the threshold values was calculated and used as a summarized scalar that is independent of single threshold selection (Zhang et al. 2011). After regressing out age, gender, and mean FD, correlation analysis was performed between the AUC value of each network metric and extraversion/neuroticism scores. Given the theoretical and statistical anticorrelation between extraversion and neuroticism, we added neuroticism (or extraversion) scores as covariate when calculating the correlation between extraversion (or neuroticism) and AUC of each network measure, to determine the effects individually driven by each personality dimension.

Nonparametric permutation test was employed to test the null hypothesis that the observed correlation result could occur by chance. Extraversion/neuroticism scores were permuted randomly and the correlations with each network measure were recalculated. This procedure was repeated 5000 times to obtain the null distribution. We then assigned a *p*-value to the correlation between extraversion/neuroticism and network parameters by computing the proportion of correlations exceeding the null distribution values (Servaas et al. 2015; Zhang et al. 2011). The significance of the corrections at each region was tested using the false-positive correction $p < (1/N) = 0.011$, where N = the number of nodes. This implied there was less than one false-positive per analysis (Fornito et al. 2011; Liao et al. 2016; Lynall et al. 2010).

A post-hoc analysis was added to gain further insights into the proper interpretation of relationships between nodal efficiency and extraversion/neuroticism. The structural connectivity (i.e., mean FA value) between each of the identified regions and 89 other regions were firstly extracted. Then, correlation was calculated between the connectivity and extraversion (or neuroticism) scores after regressing out age, gender, mean FD, and neuroticism (or extraversion). All the structural connectivity of the identified region perhaps contributed to the association of personality and node efficiency. We ranked the correlation values, and the correlation results which survived by $p < 0.05$ without uncorrected were included in our analysis. The survived structural connectivity was labeled on the basis of John Hopkins University white-matter tractography atlas (Mori et al. 2005). The results of this part was included in the Supplementary Material.

Results

Regions Where Efficiency is Related to Extraversion/Neuroticism

In this study, network global and local efficiencies showed no significant association with extraversion/neuroticism. The two personality dimensions exhibited correlation with nodal efficiency mainly in the PFC and limbic regions (permutation testing, $p < 0.011$). Extraversion was negatively correlated with local efficiency in the left medial superior frontal gyrus, and neuroticism was positively correlated with local efficiency in the right hippocampus and left cuneus (Fig. 1; Table 1). Neuroticism was also positively correlated with global efficiency in the right medial superior frontal gyrus, left medial orbital part of superior frontal gyrus, and left rectus gyrus (Fig. 2; Table 1).

Additional Analysis

In order to further test the reliability of our results, some additional works were included. First, as the edge definition of minimum ten fibers to exit between two nodes pairs seems arbitrary, we then use different threshold with at least three or five fibers to test the association between network efficiency and extraversion and neuroticism. Second, in addition to investigating the network measures on binary network, we also take into account the weighted network, which additionally providing information on the structural connectivity strength. The main results observed in our analyses were robust to different parameter settings (see Tables S3, S4, and S5).
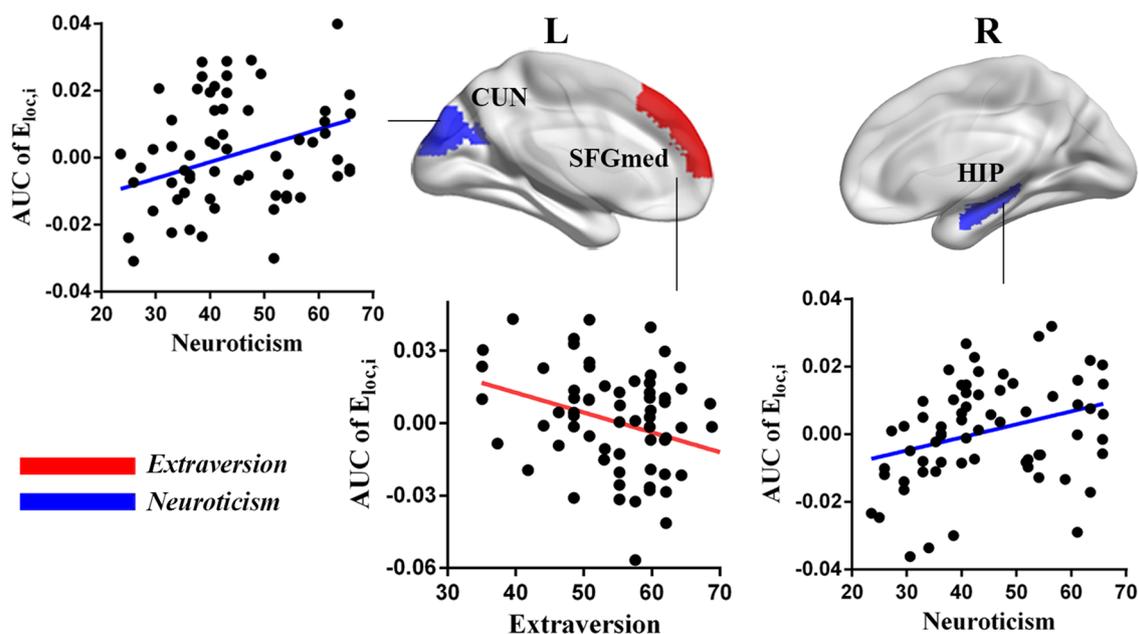

Fig. 1 Regions where nodal local efficiency was correlated with extraversion and neuroticism. AUC was calculated over the range of $0.10 \leq S \leq 0.34$ with an interval of 0.01 after regressing out age, sex, and mean FD. Region marked in red was associated with extraversion, whereas regions marked in blue were associated with neuroticism. The red and blue lines in the scatter plots represent the negative and positive correlation, respectively. *SFGmed* superior frontal gyrus, medial part; *HIP* hippocampus; *CUN* cuneus; *AUC* area under the curve; *R* right; *L* left

Table 1 Regions where efficiency are related to extraversion and neuroticism

Brain regions	r value (p)	
	Nodal global efficiency	Nodal local efficiency
Extraversion		
L_ superior frontal gyrus, medial part	–	− 0.31 (0.005)
Neuroticism		
R_ hippocampus	–	0.31 (0.004)
L_ cuneus	–	0.29 (0.009)
R_ superior frontal gyrus, medial part	0.32 (0.004)	–
L_ superior frontal gyrus, medial orbital part	0.29 (0.007)	–
L_ rectus gyrus	0.28 (0.009)	–

Regions showing association with extraversion and neuroticism in nodal global and local efficiencies (permutation testing, $p < 0.011$)
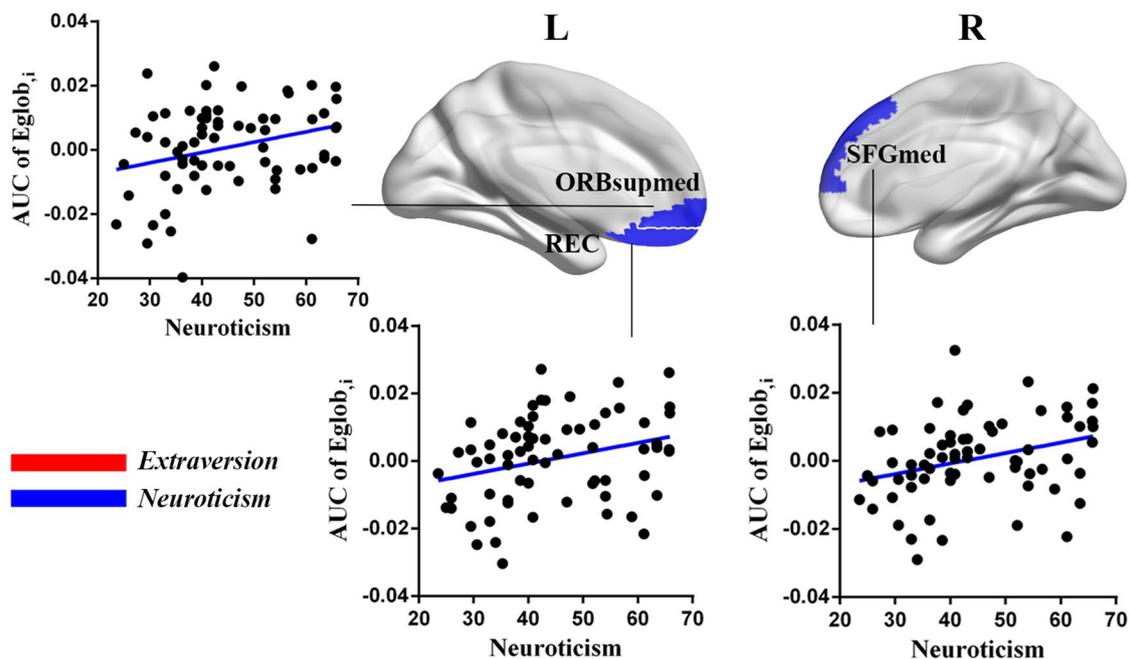
R right; *L* left

Fig. 2 Regions where nodal global efficiency was correlated with neuroticism. AUC was calculated over the range of $0.10 \leq S \leq 0.34$ with an interval of 0.01 after regressing out age, sex, and mean FD. Regions marked in blue were associated with neuroticism. The blue line in the scatter plots represents the positive correlation. *SFGmed* superior frontal gyrus, medial part; *ORBsupmed* superior frontal gyrus, medial orbital part; *REC* rectus gyrus; *AUC* area under the curve; *R* right; *L* left

Discussion

This study investigated neural mechanisms underlying extraversion and neuroticism in healthy young subjects in terms of the organization of the whole-brain structure network. The results confirm our hypothesis that extraversion and neuroticism are associated with the local and global efficiencies of nodes mainly in the PFC and limbic regions. The tracts between these identified regions and part of cortical and subcortical regions subserving the cognition–emotion function are important for neuroticism. Furthermore, the local and global efficiencies of network are uncorrelated with extraversion and neuroticism. These results highlight the role of structural network architecture in delineating extraversion and neuroticism.

Regions Where Nodal Efficiency is Related to Extraversion

The MPFC is a key region in the default mode network and implicated in social cognition, affection, and self-awareness

and is related to extraversion trait (Heatherton 2011; Mitchell et al. 2005). Compared with introverts, extraverts show decreased regional cerebral blood flow (Johnson et al. 1999), regional homogeneity (Wei et al. 2011), resting functional MRI signals (Kumari et al. 2004) in this region, as well as decreased local functional connectivity of the MPFC (Pang et al. 2015). Complementary to these findings, we revealed that the local information transfer across the MPFC in structural network is negatively associated with extraversion. The negative correlation of extraversion and MPFC supports Eysenck's predication that extraverts have low arousal level in the frontal lobe (Eysenck 1994). Due to this chronic intrinsic underaroused activity, extraverts are prone to engage in typically extraverted behavior to enhance their low arousal level (Eysenck 1994; Gao et al. 2013).

Regions Where Nodal Efficiency is Related to Neuroticism

The local efficiency in the hippocampus is positively associated with neuroticism, and the fiber connectivity of the hippocampus extends to other limbic regions through fornix, inferior fronto-occipital fasciculus, and corpus callosum tracts. The information transfer in limbic regions is implicated in emotion and memory process that related to neuroticism (Greenberg et al. 2005; Nyberg et al. 2016; Ormel et al. 2013; Sadeh et al. 2014). Higher neurotic individuals has a tendency toward fewer happy thoughts and memories (Ruizcaballero and Bermúdez 1995). They tend to recall negative information that comes from personal memories for real-life events (i.e., autobiographical memory) (Denkova et al. 2012; Kuyken and Dalgleish 2011). At the neural level, the greater limbic regions activity in individuals with high neuroticism scores during fear learning was related to improved long-term memory of learned associations (Hooker et al. 2008). The higher effective connectivity of limbic region in individuals high in neuroticism was associated with negative emotion processes (Pang et al. 2016). Accordingly, the limbic regions play an important role in the negative affective bias in emotional memory associated with neuroticism (Haas and Canli 2008; Katsumi et al. 2017).

Recent studies have introduced the association between neuroticism and MPFC region. High levels of spontaneous activity in the MPFC tended to result in a multitude of negative self-generated thoughts, which was served as the engine of neuroticism (Ochsner et al. 2005; Perkins et al. 2015; Robinson and Meier 2005). Greater sustained MPFC activity in response to sad facial expressions was associated with higher scores of neuroticism (Haas et al. 2008). Among the relationship, the role of negative self-evaluation and appraisal in this region was emphasized (Fossati et al. 2003; Ochsner et al. 2004). Here, in structural brain network, we found that the higher efficiency of global information

transform between the MPFC and other cognitive regions (e.g., dorsolateral PFC, caudate, and pallidum) is associated with higher levels of neuroticism. The connectivity of MPFC through corpus callosum and internal capsule/corona radiate contributes to the integration of cognitive process (Alexander et al. 2003; Chai et al. 2014; Neurology 1993; Shackman et al. 2009). In sum, these findings together provide a sustained neural mechanism underlies the character of sensitivity to negative information in neuroticism.

Absent Network Efficiency is Related to Extraversion/Neuroticism

While our previous functional network analysis revealed no correlation between network efficiency and personality (Gao et al. 2013), Servaas et al. (2015) suggested that neuroticism is positively correlated with network global efficiency in terms of functional brain network. The discrepant result should be ascribed to the different samples and method analysis in these two studies. The sex difference significantly influences human personality (Jorm 1987; Vianello et al. 2013; Weisberg et al. 2011). In addition, the different predefined template may also play an effect on network analysis. In the structural network, we did not obtain the expected result between personality and the global and local efficiencies of network. There are some reasons: First, the modest sample size limits the power of correlation analysis between personality dimensions and network efficiency parameters. Second, the definition node may have an effect on white matter network analysis. Third, and the structural network seems to be stable which offers a complex architecture that promotes large-scale neuronal dynamic interactions between nodes, leading to the formation of a functional network (Olaf 2013; Smith 2012).

Limitation

Our study has several limitations. First, the modest sample size limits the power of correlation analysis between structural brain network topological properties and personality dimensions, as well as justifies the multiple-comparisons correction that does not reach strong type 1 error control at the regional level of analysis. A large sample is needed to warrant our findings in the future. Second, we use AAL template to define the network nodes in our analyses. This approach is widely used in the literature, but the definition of nodes remain arbitrary. Further work examining the effects of template selection on reported findings will be important to determine their generalizability. Third, our design does not control for confounding effects of nicotine/smoking, which can affect FA in the corpus callosum and Internal capsule/corona radiate (Kochunov et al. 2013; Paul et al. 2008). Future personality studies should exclude the effects

of nicotine/smoking. Fourth, although some well-known fibers existing in human brain were successfully extracted from our tracking results (see detailed information in Supplementary Material), the non-isotropic voxel size may lead to underestimate FA values in regions with crossing fibers such as the superior longitudinal fasciculus, thalamus, and red nucleus (Basser et al. 2000; Jones and Cercignani 2010; Oouchi et al. 2007). The isotropic voxel size of DTI data is required to further test our findings in the future.

Conclusion

To the best of our knowledge, this study is the first to explore the relationship between personality and neuroanatomical structural connections from the network perspective. The node-based, rather than network-based, efficient information transfer is correlated with extraversion and neuroticism. The fiber connectivity of the PFC and limbic regions plays a specific role in explaining some aspects of the complex cognitive pattern associated with extraversion and neuroticism. These results highlight the importance of the anatomical brain network in understanding the human personality. The relationship between personality and the WM network can be a valuable index for exploring the neurobiological underpinnings of human personality.

Author Contributions YP and HC conceived and designed the experiments. ZZ and GL prepared the samples. YP, HC, and YC analyzed the data. YP, QC, and YW participated in the interpretation of data. YP wrote the paper.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interest.

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