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# ORIGINAL ARTICLE

# Longitudinal Alterations of Frontoparietal and Frontotemporal Networks Predict Future Creative Cognitive Ability

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# Abstract

Creative cognition is important to academic performance and career success during late adolescence and adulthood. However, there is a lack of longitudinal data on whether brain structural development could predict improvements in creative thinking, and how such changes interact with other cognitive abilities to support creative performance. Here we examined longitudinal alterations of brain structure and their relation to creative cognitive ability in a sample of 159 healthy young adults who were scanned using magnetic resonance imaging 2–3 times over the course of 3 years. The most robust predictor of future creative ability was the right dorsolateral prefrontal cortex (DLPFC), which in conjunction with baseline creative capacity showed a 31% prediction rate. Longitudinal analysis revealed that slower decreases in gray matter density within left frontoparietal and right frontotemporal clusters predicted enhanced creative ability. Moreoever, the relationship between longitudinal alterations within frontal-related clusters and improved creative ability was moderated by the right DLPFC and working memory ability. We conclude that continuous goal-directed planning and accumulated knowledge are implemented in the right DLPFC and temporal areas, respectively, which in turn support longitudinal gains in creative cognitive ability.

Key words: creativity, frontoparietal network, frontotemporal network, gray matter density, longitudinal, working memory

# Introduction

Creative thinking is an important predictor of academic success (Hirsh and Peterson 2008) and social adaption (Baas et al. 2008). Although creativity is a complex and broadly defined construct, it is commonly defined as the ability to produce both novel and useful outcomes (Stein 1953; Sternberg and Lubart 1996; Runco and Jaeger 2012). This cognitive capacity begins to develop in

childhood through adolescence, and further along with adaptive skills for problem solving in late adolescence and later adulthood (Jaquish and Ripple 1980; Cheung et al. 2003; Baas et al. 2008). Studies on the neural underpinnings of creative thinking have by far focused largely on the activation patterns of specific brain regions (Fink et al. 2009; Benedek et al. 2014a) and individual differences in brain structure and functional connectivity (Takeuchi et al. 2010, 2012; Zhu et al. 2013; Beaty et al. 2014; Wei et al. 2014; Jauk et al. 2015). However, there is still a lack of longitudinal data showing whether brain structural variability could predict incremental creative cognitive ability, and how changes in the pattern of structural alteration interacts with other cognitive abilities (e.g., working memory, WM) at baseline to support incremental creative capacity. Given the large improvements in creative ability during collegeaged adults, we sought to examine the relationship between brain structural variability and creative cognitive ability in a large longitudinal sample from late adolescence to early adulthood, and investigate how changes in the structural variant pattern during college support increases or decreases in creative capacity.

Neuroimaging research on creative cognition has implicated 2 broad networks consisting of lateral prefrontal regions and temporo-parietal regions (Dietrich and Kanso 2010; Wu et al. 2015). Using the classic unusual uses task, an functional magnetic resonance imaging (fMRI) study revealed that the generation of original ideas was linked to strong activation within frontal and parietotemporal cortices (Fink et al. 2009), consistent with task-related changes of electroencephalogram alpha activity within these regions (Fink et al. 2009). Activation of several subregions within prefrontal cortex (PFC) have been observed during tasks involving creative idea generation, such as anterior cingulate cortex (ACC) during divergent thinking (Howard-Jones et al. 2005; Kleibeuker et al. 2013), dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC) during novel metaphor comprehension and the generation of creative uses for common objects (Mashal et al. 2007; Abraham et al. 2012b), and frontopolar cortex during creative analogical reasoning (Green et al. 2012). Additionally, temporoparietal regions play a central role in the classic creative thinking task involving semantic-related retrieval and long-term memory (Dietrich 2004; Baas et al. 2008). These regions contain the left inferior parietal lobule (IPL), left supramarginal gyrus (SMG), right angular gyrus (Abraham et al. 2012a; Kleibeuker et al. 2013; Benedek et al. 2014a), and middle temporal gyrus (MTG; Fink et al. 2009).

A growing body of research has focused on the brain structural characterizations or biomarkers of creative cognitive ability from an individual differences perspective (Takeuchi et al. 2010; Zhu et al. 2013; Fink et al. 2014; Chen et al. 2015; Jauk et al. 2015). On the other hand, neurodevelopmental studies of creative cognition are relatively limited. To our knowledge, only 2 studies have examined age differences in functional brain activity and gray matter morphology in relation to creative cognitive ability. Kleibeuker et al. (2013) observed increased recruitment of left lateralized posterior parietal cortex (PPC) and bilateral MTG in both adolescents (15-17 years) and adults (25-30 years) associated with divergent thinking performance, whereas lateral PFC (left inferior frontal gyrus and middle frontal gyrus) was more optimized in adults than in adolescents. A subsequent structural study revealed that the ability to generate original ideas was positively related to cortical thickness of the right MTG in both late adolescence (15-20 years) and early adulthood (20-30 years). Moreoever, moderation analysis showed that cortical thickness of the SMG was negatively related to flexibility in late adolescents only, but not in early adulthood (Cousijn et al. 2014). These crosssectional studies highlight the importance of brain development to creative cognition, especially in terms of the transition from late adolescence to adulthood. Nevertheless, a longitudinal investigation of the same individuals over time has not yet been conducted. A longitudinal approach has the potential to identify

brain predictors of creative cognitive ability and to examine potential neural changes associated with creative variability.

Here we use data from 159 university students to test whether brain structural variations could predict individual creative capacity 3 years later. We focused on potential interactions between prediction-related regions, change-related regions, and future creative capacity in the context of executive functions at baseline because executive processes have been associated with creativity in previous studies (Zabelina and Robinson 2010; Takeuchi et al. 2011; Benedek et al. 2012, 2014b; Silvia et al. 2013) and they are a central factor underlying brain structural change after adolescence (Paus 2005; Bunge and Wright 2007). In light of past work reporting larger gray matter volume (GMV) or gray matter density (GMD) associated with creative performance (Takeuchi et al. 2010; Zhu et al. 2013; Fink et al. 2014; Chen et al. 2015; Jauk et al. 2015), we hypothesized that individual variability in future creative capacity could be predicted by specific regions within lateral PFC and temporoparietal cortex. In light of past research reporting a rapid decline in GMD within dorsal-frontal and parietal association cortices, as well as the interhemispheric cortex during the first half of life (Sowell et al. 2003), we hyptothesized that individuals who show higher creative cognitive ability in the future may also show lower decreases within these clusters. Specifically, we hypothesized that the relation between future creative capacity and change-related regions is moderated by a combination of WM and prediction-related regions at baseline.

#### **Materials and Methods**

#### Participants

The longitudinal sample was drawn from an ongoing project exploring the associations among individual differences in brain structure and function, creativity, and mental health (Zhu et al. 2013; Chen et al. 2014; Li et al. 2014; Wei et al. 2014; Chen et al. 2015). Participants were recruited from Southwest University by means of the campus network, advertisements on bulletin boards and leaflets, or through face-to-face communications on campus. Before enrolling in the study, each participant was screened with a set of exclusion procedures involving self-reported questionnaires as well as structuredand semi-structured interviews. All participants were required to be healthy and right-handed, and none had a history of psychiatric disorder, cognitive disability, substance abuse (including illicit drugs and alcohol), and MRI contraindications. At follow-up, participants were re-contacted by telephone. In addition to the initial screening criteria, an additional set of exclusion criteria was used: Beck Depression Inventory (Beck and Steer 1987) score of  $\leq$ 13 at both time points and a time interval of at least one year between the 2 sessions. The project was approved by the Southwest University Brain Imaging Center Institutional Review Board, and written informed consent was obtained from each subject. Participants received payment depending on time and tasks completed.

At time point 1 (tp1), 558 healthy volunteers completed the assessments. Among these, 443 completed relevant creativity assessments, such as the Torrance Tests of Creative Thinking, the Alternate Uses Task, and the Creative Achievement Questionnaire. For the follow-up study, 273 returned to complete a majority of behavioral assessments at time point 2 (tp2); of these, 45 declined to participate in the MRI scan. Of the 228 participants that completed MRI and neuropsychological testing at both time points, 26 declined to participate in the

creativity assessment due to an inconvenient test date. In addition, 2 subjects had mismatched structural images at both time points and 41 failed to finish the creative assessment at tp1. This resulted in a final follow-up sample of 159 participants (70 male), aged 18–22 (mean =  $19.58 \pm 0.96$ ), at tp1.

#### Assessments of Psychological Variables

At both time points, we measured creative cognitive ability using 2 items from the verbal form of the Torrance Tests of Creative Thinking (TTCT, Torrance 1974): the product improvement task (PIT) and Alternate Uses Task (AUT). The TTCT was revised in Chinese by the Shanghai Normal University in 1988 (Ye et al. 1988), and the scoring guide was slightly adjusted in recent studies because some responses were produced in contemporary times that were non-existent in the original guidelines (Wei et al. 2014; Chen et al. 2015). The PIT is subtest 4 of the TTCT, where participants are required to think of as many ways as possible to change a toy to make it more enjoyable and appealing. The AUT is subtest 5 of the TTCT, where participants need to list as many interesting and unusual uses for a cardboard box. Both tasks were administered using paper-pencil and limited to 10 min. The creative test score (CTS) is the sum of ideational fluency and ideational originality. Ideational fluency is defined as the number of meaningful and relevant responses. Ideational originality is the ability to produce uncommon ideas; the scoring was based on a bank of responses that are derived from a criteria table. 3 raters were asked to assess the answers of all participants based on previous guidance (Chen et al. 2015). Mean inter-rater reliabilities were ICC = 0.97 in the PIT tasks and ICC = 0.98 in the UUT tasks at tp1, and mean inter-rater reliabilities were ICC = 0.98 in the PIT tasks and ICC = 0.99 in the AUT tasks at tp2. Additionally, a parallel creativity test was carried out at tp2. This test includes 3 task types, which were used in previous studies (Fink et al. 2006; Sun et al. 2016): Alternate Uses Task (AUT), Product Improvement Task (PIT), and Utopian Situations Task (UST). For uniformity, we used the data from both AUT and PIT at tp2 for further analysis. The AUT, containing 2 items ("can" and "brick"), required subjects to generate as many novel and unusual uses as possible. The PIT required subjects to think of as many improvements as possible for 2 products ("bicycle" and "umbrella"), making it more interesting, useful, and esthetically appealing. Stimuli were presented using E-prime software (version 1.2, Psychology Tools Inc.) in white font projected onto a black background. Subjects were required to write their thoughts on an answer sheet. Each task involved 2 items and each item was limited to 3 min. In total, the test took 12 min to complete. The manner of scoring was constructed based on the instructions described above, except we used a 5-point Likert scale to assess originality. Finally, 3 raters were asked to assess all participant responses based on previous guidance, and mean inter-rater reliabilities were adequate (ICC = 0.87-0.95).

At tp1, we also assessed executive functions with the Nback, Stroop, and Go/NoGo tasks. Participants completed a three-back WM task in which they were asked to respond as soon as possible by pressing the "F" key when a word was the same as the one that appeared 3 words previously, otherwise pressing the "J" key. Words were presented in white against a black background for 750 ms in a serial fashion with a 2 250-ms ISI. There were 6 blocks of 15 words each: 6 match targets and 9 no-match trials. The score used for the analysis is equal to the sum of correct trials in this task.

The classic Stroop conflict consisted of one of 4 words in Chinese (red, orange, blue, or green) printed in one of 4 colors. The trials were either congruent (e.g., the word "blue" in blue ink) or incongruent (e.g., the word "blue" in green ink). Participants were required to categorize a color (red, orange, blue, or green) in the presence of a word by using the "D/F/J/K" keys, respectively. They were instructed to be accurate with speed. After an exercise, they completed 96 trials divided by 4 blocks. Each trail consisted of a fixation cross (+) for 500 ms followed by a color word for 3000 ms and a blank for 1000-2000 ms. Stroop performance was calculated by subtracting the mean reaction time on congruent trials from the mean reaction time on incongruent trials (MacLeod 1991) after excluding trials with extreme response times (response time out of  $\pm$  3 s.d. ms) in each participant to avoid rapid or slow responses unduly influencing average response time.

In the Go/NoGo task, participants were required to respond with a space key press to every letter except "X" as no-go stimuli, to which they were instructed to withhold their response. Each letter was presented every 500 ms with a 2000 ms fixation as the ISI at the center of the computer screen, and "X" was presented on 30% of the trials. Task performance was calculated in terms of mean reaction time on correct no-go trials.

#### Assessment of General Intelligence

To adjust for the effect of general intelligence on creativity, we assessed intelligence with the Combined Raven's Test (CRT), a widely adopted measure administered to Chinese individuals between the ages of 5 and 75 (Li et al. 1989; Qian et al. 1997; Wang et al. 2007). The CRT is based on the Color Progressive Matrices (Raven 1958) and Raven's Standard Progressive Matrices (Raven 1960). It contains 72 items in 6 segments of the CRT-RC2, corresponding to the CPM groups A, AB, and B, and the SPM groups C, D, and E in the original Raven matrices. The CRT for Adult in China (CRT-AC2) has shown good reliability and validity, and the Chinese norms for CRT-AC2 was established from a sample of 2526 people (17-64) from 20 provinces in China (Qian et al. 1997). The raw score is computed by summing the number of correct responses, and the distribution of participants is calculated with percentiles that vary from 0 to 100 in the different age groups. The percentiles were converted to z-score using a z-table and the standard CRT scores (mean = 100 and SD = 15) were calculated according to the Norm for Chinese Adult by Tianjin Medical University (Qian et al. 1997; Wang et al. 2007).

#### Personality

The 240-item version of the Neuroticism-Extraversion-Openness Personality Inventory-Revised (NEO; Costa and McCrae 1992) was used to assess personality. Participants were required to indicate the extent to which they agree or disagree with each statement on a five-point Likert scale, which produces summary scores across 5 factors of personality: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness.

#### MRI Data Acquisition

Imaging data were collected using an 8-channel head coil on a Siemens 3 T Trio scanner (Siemens Medical Systems, Erlangen, Germany) at the Brain Imaging Center, Southwest University. The same scanner and sequences were used at both time points. High-resolution, three-dimensional T1-weighted structural images were obtained using a Magnetization Prepared Rapid Acquisition Gradient-echo (MPRAGE) sequence (TR/ TE = 1900 ms/2.52 ms, FA = 9°, FOV =  $256 \times 256$  mm<sup>2</sup>; slices = 176; thickness = 1.0 mm; voxel size =  $1 \times 1 \times 1$  mm<sup>3</sup>).

#### Preprocessing of Structural Data

Data preprocessing and analysis were performed with the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm/), which is incorporated in the SPM8 software (http://www.fil.ion.ucl.ac.uk/spm/) running on MATLAB R2010a (Mathworks). We applied the longitudinal preprocessing approach implemented in the VBM8 toolbox. Firstly, the follow-up scans (tp2 scans) were registered to the baseline scans (tp1 scans) and a mean of the realigned images was produced for each subject separately; then, both realigned images were bias corrected based on the mean image. The resulting images were segmented into different tissue classes (gray matter, white matter, and CSF) and registered using linear (i.e., affine) and non-linear registration (i.e., DARTEL template). The segmentation step also incorporates an image intensity nonuniformity correction and produces gray matter density maps by using the default parameters (Ashburner et al. 2000). In order to correct for individual local volume deformations, simultaneously resulting maps were modulated by the Jacobian determinants as derived from the spatial normalization's deformation parameters (Good et al. 2001). Subsequently, all images (GMD and GMV maps) were smoothed by convolving them with an isotropic gaussian kernel of 10 mm full width at half maximum. The main analysis focused on the unmodulated data (GMD) since longitudinal development may yield small changes in total intracranial volume.

For subsequent analysis, we calculated the signal change in regional GMD/GMV between both images at each voxel for each participant using the ImCalc method implemented in SPM8, in which only value of voxels >0.10 in both images were considered in the calculation formula (CTS at tp2 – CTS at tp1) to limit the images to areas in gray matter.

#### **Statistical Analysis**

The statistical analyses of behavioral data were performed using the statistical software package SPSS 20.0 (IBM SPSS Statistics for Windows, Version 20.0, IBM Corp, Armonk, NY, USA). Intraclass correlations (ICC) were used to describe testretest reliability in longitudinal samples and homogeneity of the parallel test. To characterize the relationship between psychological variables for the cross-sectional and longitudinal samples, we computed Pearson's correlation between all measures. In addition, we used hierarchical linear regression models to examine whether the anatomical data at tp1, in conjunction with the creative capacity and other variables at tp1, could explain variance in creative capacity at tp2.

In the prediction analyses, voxel-wise analysis of covariance (ANCOVA) was used to examine the relationship between rGMD at tp1 and creative performance at tp2. The model included one discrete factor (sex) and 5 continuous factors at tp1, including CTS, age, CRT score, openness to experience, and total intracranial volume (TIV), where CTS at tp2 is the variable of interest and the others are regressed out as confounding factors. In these analyses, each covariate (except TIV) was defined as a unique relationship with rGMD for sex to assess the interaction between sex and each covariate. The mask specified voxels that showed rGMD values of > 0.10 in all subjects to limit

the images to areas in gray matter. We employed t-contrasts to examine the main effects of CTS by defining contrasts as  $(1 \ 1)$  or  $(-1 \ -1)$ . In addition, we employed the same model to test a relationship between CTS at tp2 and rGMV at tp1, as well as CTS change and rGMD at tp1.

In the longitudinal analyses, the same model was used to examine the relationship between rGMD change and creative performance at tp2. The model included one discrete factor (sex) and 5 continuous factors including CTS at tp2, age at tp1, CRT score at tp1, openness to experience at tp1, and TIV change, where CTS at tp2 is the variable of interest and the others are regressed out as confounding factors. In these analyses, each covariate (except TIV change) was defined as a unique relationship with rGMD for sex to assess the interaction between sex and each covariate. We employed t-contrasts to examine the main effects of CTS by defining contrasts as (1 1) or (-1 - 1). In addition, we employed the same model to test the relationship between rGMV change and CTS at tp2, as well as CTS change. For all analyses, the resulting maps were also corrected at a voxel level of P < 0.05, corrected for multiple comparisons across the whole brain using the family-wise error (FWE) rate. In addition, we performed a small volume correction for multiple comparisons at P < 0.05 (voxel-level) within a serial of regions of interest (ROIs), which comprised 10 spheres, each with a 12 mm radius centered around centered coordinates in each hemisphere within MNI space (Table S1). All these ROIs are chosen from the relevant VBM and task-fMRI studies (Takeuchi et al. 2010; Zhu et al. 2013; Kleibeuker et al. 2013), as well as 2 recent meta-analyses of functional imaging studies on creative thinking (Gonen-Yaacovi et al. 2013; Wu et al. 2015).

We extracted the mean signal from regions of interest (ROIs, see Table 2) within the gray matter yielded by the longitudinal analysis and performed hierarchical cluster analysis using Euclidean distances in SPSS. In addition, correlation analysis was used to explore whether the relationship between these ROIs and CTS at tp2, and ROIs with similar correlational patterns, were spatially proximal in the matrix by reorganizing the data. We also used a dendrogram to describe the level of similarity between the ROIs. To test our moderation hypotheses, we employed Hayes Process Model 3 via IBM SPSS (Hayes 2013) to determine whether individual WM capacity and predictionrelated regions moderated the effects of creative cognitive ability on the change-related networks. This approach enabled us to examine the 3-way interaction between change-related networks, WM at tp1, and prediction-related regions, controlling for sex, age at tp1, CTS at tp1, CRT score at tp1, openness to experience at tp1, and TIV change. Model 3 enabled the specification of the three-way interaction change between change-related networks (X), WM (M), and prediction-related regions (W).

# Results

#### Longitudinal Behavioral Analysis

Table 1 shows summary statistics regarding cross-sectional and longitudinal covariates of interest for the subsequent analyses. We used paired t-tests to assess the effects of these psychological variables measured at both time points. As expected, CTS (t = 2.38, P < 0.05) and originality (t = 3.85, P < 0.001) at tp2 was significantly higher than at tp1, indicating that individual creative cognitive ability increased during college. We also found that TIV significantly decreased from tp1 to tp2 (t = 9.71, P < 0.001).

	Tab	le	1 Psyc	hol	ogical	charact	eristics	of	longitudinal	study subjects
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	Time 1: Mean $\pm$ SD (range)	Time2: Mean $\pm$ SD (range)	Statistical value (P value)
Age	19.58 ± 0.96 (17–22)	22.01 ± 0.92 (19–25)	_
Interval days	_	888.94 ± 88.08 (772-1211)	_
CRT score	100.58 ± 15.17 (63–156)	_	_
Openness	158.39 ± 13.72 (129–191)	_	_
WM	0.55 ± 0.24 (-0.53-1)	_	_
Stroop	$0.13 \pm 0.06$ (-0.02-0.30)	_	_
Go/NoGo	0.79 ± 0.12 (0.38–1)	_	_
Originality	19.86 ± 8.34 (5.33–46.50)	22.95 ± 9.48 (4.33-54.00)	t(158) = 3.85; P < 0.001
Fluency	22.46 ± 8.68 (6.67-50.75)	22.96 ± 9.65 (5.00-62.33)	t(158) = 0.68; P = 0.50
CTS	42.32 ± 16.66 (12.00-97.25)	45.92 ± 18.93 (12.00–116.33)	t(158) = 2.38; P < 0.05
pCTS	_	69.47 ± 25.54 (14.33-151.67)	_
TIV(cm <sup>3</sup> )	1415.05 ± 126.38 (1143.64–1735.67)	1403.13 ± 126.37 (1143.90–1725.18)	t(158)=9.71; P < 0.001

CRT score, general intelligence measured by the combined Raven's test; WM, working memory; CTS, creative test score; pCTS, parallel creative test score; TIV, total intracranial volume.

#### **Correlations Within and Between Measures**

To test whether the CTS showed good test–retest reliability in longitudinal samples and parallel test forms, interclass correlation (ICC) values were calculated using IBM SPSS Statistics for Windows, v20. We found evidence for good reliability, including retest reliability of CTS between tp1 and tp2 (ICC = 0.60, P < 0.001), test–retest reliability between CTS at tp1 and parallel creative test score (pCTS) at tp2 (ICC = 0.52, P < 0.001), as well as parallel-forms reliability between CTS and pCTS at tp2 (ICC = 0.64, P < 0.001). All values indicated sufficient homogeneity of observations within individuals at different time points.

To assess correlations between cross-sectional (between tp1) and longitudinal CTS and other measures (tp1 and tp2), Pearson's correlations were calculated (Table S2). The cross-sectional correlation was significant between openness to experience and originality (r = 0.19, P < 0.05), fluency (r = 0.18, P < 0.05), CTS (r = 0.19, P < 0.05) at tp1, as well as between openness to experience at tp1 and pCTS (r = 0.16, P < 0.05) at tp2. The correlation between inhibitory ability and cognitive contral ability at tp1 was also significant (r = 0.21, P < 0.01). Correlations were not significant between CRT score, executive functions, and CTS at both time points.

#### Predictors of Future Creative Cognitive Ability

After correcting for sex, age at tp1, CRT score at tp1, openness to experience at tp1, TIV at tp1, and CTS at tp1, we found that CTS at tp2 was negatively associated with the right DLPFC at tp1 (x, y, z = 42,11, 41, BA9, t-value of the peak = 4.85, corrected for FWE, P < 0.05 Fig. 1a). We also considered CTS change as independent variables and found similar tendencies for an association between CTS at tp2 and rGMD at tp1 (Fig.S1a). Similar tendencies were observed when using the GMV data at tp1 as a dependent variable in the same approach (Fig. S1b).

To examine the generalizability of the right DLPFC at tp1 in predicting future creative capacity, a composite index for creative capacity was calculated using the total score (tCTS) from CTS and pCTS at tp2. A multiple regression analysis performed using the GMD of the right DLPFC at tp1 as dependent variable after correcting for the effects of sex, age at tp1, CRT score at tp1, openness to experience at tp1, and TIV at tp1 revealed that the right DLPFC was significantly and negatively correlated with tCTS at tp2 (b = -0.29, t = -3.80, P < 0.001), CTS (b = -0.33, t = -4.38, P < 0.001; Fig. 1c) and pCTS (b = -0.19, t = -2.47,

P = 0.02; Fig. 1d) at tp2, but not with CTS (b = -0.03, t = -0.33, P = 0.75; Fig. 1b) at tp1.

Next, we examined whether the anatomical data, in conjunction with the cognitive ability variables at tp1, could explain variance in future creative capacity (i.e., tp2 CTS). In a hierarchical linear regression model, CTS at tp2 was modeled as the dependent variable; sex, age at tp1, CRT score at tp1, openness to experience at tp1, and TIV at tp1 were entered as control variables in the first step (Model 1); CTS at tp1 was entered in Model 2; and the mean rGMD of right DLPFC at tp1 was entered in Model 3.

The full model, including all independent variables, showed a significant prediction effect of future creative ability ( $R^2 = 0.31$ , P < 0.001; Fig. 2a). Notably, the mean rGMD of right DLPFC at tp1 could alone could account for a significant proportion of the variance in tp2 CTS ( $R^2$  Change = 0.10, P < 0.001). Controlling for variables in the first step revealed a further effect of CTS at both time points ( $R^2$  Change = 0.17, P < 0.001), indicating that the combined index had a better prediction for future creative capacity. When the pCTS at tp2 was used as the dependent variable, a significant but relatively weak contribution of the same predictors persisted, and the optimal model showed a significant effect ( $R^2 = 0.23$ , P < 0.001; Fig. 2b).

#### Longitudinal VBM Analysis

In order to examine the association between rGMD change and CTS at tp2, we performed voxel-wise analysis of covariance (ANCOVA). In this analysis, CTS at tp2, age at tp1, CRT score at tp1, openness to experience at tp1, and TIV at tp1 were modeled as covariates to assess their unique relations with rGMD change with sex using the interactions option. T-contrasts were then conducted to identify the main effect on CTS at tp2 and other covariates as confounding factors.

Results revealed an overall positive main effect of CTS at tp2 on rGMD change in an anatomical cluster in the right MTG (x, y, z = 62, -48, -8, BA21, t-value of the peak = 4.58) and in several anatomical clusters within the PFC, including the right middle frontal gyrus (x, y, z = 48, 33, 21, BA46/10, t-value of the peak = 3.99), right inferior frontal gyrus (x, y, z = 54, 32, 4, BA45, t-value of the peak = 3.62), left inferior frontal gyrus (x, y, z = -51, 30, 16, BA44/45, t-value of the peak = 3.21), and left medial superior frontal gyrus (x, y, z = -21, 57, 16, BA10, t-value of the peak = 3.51), right DLPFC (x, y, z = 42, 12, 40, BA9, t-value of the peak = 3.54), and several additional clusters, including



Figure 1. Regional gray matter density (rGMD) within right DLPFC at tp1(MNI coordinates: x = 42, y = 11, z = 41) predicts individual creative cognitive ability at tp2 (*a*). Scatterplots with trend lines depicting correlations between residuals in multiple regression analyses with mean GMD of right DLPFC at tp1 and individual creative cognitive ability at tp2 (*c*), as well as parallel creative cognitive ability at tp2 (*d*) controlling for sex, age at tp1, CRT score at tp1, openness to experience at tp1 and TIV at tp1.



Figure 2. Associations between predicted value and individual creative cognitive ability at tp2 as well as parallel test at tp2. (a) Scatterplots with trend lines depicting correlations between CTS at tp2 and standardized predicted value in multiple regression analyses with CTS at tp2 as a dependent variable and mean GMD of right DLPFC and CRT score at tp1, openness to experience at tp1, TIV at tp1 as dependent variables. (b) Scatterplots with trend lines depicting correlations between pCTS at tp2 and standardized predicted value in multiple regression analyses with CTS at tp2 as a dependent variable and mean GMD of right DLPFC and CRT score at tp1, openness to experience at tp1, TIV at tp1 as dependent variables at tp2 as a dependent variable and mean GMD of right DLPFC and CRT score at tp1, openness to experience at tp1, TIV at tp1 as dependent variables.

left angular gyrus (x, y, z = -50, -73, 36, BA39, t-value of the peak = 3.28), right superior temporal gyrus (x, y, z = 54, -34, -3, BA22 t-value of the peak = 3.16), left inferior partial lobe (x, y, z = -54, -55, 42, BA40, t-value of the peak = 3.01). There were no significantly negative findings in the whole-brain analyses of rGMD change (Fig. 3; Table 2). All these regions were relatively stable when including CTS change as an independent variable, and when using the same approach in the whole-brain analyses of rGMV change (Fig. S2).

Among the significant clusters identified in the longitudinal analysis, the right DLPFC (x, y, z = 42, 12, 40, BA9) partially overlapped with the same region found in the prediction analysis (cluster size = 15 voxels, P < 0.001). This indicated that the right DLPFC could predict individual future creativity, and simultaneously, that its change could predict the growth rate of creative cognitive ability over time.

A correlation matrix of these regions identified in the longitudinal analysis accompanies the dendrogram by hierarchical cluster analyses, which displays 2 major blocks: a frontoparietal cluster and a frontotemporal cluster (Fig. 4a). Additional hierarchical cluster analysis was performed on these ROIs by extracting the neuroanatomic value at both time points and identifying the same clusters (Fig. S3). The last column of the correlation matrix reveals that all rGMD changes within these regions were correlated to creative cognitive ability at tp2. To further illustrate the relation between rGMD change within the cluster and CTS change, correlation analysis revealed that the growth of creative cognitive ability was significantly and strongly related to both the frontoparietal network (r = 0.31, P < 0.001; Fig. 4b) and the frontotemporal network (r = 0.28, P < 0.001; Fig. 4c).

#### **Moderator Analysis**

As expected, results from the Process Model 3 moderation analysis revealed a significant 3-way interaction (Fig. S4a) between frontoparietal clusters, WM at tp1, and the right DLPFC at tp1



**Figure 3.** Lower decreases of rGMD were associated with increases creative cognitive ability during 3 years in college. Significant correlations were observed in the right MTG, right STG, right MFG, right IFG, right DLPFC, left SFG, left ANG, left IFG, and left IPL. Results are shown with P < 0.001, uncorrected for visualization purposes. Color bar shows t-value.

for future creative capacity (b = -0.13, s.e.: 0.05, 95% confidence interval [CI]: -0.22 to -0.03, model R<sup>2</sup> = 0.42). A similar Process Model 3 analysis revealed a significant 3-way interaction (Fig. S4b) between the frontotemporal network, WM ability, and the right DLPFC at tp1 for future creative capacity (b = -0.16, s.e.: 0.06, 95% CI:-0.28, -0.03, model R<sup>2</sup> = 0.40). Finally, we added Stroop performance, response inhibition ability, and left DLPFC GMD at tp1 into the model as moderators, and found that both the main effect and 3-way interaction were not significant (Table S3–S5).

### Discussion

In the present study, we examined whether longitudinal changes in gray matter structure could predict future creative cognitive ability. We also explored potential interactions of gray matter structure and executive function on future creativity. As predicted, we found that rGMD/rGMV in lateral PFC showed a significant and negative prediction effect for creative capacity after 3 years. Longitudinal alterations of gray matter properties in prefrontal-related clusters, such as the frontotemporal network (FTN) and frontoparietal network (FPN), were positively related to future creative cognitive ability. Moderation analysis revealed that right DLPFC and WM ability at tp1 jointly moderated the relation between changes of frontorelated networks and future creative cognitive ability. The present research thus provides the first longitudinal evidence for a role of structural brain network development in predicting future creative cognitive ability.

#### The Role of Lateral PFC for Creativity

The correlation between rGMD in the right DLPFC and creative performance is consistent with several previous MRI studies that highlighted the importance of lateral PFC in creative problem solving. For example, Goel and Vartanian (2005) found increased activation in bilateral DLPFC during performance on a visual divergent thinking task in healthy adults (i.e., matchstick problems), especially within right DLPFC. Employing a visual-spatial creative task, another study reported activation of the left DFLPC, which was hypothesized to support creative processing by means of goal-directed planning (Aziz-Zadeh et al. 2013).

Moreover, a study of developmental differences in creative problem solving also reported that activation in left DLPFC is

Table 2 Correlation of regional gray matter density change with future creative cognitive ability collected 3 years later

Brain regions	R/L	ВА	Peak coordination(MNI)			voxels	T-score	P values (SVC)
			Х	Y	Z			
MTG	R	21	62	-48	-8	266	4.58*	<0.001
MFG	R	46/10	48	33	21	622	3.99	0.003
IFG	R	45	54	32	4	665	3.62	0.011
SFG	L	10	-21	57	16	717	3.51	0.015
DLPFC	R	9	42	12	40	44	3.54	0.026
ANG	L	39	-50	-73	36	73	3.28	0.028
STG	R	22	54	-34	-3	126	3.16	0.038
IFG	L	44/45	-51	30	16	116	3.21	0.044
IPL	L	40	-54	-55	42	195	3.01	0.042
SMG	L	2	-66	-27	30	29	2.82	0.084

R, right; L, left; MNI, Montreal Neurological Institute; MTG, middle temporal gyrus; MFG, middle frontal gyrus; IFG, inferior frontal gyrus; SFG, superior frontal gyrus; DLPFC, dorsolateral prefrontal cortex; ANG, angular; STG, superior temporal gyrus; IPL, inferior partial gyrus; SMG, supramarginal gyrus. \* means a significance level of *P* < 0.05 (FWE for multiple comparisons) and SVC means small volume correction for multiple comparisons at *P* < 0.05 (voxel-level) within regions of interest (ROIs).



Figure 4. Heatmap of the correlation matrix between significant ROIs for predicting creative cognitive ability at tp2, with results from a hierarchal cluster analysis displayed on the left margins (a). 2 major clusters of structures were identified: a frontoparietal network (FPN) including left SFG, right MFG, right IFG, left IFG, left ANG, left IPL and a fronto-tempor network (FTN) including right MTG, right STG, right DLPFC. Relationships between creative cognitive ability changes and FPN (b), FTN (c) changes during 3 years are shown.

generally related to successful creative problem solving. In this study, adolescents showed greater activation in right DLPFC during successful creative problem solving compared to adults, and activation of this region significantly predicted performance on creativity tasks outside the scanner (Kleibeuker et al. 2013). This suggests that a flexible mode of processing, characteristic of the PFC, is adaptive for creative problem solving at different stages of development (Son and Sethi 2009). Notably, the DLPFC is consistently involved in a range of cognitive processes associated with WM (Curtis and D'Esposito 2003; Crone et al. 2006; Jolles et al. 2011). Thus, the DLPFC may support creative problem solving by providing top-down control, focused and flexible attention, and WM capacity (de Manzano and Ullén 2012; Prakash and Du 2013).

Regarding hemispheric specialization, we found that the right DLPFC was more predictive of future creative ability than the left DLPFC, although this relationship was relatively weak. Seminal theories (Bogen and Bogen 1969) postulated that the inhibiting action of the left hemisphere, in favor of right hemispheric functions, could be detrimental to creative thought. It is now generally accepted that the coordination of the 2 hemispheres plays a key role in higher cognitive functions such as creativity (Carlsson et al. 2000; de Souza et al. 2010; Benedek et al. 2011; Sawyer 2011; Runco 2014). However, recent research indicates that hemispheric specialization depends on different domains of creative behavior. For example, the left DLPFC is thought to be responsible for semantic memory retrieval during verbal creativity tasks, while the right DLPFC is mainly associated with sustained attention and generating associations during non-verbal or visuospatial creativity tasks (Gonen-Yaacovi et al. 2013).

According to the coarse semantic coding hypothesis, the right hemisphere is relatively more prone to engage in coarser semantic coding than the left hemisphere, consistent with its involvement during the solution of creative insight problems (Beeman and Bowden 2000; de Manzano and Ullén 2012; Kounios and Beeman 2014). Lateralized cytoarchitectonic differences in language processing regions, such as Broca's area (VLPFC) and adjacent DLPFC, could synthesize highly dissimilar inputs in the right hemisphere, resulting in coarser semantic coding (Hutsler and Galuske 2003; Prakash and Du 2013). Taken together with the theory of neuronal pruning—lower cortical density or thickness via synaptic pruning processes, often associated with enhanced task performance (Kanai and Rees 2011)—we suggest that lower density in the right DLPFC at baseline reflects the optimal point of the inverted U developmental course with gray matter (Gogtay et al. 2004), which in turn predicts higher creative capacity in the future.

Notably, creative thinking does not appear to rely on a single cognitive process, brain region, or large-scale network (Dietrich 2004). Instead, it appears to arise from the dynamic interplay or coordination of several brain regions, networks, and systems (Jung et al. 2013; Beaty 2015; Beaty et al. 2016). Pinho et al. (2015) suggested that 2 different strategies during creative problem solving strongly depends on effective functional connectivity between the right DLPFC and 2 networks corresponding to extrospective and introspective neural circuits. Thus, our findings do not support an exclusive role for DLPFC in predicting creative ability, but rather provides a starting point for developing an increasingly precise predictive model of creativity. Future studies exploring static and dynamic functional brain network connectivity may be able to more precisely predict future creative ability.

#### Longitudinal Change of Fronto-related Clusters and Creativity

As expected, lower decreased GMD within 3 broad regions including frontal (PFC), temporal (STG and MTG), and PPC—significantly predicted future creative capacity 3 years later. Cluster analysis revealed that these broad regions were categorized as 2 networks (i.e., FTN and FPN), which have often been implicated in many studies or reviews on creativity. This finding is partly consistent with prior studies that reported larger volume or density in regions corresponding to the temporal, occipital, and parietal (TOP; Dietrich 2004; Cousijn et al. 2014; Fink et al. 2014; Chen et al. 2015; Jauk et al. 2015), as well as studies reporting a positive association between lateral and medial PFC density with creative capacity measured via divergent thinking tasks outside of the scanner. At first glance, these prior studies have shown seemingly paradoxical results compared to the present findings regarding brain structure (gray matter volume, density, and thickness). In this study, brain structure was positively or negatively correlated with concurrent creative performance, and the longitudinal alterations of brain structure (such as decreased GMD) was positively correlated with individual creative performance in the future.

We believe our results may help to reconcile past work and clarify the neural underpinnings of creative thought. According to maturational theories, gray matter characteristics follow a regionally specific inverted U-shape development throughout childhood and late adolescence (Raz et al. 2004; Lenroot and Giedd 2006). Previous studies on individual differences in creative thinking mainly recruited adolescents (Cousijn et al. 2014; Fink et al. 2014; Chen et al. 2015) and found a positive correlation between brain structure and creative ability. Thus, optimal morphology may be generally adaptive for creativity in adolescence. But for highly creative adolescents, a lower decreased (or maintained gray matter) level may actually support higher creative ability in the future. In addition to the maturational interpretation, a large number of longitudinal studies found that a wide range of brain areas predicted task performance in the present compared to the future (Ullman et al. 2014; Darki and Klingberg 2015). A previous review indicated that structural variants, mostly in the TOP, are associated with creative capacity (Dietrich 2004), whereas in this study, we found that 2 networks consisting of prefrontal-related clusters were associated with creative cognitive ability 3 years later. These results suggest that a dynamic of the neural systems linked to PFC support developmental changes in creative cognitive ability.

The generation of novel and useful ideas is broadly considered to result from a set spontaneous and controlled cognitive processes that arise from the default mode network (DMN) and executive control network (ECN), respectively (Dietrich and Kanso 2010; Beaty et al. 2016). A growing body of fMRI studies has shown that the control network, including PPC and lateral PFC, is responsible for goal-directed processing and evaluation to meet specific task demands, and that this network cooperates with the default network during both domain-general and domain-specific creativity tasks (Beaty et al. 2015; Liu et al. 2015; Pinho et al. 2015; Beaty et al. 2016). For example, a recent divergent thinking study found that increased functional connectivity of the ventral ACC and the left angular gyrus predicted the creative quality of divergent thinking responses (Mayseless et al. 2015). In a study of professional poets, Liu et al. (2015) demonstrated that increased coupling of the default and control systems underlies the evaluation and revision of self-generated poetry during fMRI. In line with these views, we deduce that maintained gray matter characteristics within the FPN, which reflects high-efficiency and coordination with the DMN, is beneficial to the generation and evaluation of novel and useful ideas.

A series of recent studies also provide evidence for a role of a frontotemporal network in creative performance. One recent study found that increased local GMV is related to greater volume of temporo-parieto-occipital regions, pointing to increased cooperation among auditory, visual, and conceptual representations (Seeley et al. 2008). Furthermore, a recent study on frontotemporal

dementia found that patients with this condition exhibited enhanced artistic abilities (de Souza et al. 2014); notably, artistic performance often corresponds to the absence of a clear task goal, in contrast to theory-based creativity tasks such as divergent thinking tasks. However, numerous case studies indeed reveal that neurodegeneration in PFC and posterior brain regions supports more balanced or adaptive cooperation in top-down (controlled) and bottom-up (uncontrolled) processes. A recent fMRI study using cognitive training reported enhanced verbal creativity performance after continuous engagement in divergent thinking tasks, which corresponded to increased activation in MTG, pointing to a role of more demanding semantic processes for integrating and combining novel representations (Fink et al. 2015). In addition, training using cognitive stimulation has been shown to strengthen functional connectivity within frontotemporal regions (MTG and medial SFG), which is associated with increased originality in creativity tasks (Wei et al. 2014). The MTG and other temporal regions are involved in the storage and retrieval of semantic information (Binder et al. 2009), whereas effective semantic cognition appropriate for a specific context or task is more associated with lateral PFC activation, reflecting greater semantic control process (Whitney et al. 2011). Thus, we conclude that more effective and demanding semantic processes are supported by functional coupling within frontotemporal regions involved in semantic retrieval, representations, and control, which are critical to improvements of creative performance from late adolescence to early adulthood and are reflected in maintained gray matter characteristics within the FTN.

# Interactions Between Fronto-related Networks, Right DLPFC, and WM

Above, we illustrated the importance of 2 networks (FPN and FTN) in predicting creative cognitive ability. However, the mechanisms for enhancing creativity have not yet been addressed. We suspect that the interaction of the 2 networks via the right DLPFC and WM at baseline can provide some insights into creative capacity across development. First, we found a significant interaction of the right DLPFC and rGMD change within the 2 networks, emphasizing the general role of DLPFC for enhancing creativity. Previous neuroimaging studies have suggested that the DLPFC is involved in a wide range of information processing in human cognition. Early in development, the right DLPFC does not appear to be especially important for creative actions, but its role involving other actions may be relevant for enhancing creative capacity. For example, esthetic and scientific behaviors largely depend on prefrontal activity, which is in accordance with internal goals and goaldirected planning (Miller and Cohen 2001). For individuals without clear targets and continuity of higher-order cognition, it may be difficult to engage in tasks involving innovative performance or original ideation, although other conditions may be satisfied for developing creative ability.

We suggest that DLPFC serves as a search engine and filtering system that can retrieve task-relevant information from long-term memory (Cabeza and Nyberg 2000) and withhold conventional responses from entering WM for further processing. Another possible explanation is that the relationship between DLPFC and the 2 networks corresponds to efficient cooperation of the FPN and FTN at an early stage of development. This notion is in line with a recent study showing that expertise in musical improvisational was inversely related to right DLPFC activity during improvisation, but positively related to connectivity between DFLPC and other regions within associative networks, indicating more efficient information exchange between these networks during musical creativity (Pinho et al. 2014). In this context, decreased activity of DLPFC may also coincide with increased functional coupling of this region with task-relevant networks as a function of expertise, potentially reflecting neural efficiency (Beaty 2015).

Several lines of evidence suggest that WM may play an important role in creative thinking (Damasio 2001; De Dreu et al. 2012; Lee and Therriault 2013). The WM system is thought to consist of storage and executive attention control systems (Baddeley 2000) which have been shown to influence performance on creativity tasks by providing cognitive flexibility, strategic planning, focused attention, and attention shifting during complex cognitive tasks (Dietrich 2004; Unsworth et al. 2009; Nusbaum and Silvia 2011). Notably, in this study, the relationship between longitudinal alterations within fronto-related networks and improved creativity was mediated by the right DLPFC and WM capacity at baseline, but not Stroop performance and response inhibition. Taken together, these findings suggest that specific executive functions, namely WM updating, contribute to the development of creative cognitive ability.

The results may also inform two-stage models of creative cognition (Finke et al. 1992) which emphasize generative and evaluative processes. We suspect that prior to idea evaluation, idea generation may first arise from self-generated thinking stemming from the DMN or TOP regions. From there, information can be forwarded to the WM buffer (Dietrich 2004; Beaty et al. 2016). We propose that TOP regions can be separated into 2 systems: temporary representations (e.g., visual and motor imagery) from occipital-parietal areas (Jensen et al. 2002; Fink et al. 2009; Palmiero et al. 2011; Fink and Benedek 2014) and long-term storage (e.g., episodic memory and prior knowledge) from occipital-temporal areas (Yonelinas et al. 2001; Shah et al. 2013; Madore et al. 2015). Thus, for adults, the accumulated knowledge and experience during college, such as professional knowledge, extensive interests, and creative actions, might be more critical to predict creative capacity. This interpretation is consistent with the notion that creativity involves episodic memory via the flexible recombination of stored representations (Madore et al. 2015; Addis et al. 2016; Beaty et al. 2016).

# Conclusion

The present study provides the first longitudinal evidence for a role of structural network development in creative cognitive ability. Nevertheless, some limitations should be noted. The main limitation is that creative cognitive ability was assessed by the same tasks across time, which might result in test-retest effects and overestimating the increase in creative ability during college. However, such effects may have been mitigated by the substantial time interval between test and retest (>2.5 years) and the inclusion of a novel creativity assessment at tp2 (i.e., pCTS). Nevertheless, it is challenging to completely eliminate test-retest effects, which could theoretically yield familiarity and recall when subjects complete the same tasks at tp2. Another potential limitation is that because we did not employ a targeted intervention, it was not possible to deduce whether brain structure variation or change have causal effects on creative capacity changes. Although we ruled out confounding factors related to individual creativity as previous reported (e.g., general intelligence and openness to experience), in the longitudinal analysis, several individual factors that were not assessed at follow-up could have been influential (e.g., environmental, motivation, and mood). However, the present study is

part of an ongoing project, so future analyses of these data could consider such factors for investigating behavioral and neuropsychosocial profiles of current and future creativity.

In conclusion, these results highlight increased creative cognitive ability during college, from late adolescence to early adulthood. This developmental change in behavior, in turn, is associated with individual difference variables underlying baseline rGMD in lateral PFC. This area has been widely implicated in previous studies on creative thinking, which may reflect its multiple functions, including focused attention, WM, and cognitive flexibility (de Manzano and Ullén 2012; Prakash and Du 2013). In addition, we found that future creative cognitive ability is associated with brain structure change in frontalrelated clusters, and that future creativity is influenced by baseline rGMD in lateral PFC and WM ability. We believe these results offer new insight into the neural basis of creative cognitive ability, and provide a viable method for screening and identifying highly creative individuals by combining MRI and behavioral technologies.

# **Supplementary Material**

Supplementary data is available at Cerebral Cortex online.

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