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Subcortical structures and visual divergent thinking: a resting-state functional MRI analysis

Zhenni Gao[1] · Xiaojin Liu[3,4,5] · Delong Zhang[2] · Ming Liu[2] · Ning Hao[1]

Abstract
An increasing number of studies have found that a few, specific subcortical regions are involved in creative visual divergent thinking. In addition, creative thinking is heavily reliant on the fronto-striatal dopaminergic pathways. This study aimed to explore whether spontaneous fluctuations in the subcortex, which contribute to our creative abilities, showed significant differences between individuals with different levels of creativity based on resting-state functional magnetic resonance imaging data. We calculated subcortical regions' seed-wise and dynamic functional connectivity (dFC), and then examined the differences between the high and low visual creativity groups. Furthermore, the topological properties of the subcortical network were measured, and their relationship with creative visual divergent thinking was calculated using brain–behavior correlation analyses. The results showed that functional connectivity (FC) between the putamen, pallidum, and thalamus indicated group differences within the subcortex. Whole-brain FC results showed group differences across subcortical (i.e., the thalamus and pallidum) and cerebral regions (i.e., the insula, middle frontal gyrus, and middle temporal gyrus). In addition, subcortical FC demonstrated a positive correlation with visual divergent thinking scores across the pallidum, putamen, and thalamus. Our findings provide novel insights into the relationship between visual divergent thinking and the activities of the subcortex. It is likely that not only fronto-striatal dopaminergic pathways, but also "motor" pathways, are involved in creative visual divergent thinking processing.

Keywords Visual creativity · Subcortex · Functional connectivity · Resting-state fMRI

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Introduction

Creativity encompasses a series of complex cognitive processes, that induce activity within multiple cortical structures, such as the prefrontal cortex (PFC) (Beaty et al. 2015; Wei et al. 2014), middle frontal gyrus (MFG) (Chávez-Eakle et al. 2007), middle temporal gyrus (MTG) (Kounios et al. 2008), and insula (Gao et al. 2017). It has been hypothesized that dopamine-coupled brain areas contribute to creative thought (Heilman et al. 2003). This idea suggests that many creative traits (such as extraversion and openness) result from the neural activity of dopamine-coupled regions (Schuler et al. 2019). On the other hand, some researchers have suggested that higher dopamine receptor levels cause greater cognitive flexibility, resulting in better creative performance (Ashby et al. 1999; Chermahini and Hommel 2010).

Neuroimaging techniques have been widely used to examine the potential morphological and functional changes within subcortical regions associated with creativity. An

increasing number of studies have explored the important role of dopamine-related subcortical regions in creative thinking processing (Boot et al. 2017; Chen et al. 2019). For example, increased regional gray matter volumes in the caudate nucleus and midbrain are significantly related to divergent thinking performance (Takeuchi et al. 2010). Recent burgeoning research on creative thinking is indicative of a growing conviction that subcortical regions, such as the putamen and nucleus accumbens (NAcc), are involved in the insight process, which is crucial in problem solving (Shen et al. 2018; Tik et al. 2018). A very recent publication by Chen et al. (2019) found similar results, and the results of a resting-state functional magnetic resonance imaging (r-fMRI) study have demonstrated that divergent thinking is associated with neural activity within the subcortical regions, such as the thalamus and putamen. In summary, creativity appears to be correlated with subcortical regions (Chen et al. 2019; Shen et al. 2018). Visual divergent thinking is an important component of creativity (Kowatari et al. 2009). Although the impact of dopamine levels on creative visual divergent thinking has been found not only in behavioral experiments, but also in relevant neuropsychiatric disorders (i.e., Parkinson's disease) (Faust-Socher et al. 2014; Salvi et al. 2015), the neural basis of these subcortical regions in relation to individual creative visual divergent thinking based on spontaneous fluctuations in the human brain is still unclear.

Generally, there are different dopamine loops for information transmission across subcortical regions. One of them is the "nigrostriatal pathway", and it is associated with "motor function" passing largely through the substantia nigra, which receives inputs from the motor cortex and is the primary influence on dopamine levels in the dorsal striatum (i.e., putamen and caudate nucleus) (Alexander et al. 1986, 1990; Boot et al. 2017). Another dopaminergic loop passes through the mesolimbic pathway, which receives input from the ventral tegmental area (VTA) and may influence creativity through motivation and reward prediction, most prominently the NAcc (ventral striatum) (Baliki et al. 2013; Wenzel et al. 2015). In addition, the VTA links separate circuits between the NAcc and ventral pallidum (Alexander et al. 1986; Puglisi-Allegra and Ventura 2012). Along with the mesolimbic pathway, the mesocortical pathway also projects from the VTA, from which important influences ultimately return to portions of the PFC (Alexander et al. 1986). In addition, the VTA projects to the amygdala and hippocampus (Mahler and Berridge 2011; Puglisi-Allegra and Ventura 2012). Based on current available results, however, studies investigating subcortical areas that are involved in creative thinking have mainly focused on one aspect: the "PFC" loop. For example, Boot et al. (2017) demonstrated that creative thinking is strongly based on fronto-striatal dopaminergic pathways, which contributes to flexibility in increasing creativity.

However, the authors do not suggest whether other regions, such as the pallidum and thalamus, are involved in the creativity process. Moreover, researchers have found that intranasal administration of oxytocin boosted divergent thinking, flexibility, and creative insight performance (De Dreu and Kret 2016). This may be caused by decreased cortisol responses and fear signals in the amygdalar-hippocampal circuit. Thus, the increased creative performance may be due to other neurotransmitters. However, it is unclear whether other neurotransmitters such as norepinephrine and oxytocin contribute to creative visual divergent thinking.

Neurons in the brain form complex networks (Cajal 1995), which are thought to underlie the physiological basis of information transfer and mental representation (Strogatz 2001). The human brain needs to expend 20% of the body's energy, and the brain's oxygen consumption is no lower at rest than during task performance (Sokoloff et al. 1953). Before Biswal et al. (1995) published findings on spontaneous fluctuations in the human brain using functional magnetic resonance imaging (fMRI), scientists suggested that those brain fluctuations brain are noise. However, Biswal and colleagues indicated that blood oxygen level-dependent (BOLD) signals show low-frequency fluctuations in the bilateral motor cortex (Biswal et al. 1995). That is, the human brain maintains a specific level of fluctuation in the absence of explicit external or internal stimuli. Many studies have found that spontaneous activity in the human brain can shape most neural activity underlying behavior (Dietrich and Kanso 2010; Wei et al. 2014), indicating that spontaneous fluctuations could provide resources for understanding our behavior. Therefore, the neural basis of behavior can be explored by examining the brain networks underlying spontaneous fluctuations (Zou et al. 2013), which seems to be effective because the neural basis of creativity can be explored using resting-state data. In addition, the development of complex networks has been translated into neuroimaging studies in an effort to enhance our understanding of the brain (Kenett et al. 2020; Rubinov and Sporns 2010). Generally, different brain regions are represented as sets of nodes and internodal functional or structural connectivity is represented as an edge. Previous studies have analyzed the topological properties of brain functional networks using graph theory (Gao et al. 2017; Wang et al. 2011) and inferred the relationship between network organization and different cognitive functions (Bullmore and Sporns 2009). However, it is still unclear whether the topological properties of subcortical networks related to different creativity abilities exhibit significant differences. Compared to functional connectivity (FC), which examines subcortical regions' neural activity, graph theory characterizes and depicts the functional organization of the whole subcortical network, which may reflect this network's information

transfer and local and global efficiency. This may provide novel insights into the neural mechanism of subcortical networks in relation to visual creativity ability. In this study, we applied graph theory to investigate the differences in the subcortical network's functional organization between high and low visual creativity groups. A recent study using resting-state data indicated that creative divergent thinking training gives rise to changes in human brain networks' FC patterns (Fink et al. 2018). This provides further evidence that there is consistency between the resting-state and task-state connectivity patterns related to creative thinking. However, the human brain is a complex system that is never in a static state (Marusak et al. 2017). Previous fMRI studies have revealed variations in static functional connections throughout the entire scan (Allen et al., 2014; Calhoun et al. 2014). Generally, static FC was regularly divided into several continuous sections that are considered as dynamic functional connectivity (dFC). Recent evidence has shown that dFC may reveal a great deal of information regarding the human brain's time-varying neural activity (Calhoun et al. 2014; Rashid et al. 2016). A previous study applied static and dynamic FC to investigate whether divergent thinking training could induce plasticity in the resting-state brain. Sun et al. (2020) found that static FC between the dorsal anterior cingulate cortex and inferior parietal lobule, the dorsal anterior cingulate cortex and precuneus, and the left and right dorsolateral PFC increased significantly after divergent thinking training. In addition, the temporal variability of the MTG and supplementary motor area significantly increased. These results suggest that short-term divergent thinking training induced neural plasticity in the resting-state brain. Therefore, our use of both static and dynamic FC to explore the basis of the creative brain network has provided comprehensive insight. However, it is still unclear whether significant differences in static and dynamic FC have already been observed between the high and low creativity groups.

Although previous studies have investigated the relationship between special dopamine loops and divergent thinking, subcortical-wide regional connectivity, with cortical regions contributing to individual creative visual divergent thinking, has been neglected. Additionally, dopamine loops within subcortical regions are more complex than those between subcortico-cortical regions. Whether the interactions of these subcortical regions are involved in visual creativity should also be examined. In addition, more information could likely be obtained to investigate the interactions between subcortical regions using dFC. The primary purpose of this study was to address each of the following issues: first, to identify the subcortical brain regions that contribute to our creative visual abilities; second, to determine whether highly creative individuals show different FC compared to individuals with low creativity; and third, to determine whether the cortico-subcortical network's efficiency exhibits differences between individuals with high and low levels of visual creativity.

In the present study, we recruited a high visual creativity group (HCG, $n = 22$) and a low visual creativity group (LCG, $n = 22$) based on visual divergent thinking test scores. We calculated FC maps based on r-fMRI data. The topological properties of the whole-brain network, which showed differences between the two groups, were measured using graph-based analyses. We explored the relationship between subcortical regions and creative visual divergent thinking using FC and graph-based analyses. We hypothesized that the dopamine-coupled regions may show group differences and high visual creativity would show increased FC and network efficiency compared to individuals with low visual creativity.

Methods

Participants

One hundred and eighty healthy and right-handed undergraduates (90 males and 90 females, aged 18 to 22 years old) took part in the study. In this study, we used the total scores of Torrance Tests of Creative Thinking-Figural (TTCT-F) test to measure the creative visual thinking ability of all subjects (the sum of originality, flexibility, fluency, and elaboration scores). The Torrance Tests of Creative Thinking test has shown good predictive validity ($r > 0.57$) and high reliability ($r > 0.90$) (Torrance 1990). Based on the TTCT-F scores, we selected 22 subjects from the top 12% of TTCT-F scores (11 males, 18.86 ± 1.08 years old) and 22 subjects from the bottom 12% of TTCT-F scores (11 males, 19.13 ± 0.99 years old) as the high visual creativity group (HCG) and low visual creativity group (LCG), respectively. Next, we collected the r-fMRI data of all 44 subjects in the two groups. During fMRI scanning, we asked participants that they must remain awake and not be asleep. Meanwhile, we also required them to try not to think systematically. The present study was approved by the Institutional Review Board of South China Normal University.

Resting-state fMRI data acquisition

All participants were scanned using a 3 T Siemens Trio Tim MR scanner at the Brain Imaging Center at SCNU, Guangdong, China. The r-fMRI data were collected using a GE-EPI sequence: 32 axial slices, repetition time (TR) = 2 s, echo time (TE) = 30 ms, slice thickness = 3.5 mm, no gap, flip angle (FA) = 90°, matrix = 64 × 64, and field of view (FOV) = 192 mm × 192 mm. The subjects were instructed

to lie down with their eyes closed, and to remain quiet during the scans while thinking of nothing in particular. After scanning, a total of 240 volumes were obtained from each subject.

Resting-state fMRI data preprocessing

The r-fMRI data were preprocessed using DPARSF (Yan and Zang 2010) based on SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8). First, we discarded the first 10 volumes for signal equilibrium. Second, the time delay of the intra-volume in slices, as well as head movements resulting in geometrical displacements, were corrected (none of the subjects were excluded based on the criterion of displacement of > 1 mm or angular rotation of > 1° in any direction). Third, the image data were normalized to the standard Montreal Neurological Institute (MNI) space at 3-mm isotropic resolution with an echo-planar imaging (EPI) template. The data were then band-pass filtered (0.01–0.1 Hz) to decrease the effects of low-frequency drift and high-frequency physiological noise. We also removed the linear trend and spatially smoothed the data with an 8 mm FWHW Gaussian kernel. Nuisance covariates, including head motion via the Friston 24-parameter model (Friston et al. 1996; Yan et al. 2013), white matter (WM), and cerebrospinal fluid (CSF) signals, were removed using regression.

Regions of interest (ROIs)

The regions of interest (ROIs) for subcortical regions were extracted using the Harvard–Oxford subcortical structural probabilistic atlas from Data Processing and Analysis for Brain Imaging (DPABI, http://rfmri.org/dpabi). We extracted all ROIs based on the 25% probability map, including the bilateral amygdala, accumbens, brain-stem, caudate, hippocampus, pallidum, putamen, and thalamus (16 ROIs in total). We then resampled these selected ROIs to a voxel size of 3 mm for further analyses. Figure 1 shows the different anatomical orientations of the subcortical regions in this study.

Functional connectivity maps

We constructed the whole-brain FC map of each subcortical region using a standard seed-voxel approach. In this step, each ROI was considered as a seed region. For each subject, we extracted the averaged time series of all voxels within a given seed region and the time series of each voxel in the whole brain. We then calculated FC (i.e., Pearson's correlation coefficient r) between the time series of selected seed regions and each voxel in the whole brain. Through the above analyses, we obtained a whole-brain FC map of a given subcortical region for each subject. Finally, we
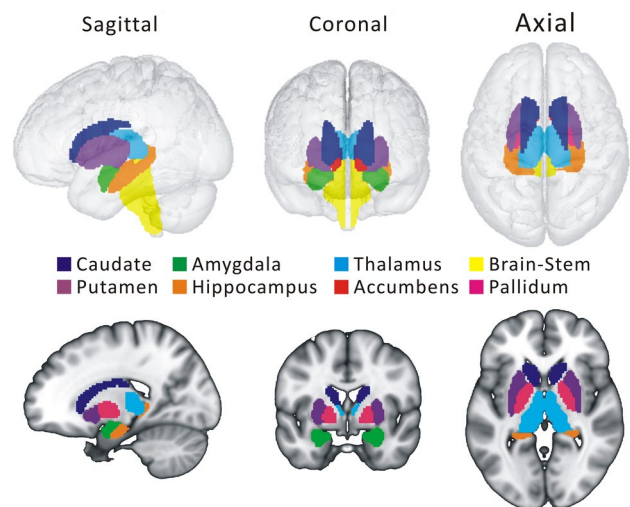

Fig. 1 Locations of the subcortical regions. Each region is labeled with different colors

performed the Fisher's r-to-z transformation to convert these FC maps to z value maps for further statistical analyses.

Constructing subcortical network

We constructed the subcortical network using a standard seed-wise method in this study. For each subject, we extracted averaged time series of all voxels within each seed region and calculated Pearson's correlation coefficient r between any two time series of these seed regions to generate the FC. Based on the above calculations, we generated a 16 × 16 FC matrix for each subject. By taking all seed regions as nodes, and all FC between any two seed regions as edges, we constructed the subcortical network for each subject in the study.

Topological properties of the subcortical network

We estimated the topological properties of the subcortical network using the GRETNA software (Wang et al. 2015) (http://www.nitrc.org/projects/gretna/). Because of the confounding effects of noisy correlations on network analyses, we set a threshold of a significance level for FC to reduce the effects. Specifically, we only kept those FCs whose corresponding p values satisfied a statistical threshold of $p < 0.05$ (family-wise error, FEW correction) compared to all others in a given FC matrix. Because the clustering coefficient (C_p), characteristic path length (L_p), global efficiency (E_{glob}), and local efficiency (E_{loc}) describe the local and global information communication of the networks and provide the altered information transferring within the brain networks, we hence selected these four parameters to examine the topological properties of

the networks in this study. Based on the corrected FC matrix, we finally calculated topological properties of the subcortical network including four global parameters: C_p, L_p, E_{glob} and E_{loc} for each subject. Graph theory have been widely used to measure the topological properties of brain networks (Bullmore and Bassett 2009; Wang et al. 2011), including the creativity-related networks (Gao et al. 2017). In addition, we also estimated the nodal parameters including the nodal strength (S_i^w) and nodal efficiency (E_i^w) of the subcortical network. Detailed definitions and mathematical descriptions of these global parameters are listed in Table S1.

Dynamic measures of the subcortical network

We estimated dFC and dynamic topological properties as dynamic measures of subcortical networks in this study. The sliding-window approach (Allen et al. 2014) was applied to dynamic measures using the DynamicBC toolbox (Liao et al. 2014). Specifically, we first segmented the whole time series of each seed region into several sliding windows. Then, the fixed length of the sliding window was set to 22 TRs (i.e., 44 s) and the subsequent sliding-window began with the step of 1 TR. The entire scanning lasted for about 8 min, including 240 TRs. After removing 10 TR in the preprocessing step, only 230 TRs were conserved for this analysis. We hence obtained 209 sliding windows based on the above calculations for each subject. Next, we extracted the time series (22 TRs, 44 s) of each seed region in each sliding window and calculated the Pearson's correlation coefficient r between any two time series of seed regions to generate the dFC of the subcortical network. We also calculated four global parameters in each sliding window, which were considered as dynamic topological properties of subcortical networks. Finally, we estimated both the mean (i.e., averaged) and the variance of dFC, as well as the variance of dynamic topological properties across all sliding windows for each subject.

Brain–behavior correlation analyses

We used Spearman's correlation analysis to examine correlations between brain measures (i.e., FC and global parameters) and TTCT-F scores. We only considered those FC or global parameters that showed significant between-group differences in the correlation analyses. We also explored a partial correlation (Pearson's correlation) between the subcortical nodal degree and TTCT-F scores. Age and sex

were controlled, and the statistical significance was set to $p < 0.05$ (false discovery rate, FDR correction).

Statistical analyses

We used a two-sample t test to detect between-group differences in whole FC maps of the subcortical region. We determined that the clusters showed statistical differences between HCG and LCG with two criteria: (1) significant threshold $p < 0.05$, with a strict multiple comparison correction strategy, Threshold-Free Cluster Enhancement correction (TFCE-correction); (2) the number of voxels in each cluster should be more than 50 voxels.

In addition, a nonparametric permutation t test was used to determine the between-group differences in each FC within the subcortical network, topological properties of the subcortical network, as well as the mean and variance of dynamic measures. In the calculation, for a given parameter (either FC or global parameter), we randomly paired the parameter values between HCG and LCG to generate two new groups. Subsequently, we calculated the mean value of each new group and estimated their differences. This permutation was repeated 5000 times to obtain the empirical distribution of the difference between new paired groups. We then selected a significance level at $p < 0.05$ to determine significant differences between HCG and LCG at 95% of the empirical distribution in a two-tailed test. Given the small sample size of the participants in our study (22 participants in each group), when significant between-group differences were determined in any parameter, we also calculated the corresponding effect size (Cohen's d) according to Cohen (2013).

Results

FC maps of subcortical regions

Figure 2 and Table S2 show significant differences in the whole-brain FC maps of the subcortical regions between the HCG and LCG. To illustrate our results conveniently, we have used L. to denote the left hemispheric lobules and R. to denote the right hemispheric lobules below. We found significantly ($p < 0.05$, TFCE-correction) higher FC between the left thalamus (L.THA) and left insula (L.INS) in the HCG compared to the LCG. In addition, statistical analyses showed that the right pallidum (R.PAL) was more strongly connected to five regions, including the bilateral parahippocampal gyrus (L/R.PHG), left fusiform gyrus (L.FFG), left middle temporal gyrus (L.MTG), and left middle frontal gyrus (orbital part, ORBmid), in the HCG compared to the LCG.
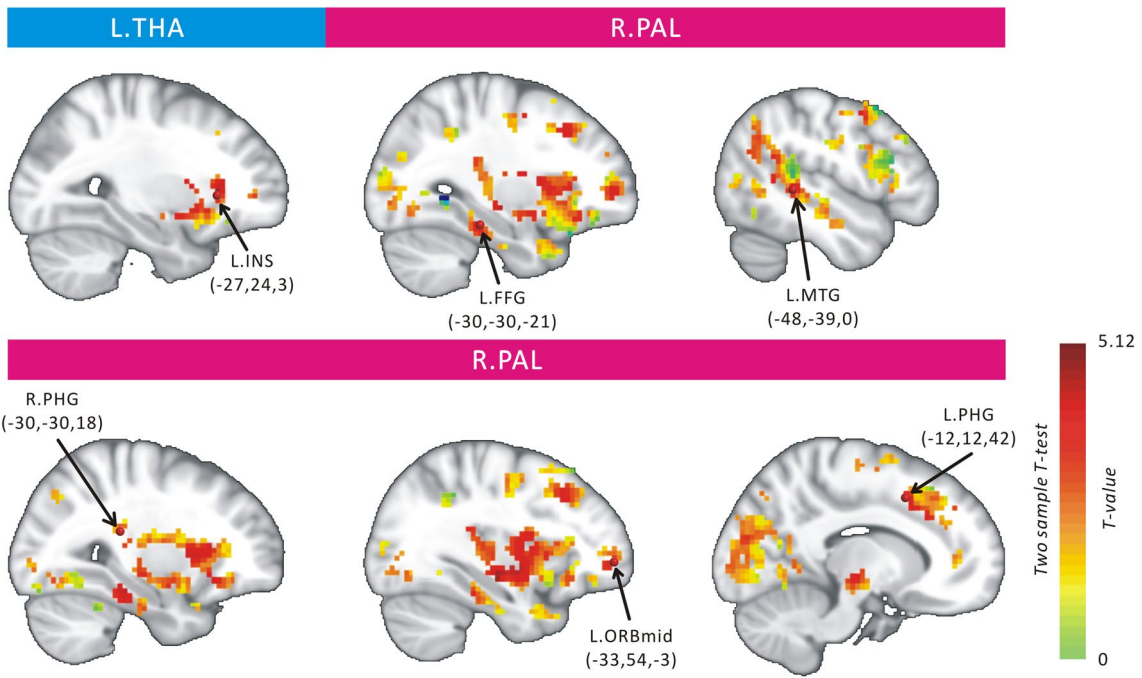
Fig. 2 Cluster corresponding to the significant difference ($p < 0.05$, Threshold-Free Cluster Enhancement correction, TFCE-correction) in the whole-brain map of subcortical region between high visual cre-ative group (HCG) and low visual creative group (LCG). *THA* thala-mus, *PAL* pallidum, *L (R)* left (right) hemisphere
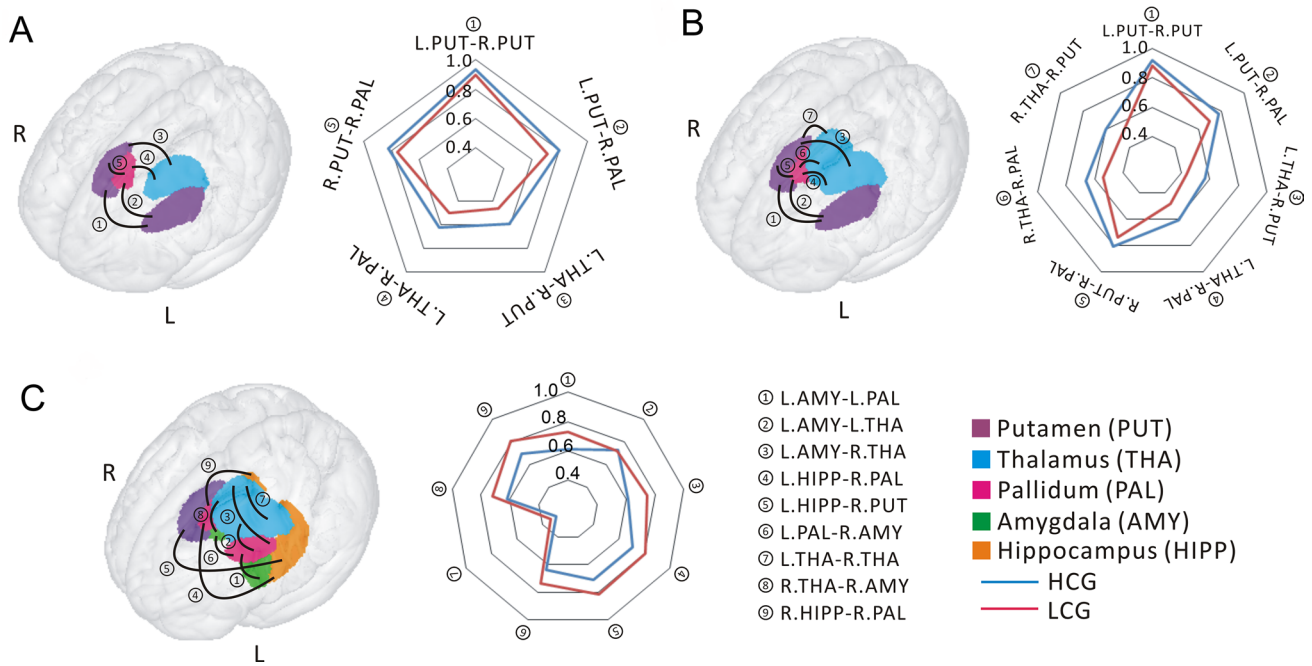

Fig. 3 Significant differences ($p < 0.05$, false discovery rate correction, FDR correction) in **A** function connectivity (FC); **B** averaged dynamic FC (dFC) between high visual creativity group (HCG) and low visual creativity group (LCG); and **C** dFC variance across all sliding windows between the HCG and LCG

FC within the subcortical network

Figure 3A and Table S3 illustrate the significant between-group differences ($p < 0.05$, FDR correction) of FC within the subcortical network. We found significantly higher FC between the putamen (PUT), PAL, and THA in the HCG than in the LCG. In particular, we found significantly higher FC between the bilateral PUT ($p = 0.0012$), the L.PUT and R.PAL ($p = 0.0006$), the L.THA and the R.PUT ($p = 0.0002$) and R.PAL ($p = 0.0010$), as well as the R.PUT and R.PAL ($p = 0.0014$) in the HCG than in the LCG.

Topological properties of the subcortical network

Global parameters of the subcortical network for both the HCG and LCG are shown in Fig. 4A and Table S4. Statistical analysis ($p < 0.05$) revealed a significantly higher clustering coefficient ($p = 0.0330$) and local efficiency ($p = 0.0190$) in the HCG compared to the LCG. Moreover, we found a marginally significant difference in global efficiency ($p = 0.0550$) between HCG and LCG. In addition, we found that the nodal strength was significantly lower ($p = 0.0008$) in the L.PUT for the HCG than in the LCG.

Dynamic measures of the subcortical network

Averaged dFC

Significant ($p < 0.05$, FDR correction) differences in the averaged dFC of the subcortical network between HCG and LCG are shown in Fig. 3B and Table S5. Across all sliding windows, we found significantly higher dFC between the PUT, PAL, and THA in the HCG than in the LCG. These results were consistent with the findings of FC within the subcortical network. We additionally found a significantly

higher dFC between the R.THA and R.PAL ($p = 0.0006$), as well as the R.THA and R.PUT ($p = 0.0010$).

dFC variance

We found significant ($p < 0.05$, FDR correction) between-group differences in the dFC variance across all sliding windows between the HCG and LCG (Fig. 3C; Table S6). We found that HCG showed significantly decreased dFC variance between the left amygdala (L.AMY) and the L.PAL ($p = 0.0002$), L.THA ($p = 0.0012$), and R.THA ($p = 0.0002$) than LCG. Meanwhile, significant between-group differences (HCG < LCG) were found in the dFC variance between the left hippocampus (L.HIPP) and the L.PAL ($p = 0.0020$) and L.PUT ($p = 0.0008$). Moreover, significantly decreased dFC variance between the bilateral THA ($p = 0.0024$), the L.PAL and R.AMY ($p = 0.0024$), the R.HIPP and R.PAL ($p = 0.0008$), and the R.THA and R.AMY ($p = 0.0016$) were found in the HCG compared to the LCG.

Global parameters variance

We found significantly decreased variance of clustering coefficient ($p = 0.0180$), characteristic path length ($p = 0.0196$), and local efficiency ($p = 0.0052$) in the HCG compared to the LCG. Figure 4B and Table S7 show detailed results of variance of global parameters of the subcortical network for both the HCG and LCG.

Brain–behavior correlation analyses

A significant ($p < 0.05$, FDR correction) positive correlation was found between the FC values within the subcortical network and the TTCT-F scores (Figure S1). We found that FC between the bilateral PUT ($r = 0.48$, $p = 0.0010$), the L.PUT
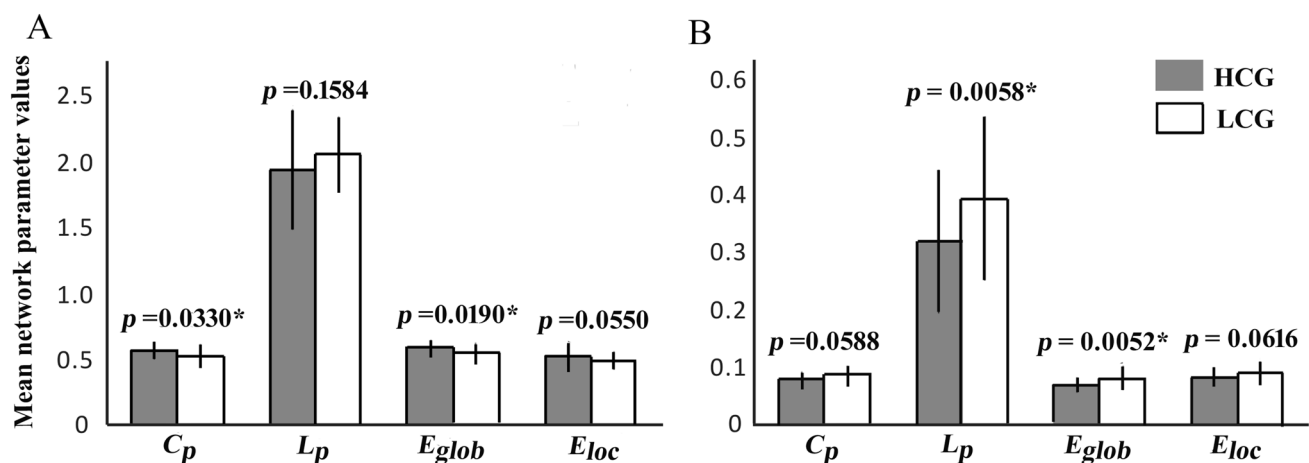

Fig. 4 **A** Global parameters of subcortical network for both high visual creativity group (HCG) and low visual creativity group (LCG); and **B** Global parameters variance of subcortical network for both the HCG and LCG. *$p < 0.05$

and R.PAL ($r = 0.43$, $p = 0.0050$), the L.THA and R.PUT ($r = 0.44$, $p = 0.004$), the L.THA and R.PAL ($r = 0.42$, $p = 0.006$), and between the R.PUT and R.PAL ($r = 0.42$, $p = 0.006$) were all significantly positively correlated with the TTCT-F scores. We found a significant ($p < 0.05$, FDR correction) positive correlation between the nodal strength of the L.PUT and TTCT-F scores.

Discussion

The present study investigated the cortico-subcortical network involved in visual creativity from a novel point of view and examined the functional brain connectivity of the subcortex and cortico-subcortical regions underlying creative visual thinking in terms of brain–behavior correlations and group differences. The main results are summarized as follows. First, static/dynamic FC between the bilateral putamen, between the right pallidum and bilateral putamen, and between the left thalamus and right putamen and right pallidum indicated group differences within the subcortex. Second, information translation efficiency was higher in the HCG than in the LCG, along with network stabilization in the subcortical network. Third, the voxel-wise FC results showed group differences across the subcortical (i.e., the left thalamus and right pallidum) and cerebral regions (i.e., insula, MFG, and MTG). Fourth, dFC variance indicated significant differences between the HCG and LCG across the putamen, thalamus, pallidum, amygdala, and hippocampus. Fifth, the FC between the bilateral putamen, the right pallidum and bilateral putamen, and the left thalamus/right putamen and right pallidum demonstrated a positive correlation with TTCT-F scores. Additionally, the TTCT-F scores and nodal degree of the subcortical regions showed a significantly positive correlation in the left putamen.

The results of the graph-based network analyses showed group differences within subcortical regions. We explored the subcortical topological network organization using two different creativity groups to analyze path length and network efficiency, which potentially underlie group differences. Our results demonstrated that the subcortical networks of participants with higher visual creativity exhibited better network efficiency. This means that information translation efficiency was higher in the HCG than in the LCG. In total, the subcortical network of participants with high visual creativity indicated a better optimized network organization compared with participants with low creativity. Furthermore, the indicator of subcortical network variance was smaller in the HCG, indicating that individuals with high visual creativity exhibited a more stable subcortical network. This finding is consistent with our expectations.

In particular, the FC of three subcortical regions, namely the putamen, pallidum, and thalamus, showed group

differences. Cortical signals are transmitted through the basal ganglia-thalamocortical circuits. The elements of each circuit include the cortex, striatum, pallidum, and thalamus (Alexander et al. 1986). Each circuit receives multiple, partially overlapping cortico-striate inputs, which are progressively integrated during their subsequent passage through the pallidum to the thalamus and from the thalamus back to the cortex (Alexander et al. 1986). Our FC results indicated that participants with higher visual creativity exhibited better FC strength within the information transmission circuit.

We investigated static and dynamic FC within the subcortical regions between the HCG and LCG. The conventional (static) FC assumes that activity in the brain region is a static phenomenon and that the mean BOLD imaging signal over the entire scan period can be calculated to represent brain activity patterns (Navalpotro-Gomez et al. 2020). In fact, recent studies (Hutchison et al. 2013; Calhoun et al. 2014) in both animals and humans have shown that spontaneous oscillations occur in the resting brain, forming a highly dynamic system. The assumption of a static brain seems to be an oversimplification of brain activation patterns, and multiple dFC patterns may be present in the brain network during a r-fMRI scan. Static and dynamic FC have been applied to explore the neural plasticity of the resting-state brain (Sun et al. 2020) and the configuration of the brain functional networks associated with creative cognition (Patil et al. 2021). In our study, a higher dFC in subcortical regions (R.THA-R.PAL, R.THA-R.PUT) was found for the HCG, but this was not found when calculating the static FC. As dynamic analysis involves altered temporal information, results may reflect temporal information and further reveal different neural activity in subcortical subregions related to creativity ability. However, this should be examined in future studies to determine whether such differences in dFC between the R.THA and R.PAL/PUT can be detected during different creativity tasks.

Many previous studies have linked the dopaminergic system to creative performance (De Manzano et al. 2010; Mayseless et al. 2013; Zabelina et al. 2016). Creativity appears to be associated with the neural activity of the striatum, which is involved in dopaminergic modulation (Boot et al. 2017). The release of dopamine in the striatum is thought to be beneficial for cognitive flexibility, as it broadens attentional focus and perspective switching, which are important for creativity (Boot et al. 2017). Furthermore, the putamen, which is a part of the striatum, has a high density of D2 dopaminergic receptors (Willeit et al. 2016). In addition, the putamen contributes to behavioral inhibition (Sweitzer et al. 2018). Peterson et al. (2002) found that behavioral inhibition is a gating process that allows ignoring prior related information; individuals with decreased behavioral inhibition are more likely to develop their creative potential. However, it is worth noting that previous studies have drawn attention

to the fronto-striatal pathways underlying the dopaminergic modulation of creativity (Boot et al. 2017; Schuler et al. 2019), which exist in a "mesocortical" loop passing through the PFC, VTA, and caudate nucleus (another part of the striatum) (Alexander et al. 1986).

Although the putamen, which participates in the nigrostriatal pathway related to the motor loop, has a high density of D2 receptors and is intensively involved in creative performance (Alexander et al. 1986), we also found group differences between the insula (sensorimotor cortex) and thalamus. The results further suggest that modulation of the "motor" pathway (nigrostriatal pathway) may be involved in the creative thinking process. Previous studies (de Manzano and Ullén 2012; Pinho et al. 2015) found that the sensorimotor cortex is related to creative visuospatial activity. The sensorimotor cortex plays an important role in planning, motor execution, and goal-directed behavior during visual divergent thinking. In addition, cognitive embodied theory explains the relationship between the human body and mind, which means that humans' cognitive and mental processes can be embodied in our bodies based on specific activity patterns (Thelen et al. 2001). In other words, cognition and body movements are closely related. We did not find any group differences in FC in the caudate. However, this does not necessarily imply that dopaminergic modulation of the fronto-striatal pathway is not involved in creative thinking. Although there were no differences in the caudate, we found group differences between the pallidum and association areas (FFG and MTG), and the PFC (i.e., ORBmid). Creative processing requires persistence, which involves focused, convergent, systematic thinking and prolonged idea searching (Baas et al. 2013). Effortful, focused creative thinking, has been implicated in the activation of the PFC pathway (Benedek et al. 2014). Further, activation in the PFC enhances creative insightful behavior and increases original idea generation (Mayseless and Shamay-Tsoory 2015). Nonetheless, there may be more complex mechanisms involved in the creative thinking process that need to be further explored.

Our results showed novel group differences between the respective motor-related pathways in the HCG and LCG. The differences between motor-related loop pathways may be a result of other neuromodulators, such as noradrenaline and oxytocin. Although previous studies have focused on dopamine (fronto-striatal pathway) as the key neurotransmitter involved in creative thinking (Boot et al. 2017; Schuler et al. 2019), cognition and behavior are modulated by other neurotransmitters such as noradrenaline (Aston-Jonnes and Cohen 2005; Berridge and Waterhouse 2003), in addition to dopamine. Noradrenaline is thought to modulate the balance between exploitation and exploration by promoting the stabilization of salient information in working memory and attention shifting (Aston-Jonnes

and Cohen 2005; Berridge and Waterhouse 2003) and may enable the persistence of creative thinking. In addition, oxytocin facilitates flexibility and divergent thinking, which are crucial for creative thinking (De Dreu et al. 2014). The differences may also be caused by decreased cortisol responses and fear signals in the amygdalar–hippocampal circuit. Our results showed that dFC variance indicated significant differences between the HCG and LCG across the amygdala and hippocampus. This finding offers the possibility that not only a single neurotransmitter (i.e., dopamine), but also additional neurotransmitters (such as norepinephrine and oxytocin), contribute to creative thinking.

Our findings provide insights into the results and possibilities. First, we used static/dynamic FC and graph theory methods to explore group differences in brain subcortical regions. Apart from the brain regions in the fronto-striatal pathway, we also found that other regions of the "motor" loop exhibited group differences. These results enrich our previous findings. In addition, we found significant differences between the HCG and LCG in the amygdalar–hippocampal circuit. Thus, there may be other neurotransmitters that contribute to creative behavior in addition to dopamine.

Although the present study has some limitations that could be improved, the results have some theoretical and practical implications. This study provides a new perspective on the relationship between subcortical regions and creativity. A limitation is that the analyses were based on resting-state data. We investigated alterations in static and dynamic FC between the high and low creativity groups using r-fMRI data. It is not clear how subcortical regions would perform during creative thinking tasks. The nature of the interaction between the cortex and subcortex during creative thinking is also unclear. As discussed above, dynamic reconfiguration of brain regions or functional networks during creativity tasks between high and low visual creativity groups should be examined in future studies. Another of our study's limitation is that we only measured visual creativity based on TTCT-F scores. The relationship between verbal creativity and brain activity in subcortical regions remains unclear. This will be explored in future research.

Author contributions ZG, XL, DZ, ML, and NH conceived the experiment. ZG, XL, and DZ performed the research. XL, and ZG analyzed the data. ZG, XL, and NH wrote the paper.

Declarations

Conflict of interest The authors have nothing to disclose.

References

Alexander GE, DeLong MR, Strick PL (1986) Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci 9:357–381

Alexander GE, Crutcher MD, DeLong MR (1990) Basal ganglia-thalamocortical circuits: parallel substrates for motor, oculomotor, prefrontal and limbic functions. Prog Brain Res 85:119–146

Allen EA, Damaraju E, Plis SM, Erhardt EB, Eichele T, Calhoun VD (2014) Tracking whole-brain connectivity dynamics in the resting state. Cereb Cortex 24:663–676

Ashby FG, Isen AM, Turken AU (1999) A neuropsychological theory of positive affect and its influence on cognition. Psychol Rev 106:529–550

Aston-Jones G, Cohen JD (2005) An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. Annu Rev Neurosci 28:403–450

Baas M, Roskes M, Sligte D, Nijstad BA, De Dreu CK (2013) Personality and creativity: the dual pathway to creativity model and a research agenda. Soc Pers Psychol Compass 7:732–748

Baliki MN, Mansour A, Baria AT, Huang LJ, Berger SE, Fields HL, Apkarian AV (2013) Parceling human accumbens into putative core and shell dissociates encoding of values for reward and pain. J Neurosci 33:16383–16393

Beaty RE, Benedek M, Kaufman SB, Silvia PJ (2015) Default and executive network coupling supports creative idea production. Sci Rep 5:10964

Benedek M, Beaty R, Jauk E, Koschutnig K, Fink A, Silvia PJ, Dunst B, Neubauer AC (2014) Creating metaphors: the neural basis of figurative language production. Neuroimage 90:99–106

Berridge CW, Waterhouse BD (2003) The locus coeruleus–noradrenergic system: modulation of behavioral state and state-dependent cognitive processes. Brain Res Rev 42:33–84

Biswal B, Yetkin FZ, Haughton VM, Hyde JS (1995) Functional connectivity in the motor cortex of resting human brain using echoplanar MRI. Magn Reson Med 34:537–541

Boot N, Baas M, van Gaal S, Cools R, De Dreu CK (2017) Creative cognition and dopaminergic modulation of fronto-striatal networks: Integrative review and research agenda. Neurosci Biobehav Rev 78:13–23

Bullmore E, Sporns O (2009) Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci 10:186–198

Cajal SR (1995) Histology of the nervous system of man and vertebrates, vol 1. Oxford University Press, Oxford

Calhoun VD, Miller R, Pearlson G, Adalı T (2014) The chronnectome: time-varying connectivity networks as the next frontier in fMRI data discovery. Neuron 84:262–274

Chávez-Eakle RA, Graff-Guerrero A, García-Reyna JC, Vaugier V, Cruz-Fuentes C (2007) Cerebral blood flow associated with creative performance: a comparative study. Neuroimage 38:519–528

Chen Q, Beaty RE, Cui Z, Sun J, He H, Zhuang K, Ren Z, Liu G, Qiu J (2019) Brain hemispheric involvement in visuospatial and verbal divergent thinking. Neuroimage 202:116065

Chermahini SA, Hommel B (2010) The (b)link between creativity and dopamine: spontaneous eye blink rates predict and dissociate divergent and convergent thinking. Cognition 115:458–465

Cohen J (2013) Statistical power analysis for the behavioral sciences. Routledge Academic, London

De Dreu CKW, Baas M, Roskes M, Sligte DJ, Ebstein RP, Chew SH, Tong T, Jiang Y, Mayseless N, Shamay-Tsoory SG (2014) Oxytonergic circuitry sustains and enables creative cognition in humans. Soc Cogn Affect Neurosci 9:1159–1165

De Dreu CKW, Kret ME (2016) Oxytocin conditions intergroup relations through upregulated in-group empathy, cooperation, conformity, and defense. Biol Psychiatry 79:165–173

de Manzano Ö, Ullén F (2012) Goal-independent mechanisms for free response generation: Creative and pseudo-random performance share neural substrates. Neuroimage 59:772–780

De Manzano Ö, Cervenka S, Karabanov A, Farde L, Ullen F (2010) Thinking outside a less intact box: thalamic dopamine D2 receptor densities are negatively related to psychometric creativity in healthy individuals. PLoS ONE 5:e10670

Dietrich A, Kanso R (2010) A review of EEG, ERP, and neuroimaging studies of creativity and insight. Psychol Bull 136:822

Faust-Socher A, Kenett YN, Cohen OS, Hassin-Baer S, Inzelberg R (2014) Enhanced creative thinking under dopaminergic therapy in Parkinson disease. Annals Neurol 75:935–942

Fink A, Benedek M, Koschutnig K, Papousek I, Weiss EM, Bagga D, Schöpf V (2018) Modulation of resting-state network connectivity by verbal divergent thinking training. Brain Cogn 128:1–6

Gao Z, Zhang D, Liang A, Liang B, Wang Z, Cai Y, Li J, Gao M, Jiao B, Huang R, Liu M (2017) Exploring the associations between intrinsic brain connectivity and creative ability using functional connectivity strength and connectome analysis. Brain Connectivity 7:590–601

Heilman KM, Nadeau SE, Beversdorf DO (2003) Creative innovation: possible brain mechanisms. Neurocase 9:369–379

Hutchison RM, Womelsdorf T, Gati JS, Everling SM, Ravi S (2013) Resting-state networks show dynamic functional connectivity in awake humans and anesthetized macaques. Hum Brain Mapp 34:2154–2177

Kenett YN, Betzel RF, Beaty RE (2020) Community structure of the creative brain at rest. Neuroimage 210:116578

Kounios J, Fleck JI, Green DL, Payne L, Stevenson JL, Bowden EM, Jung-Beeman M (2008) The origins of insight in resting-state brain activity. Neuropsychologia 46:281–291

Kowatari Y, Lee SH, Yamamura H, Nagamori Y, Levy P, Yamane S, Yamamoto M (2009) Neural networks involved in artistic creativity. Hum Brain Mapp 30:1678–1690

Liao W, Wu G-R, Xu Q, Ji G-J, Zhang Z, Zang Y-F et al (2014) DynamicBC: a MATLAB toolbox for dynamic brain connectome analysis. Brain Connectivity 4(10):780–790

Mahler SV, Berridge KC (2011) What and when to "want"? Amygdala-based focusing of incentive salience upon sugar and sex. Psychopharmacology 221:407–426

Marusak HA, Calhoun VD, Brown S, Crespo LM, Sala-Hamrick K, Gotlib IH, Thomason ME (2017) Dynamic functional connectivity of neurocognitive networks in children. Hum Brain Mapp 38:97–108

Mayseless N, Shamay-Tsoory SG (2015) Enhancing verbal creativity: modulating creativity by altering the balance between right and left inferior frontal gyrus with tDCS. Neuroscience 291:167–176

Mayseless N, Uzefovsky F, Shalev I, Ebstein RP, Shamay-Tsoory SG (2013) The association between creativity and 7R polymorphism in the dopamine receptor D4 gene (DRD4). Front Hum Neurosci 7:502

Navalpotro-Gomez I, Kim J, Paz-Alonso PM, Delgado-Alvarado M, Quiroga-Varela A, Jimenez-Urbieta H, Carreiras M, Strafella AP, Rodriguez-Oroz MC (2020) Disrupted salience network dynamics in Parkinson's disease patients with impulse control disorders. Parkinsonism Relat Disord 70:74–81

Patil AU, Ghate S, Madathil D, Tzeng OJL, Huang H-W, Huang C-M (2021) Static and dynamic functional connectivity supports the configuration of brain networks associated with creative cognition. Sci Rep 11:1–17

Peterson JB, Smith KW, Carson S (2002) Openness and extraversion are associated with reduced latent inhibition: replication and commentary. Pers Individ Differ 33:1137–1147

Pinho AL, Ullén F, Castelo-Branco M, Fransson P, de Manzano Ö (2015) Addressing a paradox: dual strategies for creative performance in introspective and extrospective networks. Cereb Cortex 26:3052–3063

Puglisi-Allegra S, Ventura R (2012) Prefrontal/accumbal catecholamine system processes high motivational salience. Front Behav Neurosci 6:31

Rashid B, Arbabshirani MR, Damaraju E, Cetin MS, Miller R, Pearlson GD, Calhoun VD (2016) Classification of schizophrenia and bipolar patients using static and dynamic resting-state fMRI brain connectivity. Neuroimage 134:645–657

Rubinov M, Sporns O (2010) Complex network measures of brain connectivity: uses and interpretations. Neuroimage 52:1059–1069

Salvi C, Bricolo E, Franconeri SL, Kounios J, Beeman M (2015) Sudden insight is associated with shutting out visual inputs. Psychon Bull Rev 22:1814–1819

Schuler AL, Tik M, Sladky R, Luft CDB, Hoffmann A, Woletz M, Zioga I, Bhattacharya J, Windischberger C (2019) Modulations in resting state networks of subcortical structures linked to creativity. Neuroimage 195:311–319

Shen W, Tong Y, Li F, Yuan Y, Hommel B, Liu C, Luo J (2018) Tracking the neurodynamics of insight: a meta-analysis of neuroimaging studies. Biol Psychol 138:189–198

Sokoloff L, Wechsler RL, Mangold R, Balls K, Kety SS (1953) Cerebral blood flow and oxygen consumption in hyperthyroidism before and after treatment. J Clin Investig 32:202

Strogatz SH (2001) Exploring complex networks. Nature 410:268–276

Sun J, Zhang Q, Li Y, Meng J, Chen Q, Yang W, Wei D, Qiu J (2020) Plasticity of the resting-state brain: static and dynamic functional connectivity change induced by divergent thinking training. Brain Imaging Behav 14:1498–1506

Sweitzer MM, Kollins SH, Kozink RV, Hallyburton M, English J, Addicott MA, Oliver JA, McClernon FJ (2018) ADHD, smoking withdrawal, and inhibitory control: results of a neuroimaging study with methylphenidate challenge. Neuropsychopharmacology 43:851

Takeuchi H, Taki Y, Sassa Y, Hashizume H, Sekiguchi A, Fukushima A, Kawashima R (2010) Regional gray matter volume of dopaminergic system associate with creativity: evidence from voxel-based morphometry. Neuroimage 51:578–585

Thelen E, Schöner G, Scheier C, Smith LB (2001) The dynamics of embodiment: a field theory of infant perseverative reaching. Behav Brain Sci 24:1–34

Tik M, Sladky R, Luft CDB, Willinger D, Hoffmann A, Banissy MJ, Bhattacharya J, Windischberger C (2018) Ultra-high-field fMRI insights on insight: neural correlates of the Aha!-moment. Hum Brain Mapp 39:3241–3252

Torrance EP (1990) Torrance tests of creative thinking. Figural forms A and B: directions manual. Scholastic testing service

Wang J-H, Zuo X-N, Gohel S, Milham MP, Biswal BB, He Y (2011) Graph theoretical analysis of functional brain networks: test-retest evaluation on short-and long-term resting-state functional MRI data. PLoS ONE 6:e21976

Wang J, Wang X, Xia M, Liao X, Evans A, He Y (2015) GRETNA: a graph theoretical network analysis toolbox for imaging connectomics. Front Hum Neurosci 9:386

Wei D, Yang J, Li W, Wang K, Zhang Q, Qiu J (2014) Increased resting functional connectivity of the medial prefrontal cortex in creativity by means of cognitive stimulation. Cortex 51:92–102

Wenzel JM, Rauscher NA, Cheer JF, Oleson EB (2015) A role for phasic dopamine release within the nucleus accumbens in encoding aversion: a review of the neurochemical literature. ACS Chem Neurosci 6:16–26

Willeit M, Popovic A, Bartova L, Sauerzopf U, Bauer M, Praschak-Rieder N (2016) In vivo imaging of dopamine metabolism and dopamine transporter function in the human brain. Neurotransmitter transporters. Humana Press, New York, pp 203–220

Yan CG, Zang Y-F (2010) DPARSF: a MATLAB toolbox for pipeline data analysis of resting-state fMRI. Front Syst Neurosci 4:1–7

Yan C, Cheung B, Kelly C, Colcombe S, Craddock RC, Di Martino A, Li Q, Zuo X, Castellanos FX, Milham MP (2013) A comprehensive assessment of regional variation in the impact of head micromovements on functional connectomics. Neuroimage 76:183–201

Zabelina DL, Colzato L, Beeman M, Hommel B (2016) Dopamine and the creative mind: Individual differences in creativity are predicted by interactions between dopamine genes DAT and COMT. PLoS ONE 11:e046768

Zou Q, Ross TJ, Gu H, Geng X, Zuo XN, Hong LE, Gao J-H, Stein EA, Zang Y-F, Yang Y (2013) Intrinsic resting-state activity predicts working memory brain activation and behavioral performance. Hum Brain Mapp 34:3204–3215