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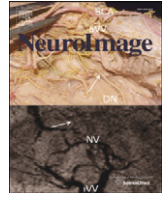
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## Fiber connectivity between the striatum and cortical and subcortical regions is associated with temperaments in Chinese males



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### ABSTRACT

The seven-factor biopsychosocial model of personality distinguished four biologically based temperaments and three psychosocially based characters. Previous studies have suggested that the four temperaments—novelty seeking (NS), reward dependence (RD), harm avoidance (HA), and persistence (P)—have their respective neurobiological correlates, especially in the striatum-connected subcortical and cortical networks. However, few studies have investigated their neurobiological basis in the form of fiber connectivity between brain regions. This study correlated temperaments with fiber connectivity between the striatum and subcortical and cortical hub regions in a sample of 50 Chinese adult males. Generally consistent with our hypotheses, results showed that: (1) NS was positively correlated with fiber connectivity from the medial and lateral orbitofrontal cortex (mOFC, IOFC) and amygdala to the striatum; (2) RD was positively correlated with fiber connectivity from the mOFC, posterior cingulate cortex/retrosplenial cortex (PCC), hippocampus, and amygdala to the striatum; (3) HA was positively linked to fiber connectivity from the dorsolateral prefrontal cortex (dlPFC) and PCC to the striatum; and (4) P was positively linked to fiber connectivity from the mOFC to the striatum. These results extended the research on the neurobiological basis of temperaments by identifying their anatomical fiber connectivity correlates within the subcortical–cortical neural networks.

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### Introduction

In the seven-factor biopsychosocial model of personality, Robert Cloninger distinguished four temperaments (novelty seeking, reward dependence, persistence, and harm avoidance) and three characters (cooperativeness, self-directedness, and self-transcendence) (Cloninger, 1987, 1994b; Cloninger et al., 1993). Temperaments represent individuals' congenital and automatic behavioral responses to the environmental stimuli of novelty, reward and danger, whereas characters represent individuals' adaptation to complex social contexts (Cloninger, 1994a,b).

**Abbreviations:** NS, novelty seeking; RD, reward dependence; P, persistence; HA, harm avoidance; TCI, the Temperament and Character Inventory; DTI, diffusion tensor imaging; mOFC, the medial orbitofrontal cortex; IOFC, the lateral orbitofrontal cortex; lPFC, the lateral prefrontal cortex; dlPFC, the dorsolateral prefrontal cortex; PCC, the posterior cingulate cortex/retrosplenial cortex; dACC, the dorsal anterior cingulate cortex; ACC, the anterior cingulate cortex.

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Consequently, the four temperaments are proposed to be more dependent on biological (genetic and neural) factors, whereas characters depend more on socio-cultural factors. Extreme/abnormal personality traits (especially temperaments) are common characteristics of a wide spectrum of prevalent personality and psychiatric disorders (Richter and Brandstrom, 2009; Svrakic et al., 1993), such as depression (Celikel et al., 2009; Farmer et al., 2003; Sandi and Richter-Levin, 2009), bipolar disorder (Olvera et al., 2009), borderline personality disorder (Barnow et al., 2007), obsessive–compulsive disorder (Ettelt et al., 2008), and schizophrenia (Hori et al., 2008; Smith et al., 2008). These disorders have been found to be accompanied by abnormal/pathological neurobiological changes in the brain (Hazlett et al., 2005; Nakamura et al., 2005). In order to have a better understanding of the neurobiological basis of temperaments and a deeper insight into the pathogenesis of the temperament-related neuropsychiatric disorders, the current study investigated the associations between temperaments and fiber connectivity from the cortical and subcortical regions to the striatum.

Several lines of research have reported that extensive subcortical and cortical regions are involved in temperaments. In the following paragraphs, we briefly introduce the four temperaments as identified by Cloninger and summarize previous neuroimaging results (see

**Table 1.** Novelty seeking (NS) is linked to the behavioral activation system and refers to one's tendency to initiate an exploratory behavior towards novelty as well as one's excessive response to cues of rewards. A recent diffusion tensor imaging (DTI) study (Cohen et al., 2009) reported that fiber connectivity between the striatum, hippocampus, and amygdala could predict individual differences in NS. Two brain anatomical studies also found that NS was correlated with white matter volume in the frontal cortex and gray matter volume in the frontal cortex and PCC (Gardini et al., 2009; Van Schuerbeek et al., 2011). Consistent with the structural data, functional brain studies reported that the striatum, substantia nigra and ventral tegmental regions (Krebs et al., 2009), and prefrontal cortical regions (Bermppohl et al., 2008) were involved in NS.

Reward dependence (RD) refers to the behavioral dependence system and reflects one's tendency to stimulate and maintain reward behavior. As shown in Table 1, the mesolimbic-dopamine-centered network, especially the striatum and frontal cortex (Berridge and Robinson, 2003; Schultz, 2000, 2002), plays a key role in RD. Cohen et al., 2009 found that fiber connectivity between the striatum and frontal cortex was associated with individual differences in RD. RD

has also been correlated with gray matter volumes of the frontal and temporal regions and caudate nucleus (Gardini et al., 2009; Van Schuerbeek et al., 2011), and gray matter densities of the medial orbitofrontal cortex, ventral striatum, and putamen (Lebreton et al., 2009). Functional brain imaging studies confirmed the key role of the striatum and orbitofrontal cortex in RD and reward processing (Krebs et al., 2009).

Harm avoidance (HA) is similar to the behavioral inhibition system and refers to one's tendency to inhibit behavior to avoid punishment, loss, and non-reward. The amygdala, anterior cingulate cortex, and medial orbitofrontal cortex had been found to contribute significantly to HA in several previous studies (Buckholtz et al., 2008; lidaka et al., 2006; Pezawas et al., 2005; Pujol et al., 2002; Yamasue et al., 2008a; Yang et al., 2009, see Table 1). Recent studies also found that HA was associated with local structural integrity indexed by fractional anisotropy as well as mean and radial diffusivity within most main white matter fibers in the brain (Kim and Whalen, 2009; Westlye et al., 2011). There appears to be a widely distributed, interconnected neural network of HA, including the limbic system and the higher-function cortical regions.

**Table 1**  
Previous brain imaging studies showing neural correlates of temperaments.<sup>a</sup>

Temperaments	Studies	Frontal cortex	Temporal cortex	Parietal/occipital cortex	Subcortical nucleus	
NS	Sugiura et al. (2000)	ACC,SFG, anterior insula	STG			
	Turner et al. (2003)		ITG & MTG	PCC		
	Suhara et al. (2001)	Right insula				
	Youn et al. (2002)	Right MFG	MTG			
	Hakamata et al. (2006)		Left STG	IPG & PCC		
	Cohen et al. (2009)				Striatum, hippocampus, amygdala	
	lidaka et al. (2006)	Left MFC				
	Gardini et al. (2009)	PFC		PCC		
	Van Schuerbeek et al. (2011)	IFC		PCC		
	Bermppohl et al.(2008)	MFG, pregenual ACC				
	Krebs et al. (2009)				SN/VTA	
	RD	Sugiura et al. (2000)	ACC,SFG, anterior insula	STG		
		Turner et al. (2003)		ITG & MTG	MOG & SOG	
Youn et al. (2002)		Left OFC	ITG & MTG			
Hakamata et al. (2006)		Left insula	MTG	Right IOG	Caudate head	
Cohen et al. (2009)		OFC, lateral and dorsal PFC			Striatum	
lidaka et al. (2006)					Right caudate nucleus	
Gardini et al. (2009)		Rectal PFC			Caudate nucleus	
Lebreton et al. (2009)		Medial OFC			Ventral striatum, left putamen	
Van Schuerbeek et al. (2011)		Left MFG, right IFG		PCC	Thalamus, putamen	
Krebs et al. (2009)					SN/VTA	
HA		Sugiura et al. (2000)	Right orbito-insular junction, SFG	Left ITG		
		Turner et al. (2003)		ITG & MTG	MOG & SOG	
		Youn et al. (2002)	Right ACC	Left MTG, ITG		
	Hakamata et al. (2006)	Left MFG	Left MTG	Right PCC	Right thalamus	
	Inada et al. (2009)	Right SFG & MFG in females				
	Cohen et al. (2009)				Striatum & hippocampus	
	Pujol et al. (2002)	Right ACC				
	lidaka et al. (2006)	OFC			Left amygdala	
	Yamasue et al. (2008b)	Left anterior PFC			Right hippocampus	
	Gardini et al. (2009)	Orbito-frontal regions		Occipital cortex		
	Van Schuerbeek et al. (2011)	Left SFG & IFG, ACC				
	Pezawas et al. (2005)	ACC			Amygdala	
	Most et al.(2006)	Subgenual ACC			Amygdala	
P	Yang et al. (2009)	Subgenual ACC				
	Westlye et al. (2011)	Subgenual ACC, OFC			Amygdala	
	Turner et al. (2003)		ITG & STG			
	Hakamata et al. (2006)	Right MFG & insula	Left MTG	PCC	Striatum	
	Cohen et al. (2009)	mOFC				
	Gardini et al. (2009)			PCC		
	Van Schuerbeek et al. (2011)	Right ACC	ITG	PCC		
Gusnard et al.(2003)	OFC			Ventral striatum		

Abbreviation: ACC, the anterior cingulate cortex; OFC, the orbitofrontal cortex; SFG, the superior frontal gyrus; MFG, the middle frontal gyrus; IFG, the inferior frontal gyrus; PFC, the prefrontal cortex; STG, the superior temporal gyrus; MTG, the middle temporal gyrus; ITG, the inferior temporal cortex; PCC, the posterior cingulate cortex/precuneus; SPG, the superior parietal gyrus; MPG, the middle parietal gyrus; IPG, the inferior parietal gyrus; SOG, the superior occipital cortex; MOG, the middle occipital cortex; IOG, the inferior occipital cortex; SN/VTA, the substantia nigra/ventral tegmental area; NS, novelty seeking; RD, reward dependence; HA, harm avoidance; P, persistence.

<sup>a</sup> This table includes all PET/SPECT studies and functional and structural MRI studies of TCI (Temperament and Character Inventory) or TPQ (Tridimensional Personality Questionnaire) in healthy and normal samples that were published between 2000 and 2011. Excluded were studies that did not use the original TCI or TPQ scales or subscales (e.g., Schweinhardt et al. (2009), who used principal component analysis to extract a main component from NS, HA, and subscales of the Behavioral Appetitive System Scale [Carver and White, 1994]).

Persistence (P) refers to one's tendency to maintain an ongoing behavior despite the absence or omission of reward. The orbitofrontal cortex and striatum have been reported to play a role in P (see Table 1). A functional brain imaging study reported that individual differences in P were associated with activation in the orbital and medial frontal cortex and ventral striatum during a picture-viewing task (Gusnard et al., 2003). In a separate study (Cohen et al., 2009), P was positively correlated with fiber connectivity from the mOFC to the striatum. P was also linked to gray and white matter volume of the cortices and limbic regions, such as the paracentral lobule, precuneus and cingulate gyrus (Gardini et al., 2009; Van Schuerbeek et al., 2011).

Taken together, these previous studies showed that the amygdala, striatum, hippocampus, cingulate, and frontal cortex play critical roles in temperaments. RD, NS and P were positively correlated with the striatal–frontal fiber connectivity and HA was positively correlated with the striatal–hippocampal fiber connectivity (Cohen et al., 2009). Integrity of white matter microstructure in pathways connecting hubs of the corticolimbic circuit was also correlated with HA (Westlye et al., 2011). Voxel-based morphometric studies provided further support for the involvement of subcortical regions (the amygdala, striatum, and hippocampus) and the frontal cortex in temperaments (Gardini et al., 2009; Lidaka et al., 2006; Van Schuerbeek et al., 2011; Yamasue et al., 2008b).

Although extensive subcortical and cortical brain regions have been found to be involved in temperaments (see Table 1), these studies focused on local brain structural/functional markers, especially on gray matter (gray matter volume, gray matter density, cortical thickness, task-elicited functional activation). Little attention has been paid to white matter, even though white matter makes up half of the human brain and has been gradually acknowledged to play an important role in human higher functions (Fields, 2010). Thus far only two studies have looked at white matter and temperaments. One focused on correlations between HA and local white matter integrity (Westlye et al., 2011) and the other focused on correlations of NS and RD with fiber connectivity between the striatum and the amygdala, hippocampus, and frontal cortical regions (Cohen et al., 2009).

The present study was designed to expand the literature on the neurobiological basis of temperaments by focusing on striatum-projected white-matter connectivity in Chinese males. Based on previous findings and suggestions, we hypothesized that different temperaments would be differentially correlated with fibers connecting the striatum with the subcortical and cortical regions. Specifically, three temperaments (NS, RD and P), which are closely linked to the mesolimbic-dopamine-centered networks, were hypothesized to be correlated with fiber connectivity between the striatum and the medial frontal cortex; HA was hypothesized to be correlated with fiber connectivity between the striatum and the medial and dorsal frontal cortex.

## Materials and methods

### Participants

Fifty male college students (mean age 20.10 yrs; range 19–22 yrs) were recruited from the Beijing Normal University. All participants were Han Chinese with normal or corrected-to-normal vision and no neurological or psychiatric history. They also passed the physical and clinical examinations for all freshmen administered by the university. They were asked to complete the Chinese version of the Temperament and Character Inventory-Revised (TCI-R) (Cloninger, 1994b; Zhu et al., 2010), the Beck Depression and Anxiety Inventories (BDI and BAI) (Beck, 1990; Beck et al., 1996), the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993) and the Fagerstrom Test for Nicotine Dependence (FTND) (Heatherton et al., 1991), and were scanned for diffusion tensor and high resolution 3D anatomical images. All participants gave informed written consents and the study

was approved by the Beijing Normal University Institutional Review Board.

### Image acquisition

Participants were scanned on a Siemens Trio 3 T scanner with an eight-channel head coil in the Beijing Normal University Imaging Center for Brain Research. The diffusion-weighted data were acquired using a twice-refocused spin-echo EPI sequence with the following parameters: TR/TE = 7200 ms/104 ms, 49 transverse slices, field-of-view = 230 \* 230 mm, matrix = 128 \* 128, slice thickness = 2.5 mm, 1 direction with  $b$ -value = 0 s/mm<sup>2</sup>, 64 directions with  $b$ -value = 1000 s/mm<sup>2</sup>. In addition, a high resolution 3D anatomical image was obtained using T1-weighted MP-RAGE sequence with the following parameters: TR/TE/FA = 2530 ms/3.75 ms/7°, FOV = 220 \* 220 mm, matrix = 256 \* 256, slice thickness = 1 mm, 128 sagittal slices. For each participant, scanning lasted 18 min.

### Image preprocessing

Diffusion tensor images (DTI) were processed using the FMRIB's Diffusion Toolbox (FDT 2.0) and Tract-Based Spatial Statistics (TBSS 1.2) (Smith et al., 2006) from the FMRIB's Software Library (FSL, version 4.1.4; www.fmrib.ox.ac.uk/fsl; Jenkinson et al., 2012; Smith et al., 2004; Woolrich et al., 2009). The standard processing procedure was used for the probabilistic tractography of DTI data: eddy correction, brain extraction (Smith, 2002), fitting of diffusion tensors, sampling of the diffusion parameters for each voxel in the seed region, and probabilistic tractography within each participant's diffusion space using FSL bedpostX (Behrens et al., 2003a, 2003b, 2007). Correction of the diffusion data for eddy currents and head motion was performed through the affine alignment to the no-diffusion-weighted reference volume ( $b$ -value = 0). The diffusion tensor was then constructed by FDT. Diffusion-weighted images were spatially normalized into the Montreal Neurological Institute (MNI) standard space with the FMRIB's Linear Image Registration Tool (FLIRT) (Greve and Fischl, 2009; Jenkinson et al., 2002) and the FMRIB's Nonlinear Image Registration Tool (FNIRT) on the individual's high resolution T1-weighted structural image. Visual inspection was done to confirm that the registration was successful. In addition, the transformation matrix and warp field between individual diffusion space and the MNI standard space were acquired with the tools "convert\_xfm" and "invwarp".

We created one seed mask of the striatum and nine target masks for each hemisphere based on the automated anatomical labeling template (Tzourio-Mazoyer et al., 2002) and the previous study (Cohen et al., 2009) (Supplementary Fig. S1). They included the medial orbitofrontal cortex (mOFC, consisting of Frontal\_Sup\_Orb, Rectus and Frontal\_Med\_Orb), lateral orbitofrontal cortex (lOFC, consisting of Frontal\_Mid\_Orb and Frontal\_Inf\_Orb), lateral prefrontal cortex (lPFC, consisting of Frontal\_Inf\_Tri\_R), dorsolateral prefrontal cortex (dlPFC, consisting of Frontal\_Sup\_R and Frontal\_Mid\_R), posterior cingulate cortex/retrosplenial cortex (PCC, consisting of Precuneus), anterior cingulate cortex (ACC, consisting of Cingulum\_Ant), dorsal anterior cingulate cortex (dACC, consisting of Cingulum\_Mid), hippocampus, amygdala, and striatum. Due to the fact that the probabilistic tractography must be conducted in the individual's diffusion space using the FMRIB Diffusion Toolbox, all masks in the MNI standard space were transformed to the individual diffusion space by using the tool "applywarp" to apply the inverse transformation matrix and warp field produced in the previous step.

For each participant, Bayesian estimation of diffusion parameters based on the Samples Techniques was conducted by the BedpostX program implemented in FMRIB's Diffusion Toolbox. Probabilistic tractography with a model allowing for crossing fibers (Behrens et al., 2003b) was performed from the striatum to the nine target regions (mOFC, lOFC, dlPFC, lPFC, ACC, dACC, PCC, hippocampus,

and amygdala) in individuals' diffusion space with 5000 tract-following samples for each voxel in the striatum, resulting in a probabilistic map of fiber connectivity for each of the nine target regions. The value of each voxel in the tractographic images represented the number of the fiber projections to the particular target area and was divided by the voxel's total number of fiber projections to all regions (i.e., a proportional ratio). These images were transformed back to the MNI standard space for group statistical analyses. Images in the MNI standard space were entered into general linear models (GLMs) for voxel-wise analyses. The method has been well validated and used in diffusion tensor imaging studies (Cohen et al., 2009; Croxson et al., 2005; Johansen-Berg and Rushworth, 2009).

#### Data analysis

All GLM analyses were conducted with the tool “randomise” with 5000 permutations. The “randomise” tool uses permutation-based non-parametric testing with the Threshold-Free Cluster Enhancement (TFCE) to perform voxel-wise group statistics (Nichols and Holmes, 2002; Smith and Nichols, 2009), which is highly recommended by the FSL group for finding statistically significant cluster-like structures in an image. Preprocessed tractographic images were entered into GLMs with demeaned temperament scores as covariates of interest. The voxel-wise p-values were corrected for multiple comparisons with the TFCE algorithm (Smith and Nichols, 2009) within analyses, and then further corrected for multiple tests across analyses by dividing the significance level by the number of analyses (4 traits  $\times$  9 ROIs = 36) in the current study.

Additional analyses were performed to examine whether the results were confounded by the following factors: depression, anxiety, alcohol use, and cigarette smoking. Scores of BDI, BAI, alcohol use and cigarette smoking were entered into GLMs as covariates of no-interest in additional GLM analyses.

We also tested whether temperaments were correlated with gray matter density, which might blunt the correlations between temperaments and fiber connectivity between brain regions. Structural data were analyzed with FSL-VBM (Douaud et al., 2007, [www.fmrib.ox.ac.uk/fslvbm](http://www.fmrib.ox.ac.uk/fslvbm)), an optimized VBM protocol (Good et al., 2001) carried out with FSL tools (Andersson, 2007; Smith et al., 2004). Furthermore, the tool “fslstats” in FSL was used to extract the fiber connectivity from significant clusters and the volumes of individuals' target regions. Pearson's and partial correlations between the extracted connectivity and the correlated temperament were assessed in SPSS 16.0 with the volume of the corresponding target region as a covariate.

## Results

Basic descriptive statistics and inter-correlations among the four temperaments are presented in Supplementary Table S1. These

correlations were similar to those reported by previous studies (Chen et al., 2002; Hansenne et al., 1999; Sung et al., 2002).

Tractography-based classification of the striatum (Supplementary Figs. S2 and S3) was consistent with the segmentation pattern reported in previous studies (Cohen et al., 2009; Croxson et al., 2005; Lehericy et al., 2004; Voorn et al., 2004), which confirmed the probabilistic tracking process of diffusion tensor images in the present study.

Results of GLMs showed that fiber connectivity between the striatum and hippocampus, amygdala, and hub cortical regions were extensively and differentially involved in temperaments. As shown in Table 2 and Figs. 1a–d, NS was positively correlated with fiber connectivity from the mOFC, IOFC, and amygdala to the striatum; RD with fiber connectivity from the mOFC, PCC, hippocampus and amygdala to the striatum; HA with fiber connectivity from the dlPFC and PCC to the striatum; and P with fiber connectivity from the mOFC to the striatum. Overlay of the correlations on the connectivity maps showed regions with low to high average connectivity probabilities (see Supplementary Fig. S4). These results did not change in the additional analysis with BDI, BAI, alcohol use, and cigarette smoking as covariates of no-interest. VBM analysis found no significant results between gray matter density and temperaments. Correlational analyses showed no significant differences between Pearson's and partial correlations, the latter of which excluded the potential confound from the volume of the specified target region.

## Discussion

In the present study, we used the noninvasive DTI technique to examine the neurobiological basis of temperaments in the form of fiber connectivity underlying the neuronal intercommunication between the striatum and cortical or subcortical hub regions. As expected, results showed variations in the extensive fiber connectivity between the striatum and cortical or subcortical regions underlying individual differences in temperaments (Table 2). These results extended previous research on the neurobiological basis of temperaments to the anatomical fiber connectivity within the subcortical–cortical neural networks. Given that functional connectivity relies on structural connectivity (Boorman et al., 2007; Haberling et al., 2011), these temperament-related neuroanatomical circuits also provided anatomical support for previous findings of functional networks for temperaments (Gusnard et al., 2003; Jung et al., 2010; Krebs et al., 2009).

#### Novelty seeking

As shown in Fig. 1a, the present study observed that NS was positively linked to fiber connectivity between the mOFC and IOFC and the striatum. Previous studies have clearly documented the involvement of the OFC and striatum in NS, especially the dopamine-innervated intercommunicated subcortical-to-cortical networks. The current findings further confirmed this in the form of anatomical fiber connectivity within this network.

**Table 2**  
Correlational results for temperaments.

Traits	Fiber-originated regions	Fiber-terminated regions in the striatum	Volume in the striatum (mm <sup>3</sup> )	Tmax	MNI coordinates (mm)
NS	mOFC	Left posterior medial putamen, right caudate	1010	6.66	(−26, −10, 8)
	IOFC	Left posterior ventral putamen	458	4.76	(−31, 3, 4)
	Amygdala	Left putamen	70	4.43	(−24, 8, 2)
RD	PCC	Left putamen, right caudate	669	3.09	(14, 10, 21)
	mOFC	Right caudate	270	4.21	(20, 18, 7)
	Hippocampus	Right caudate	128	3.69	(10, 10, 4)
	Amygdala	Right putamen and caudate	129	3.25	(18, 6, 25)
HA	dlPFC	Bilateral caudate, right putamen	704	5.06	(20, 12, 17)
	PCC	Left caudate	364	4.57	(−12, 9, 6)
P	mOFC	Left putamen	615	3.66	(−28, 12, −5)

Abbreviations: mOFC, the medial orbitofrontal cortex; IOFC, the lateral orbitofrontal cortex; PCC, the posterior cingulate cortex/retrosplenial cortex; dlPFC, the dorsolateral prefrontal cortex; NS, novelty seeking; RD, reward dependence; HA, harm avoidance; P, persistence.



As a key region of the mesolimbic dopamine system, the striatum plays a role in coding and transmitting primary novelty-related dopaminergic signals to the cortical regions. Anatomically, the striatum widely accepts fiber projections from subcortical and cortical regions such as the amygdala, hippocampus and medial frontal cortex, making up an interconnected neural network (Cohen et al., 2009; Lehericy et al., 2004). Functional studies found that these regions' response to novelty was positively correlated with NS (Krebs et al., 2009).

The prefrontal cortical regions such as IOFC and mOFC were suggested to exert top-down modulation during novelty processing (Lovstad et al., 2011). Brain anatomical studies found that NS was correlated with white matter volume in the frontal cortex, and gray matter volume in the frontal cortex and PCC (Gardini et al., 2009; Van Schuerbeek et al., 2011), and cortical thickness of the OFC, superior frontal gyrus and left middle frontal gyrus (Schilling et al., 2012). Functionally, patients with lesions centered in either the OFC or IPFC showed reduction of the frontal P3 response to novel stimuli compared to controls (Lovstad et al., 2011). Responses in the medial prefrontal cortex and pregenual anterior cingulate cortex towards emotional expectancy were positively correlated with NS (Berpohl et al., 2008). NS is closely related to exploratory/excessive and impulsive/risk-taking behaviors towards novelty and cues of potential rewards (Kelley et al., 2004; Roussos et al., 2009). Disruption of the right prefrontal cortex by low-frequency and repetitive transcranial magnetic stimulation produced more risk-taking human behaviors (Knoch et al., 2006). Baseline/tonic cortical activity in the right prefrontal cortex was also reported to be positively correlated with individual risk-taking behaviors (Gianotti et al., 2009).

#### Reward dependence

In the present study, fiber connectivity from the PCC, mOFC, hippocampus and amygdala to the striatum were correlated with RD, as shown in Table 2 and Fig. 1b. These results were consistent with many previous studies on RD-correlated brain regions.

First, white matter microstructure in the uncinate/inferior fronto-occipital fasciculus, which can partially participate in interconnections between the PCC, ventral anterior thalamic nuclei, and orbitofrontal cortex, has been correlated with response of the nucleus accumbens to reward (Camara et al., 2010). Second, brain structural studies found RD to be correlated with the gray matter volume in the left middle frontal gyrus, right inferior frontal gyrus, left posterior cingulate and left thalamus (Van Schuerbeek et al., 2011), as well as the caudate nucleus and rectal frontal gyrus (Gardini et al., 2009). Third, a large number of brain functional studies have found that widely distributed brain regions, including the substantia nigra, ventral tegmental regions, striatum, amygdala, and frontal cortex, played important roles in reward processing. Activations of the substantia nigra/ventral tegmental area elicited by novel cues that predicted reward was positively related to RD (Krebs et al., 2009). Individual differences in reward-related temperaments (reward sensitivity measured by the Behavioral Activation Scale [Carver and White, 1994]) also predicted response variations of the brain reward network (Beaver et al., 2006; Engelmann, 2006). Individual variation in reward sensitivity was also highly correlated with activation elicited by appetizing foods in the fronto-striatal-amygdala-midbrain network (Beaver et al., 2006), with activation of the ventral striatum during the reception of a reward (Simon et al., 2010), and with stronger medial orbitofrontal activity during both the reception and omission of a reward.

The OFC has been found to play an important role in reward processing (Burke et al., 2008; Padoa-Schioppa and Assad, 2006, 2008). It is believed to form relative reward values to guide or top-down regulate human RD-oriented behaviors during reward processing (Rolls, 2000; Wallis, 2007). The medial frontal cortex was proposed to integrate and transmit representations of reward to the mesolimbic and mesocortical dopamine systems, to modulate striatal reward encoding during reappraisal of reward anticipation and to contribute to successful

regulation of reward (Glascher et al., 2009; Xue et al., 2009). Human electrophysiological studies showed a dynamic interaction between the striatum and medial frontal cortex underlying reward-guided learning and decision-making (Cohen, 2007; Cohen et al., 2009). The amygdala was reported to facilitate reward-seeking behaviors by the glutamatergic or dopaminergic neurotransmission in the amygdala-striatum pathway (Lintas et al., 2011; Prevost et al., 2011; Stuber et al., 2011). Bilateral amygdala and nucleus accumbens showed significantly greater response to wins than to losses in both adolescents and adults (Ernst et al., 2005).

#### Harm avoidance

As shown in Fig. 1c, fiber connectivity from the PCC and dlPFC to the striatum was correlated with HA in the present study. The significant role of the striatal-frontal pathway in HA can be easily integrated with previous research. A recent study found that increased HA was associated with decreased fractional anisotropy and increased mean and radial diffusivity in major fiber tracts, such as anterior thalamic radiation, dorsal cingulum bundle, inferior longitudinal fasciculus, superior longitudinal fasciculus, and uncinate fasciculus, which underlie pathways connecting critical hubs in the limbic-cortical and striatal-frontal circuits including the mOFC, dlPFC, PCC, ACC, amygdala, striatum and so on (Westlye et al., 2011). Structural integrity of white matter indexed by fractional anisotropy in a pathway connecting the amygdala, ventral striatum, and frontal cortex was also inversely correlated with anxiety, a trait closely correlated with HA (Kim and Whalen, 2009). In addition, HA was found to be positively correlated with gray matter volume in the left superior frontal gyrus, and negatively correlated with gray matter volume in the left inferior frontal gyrus (Gardini et al., 2009; Van Schuerbeek et al., 2011; Yamasue et al., 2008a), anterior cingulate (Van Schuerbeek et al., 2011), and occipital and parietal structures such as PCC (Gardini et al., 2009). Finally, a previous study reported that HA was positively associated with activation of the dorsal medial PFC and PCC during self-referential processing (Lemogne et al., 2011).

It should be noted that no significant results were observed for the amygdala, ACC, and OFC in relation to HA in the present study, which was inconsistent with previous reports (Iidaka et al., 2006; Pezawas et al., 2005; Pujol et al., 2002). It seemed that even though studies have found the amygdala-ACC-mOFC pathway to play a role in HA (Most et al., 2006; Pezawas et al., 2005), the striatum-amygdala/ACC/mOFC pathways might not contribute to HA as much as originally assumed. For example, Cohen et al., (2009b) found only one significant correlation (i.e., between HA and fiber connectivity between the hippocampus and striatum). Second, females showed higher HA overall than males did and these gender differences were largely explained by gender differences in the right ACC (Pujol et al., 2002). The current study was conducted with males, which might partly account for the lack of findings of the amygdala, ACC and mOFC.

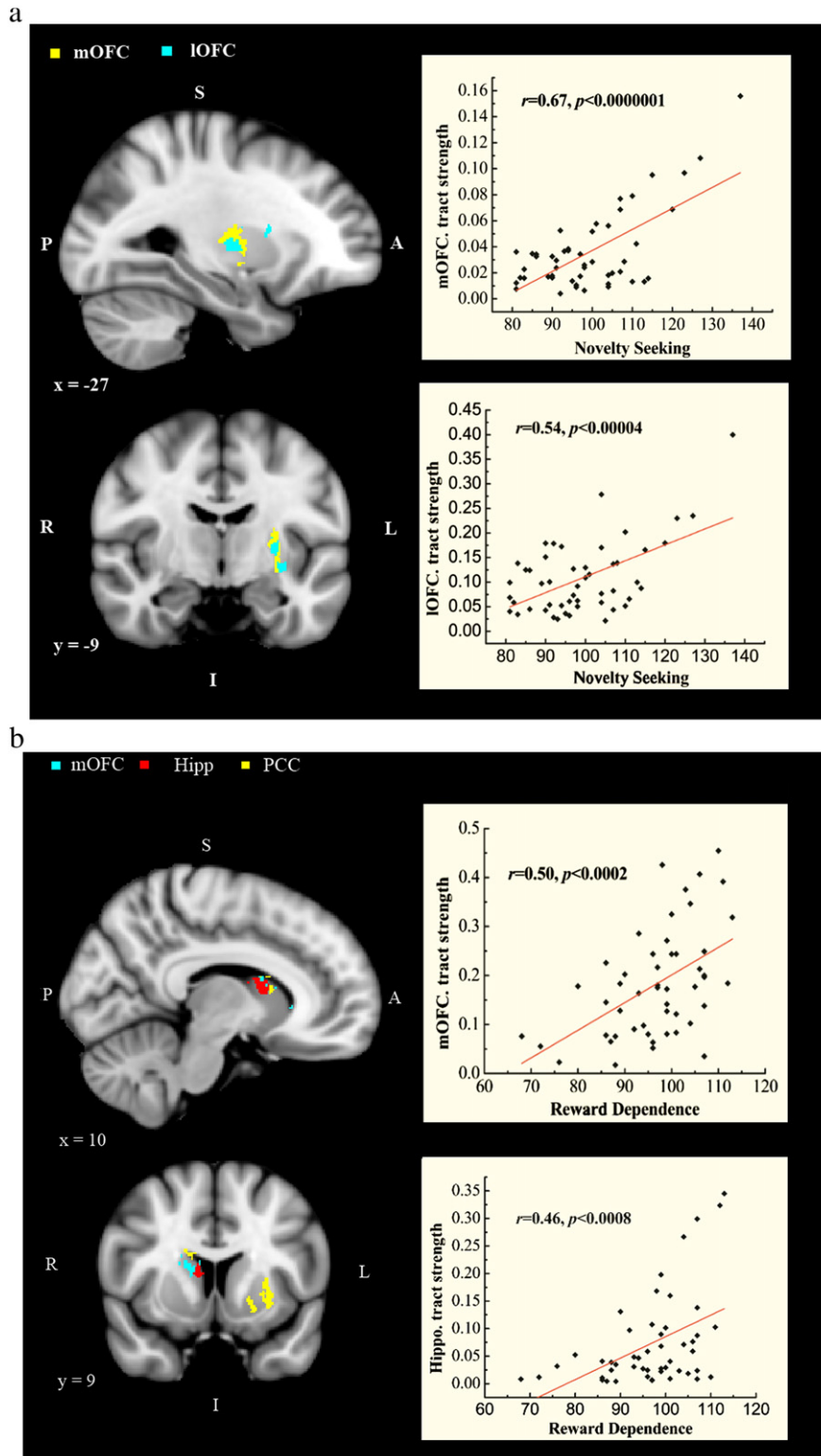
#### Persistence

Consistent with the results of Cohen et al. (2009b) study, P was positively correlated with fiber connectivity from the mOFC to striatum in the present study (Fig. 1d). Two other functional brain studies further confirmed the involvement of the OFC and striatum in P. The first one (Gusnard et al., 2003) found that individual difference in P was correlated with change in activation of the orbital and medial frontal cortex and ventral striatum during a picture-viewing task. Individuals high in P showed increasing activation in the OFC and ventral striatum with increasing percentage of neutral pictures from 10% to 90%, whereas individuals low in P showed decreasing activation of these regions in the same task condition (Gusnard et al., 2003). The second study demonstrated that the mOFC-striatum functional connectivity modulated behavioral persistence during uncertain decision-making (Jung et al., 2010). Strength of functional connectivity was found to be positively correlated with the number of persistent responses made during the task. In addition, patients with

lesion to the ventral medial prefrontal cortex showed a lack of persistence (Barrash et al., 2000). Some structural studies also linked P to gray matter volume in the limbic regions (Gardini et al., 2009; Van Schuerbeek et al., 2011).

Although P as a temperament trait was paid less attention by researchers compared to other three temperaments, similar behavioral

constructs such as “perseveration” (de Ruiter et al., 2009; Serpell et al., 2009) and “habit formation”/goal-directed behaviors (de Wit et al., 2009, 2012) in humans and animals have been extensively discussed in the fields of neuropsychology, neurology, and psychiatry (de Wit and Dickinson, 2009). Results of these studies also showed that the ventromedial prefrontal cortex played an important role in “perseveration”



**Fig. 1.** Fiber connectivity from different brain regions to the striatum were correlated with different temperaments. (a) Fiber connectivity from the mOFC and IOFC to the striatum was correlated with NS. (b) Fiber connectivity from the PCC, mOFC, and hippocampus to the striatum was correlated with RD. (c) Fiber connectivity from the dlPFC and PCC to the striatum was correlated with HA. (d) Fiber connectivity from the mOFC into the striatum was correlated with P.

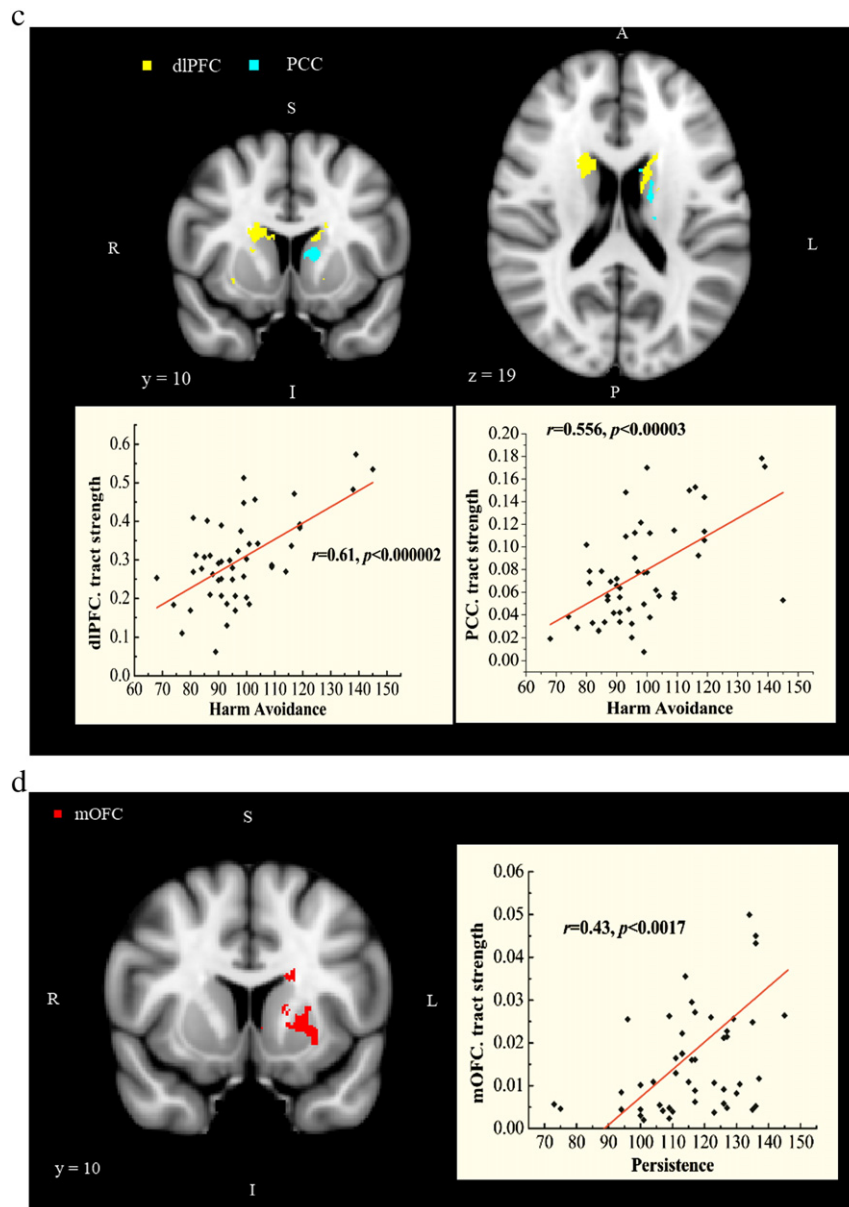


Fig. 1 (continued).

(de Ruiter et al., 2009) and habitual and goal-directed behaviors (de Ruiter et al., 2009).

### Limitations

Three main limitations of the current study should be mentioned. First, this study was conducted in males. One reason for focusing on males was that some temperaments have shown gender differences at both behavioral and neurobiological level (Raine et al., 2011; Yamasue et al., 2008a). Future research needs to replicate and extend our findings to Chinese females. Second, the current study was conducted with young college males with a narrow age range to avoid the confounding effect of age. Because aging of the brain might affect the neurobiological correlates of personality traits (Wright et al., 2007), future studies should include samples of a broader age range. Finally, several studies have found genetic effects, gene  $\times$  brain interactions, and even gender  $\times$  gene  $\times$  brain three-way interactions for RD, NS, and HA (Buckholtz et al., 2008; Marco-Pallares et al., 2010; Pezawas et al., 2005; Williams et al.,

2009). In the future, investigations need to be extended to include genetic factors.

### Conclusions

Using probabilistic tracking of diffusion tensor images, the current study investigated the neurobiological correlates of temperaments in the form of fiber connectivity between the striatum and subcortical and cortical regions in Chinese males. Results showed that different temperaments were associated with different fiber connectivity. Generally consistent with our hypotheses, three temperaments (NS, RD and P, which are closely linked to the mesolimbic-dopamine-centered networks) were correlated with fiber connectivity between the striatum and medial frontal cortex. HA was correlated with fiber connectivity between the striatum and dorsal frontal cortex. These results were not confounded by factors such as depression, anxiety, alcohol dependence, and smoking, nor by the local gray matter structure and the volume of the local brain region.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2013.04.043>.



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## Conflict of interest

The authors declare no conflict of interest.

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