

## The Association between Resting Functional Connectivity and Creativity

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**The analysis of functional connectivity at rest (rFC) enables us to know how brain regions within and between networks interact. In this study, we used resting-state functional magnetic resonance imaging and a creativity test of divergent thinking (DT) to investigate the relationship between creativity measured by DT and rFC. We took the medial prefrontal cortex (mPFC) to be the seed region and investigated correlations across subjects between the score of the DT test and the strength of rFC between the mPFC and other brain regions. Our results showed that the strength of rFC with the mPFC significantly and positively correlated with creativity as measured by the DT test in the posterior cingulate cortex (PCC). These results showed that higher creativity measured by DT is associated with rFC between the mPFC and the PCC, the key nodes of the default mode network (DMN). Increased rFC between these regions is completely opposite from that is generally expected from the association between higher creativity and reduced deactivation in DMN during an externally directed attention-demanding task shown in our previous study but is similar to the pattern seen in relatives of schizophrenia. These findings are comparable to the previously reported psychological associations between schizotypy and creativity.**

**Keywords:** creativity, default mode network, functional connectivity, posterior cingulate cortex, rest

### Introduction

Creativity is commonly agreed to involve bringing something into being that is original and also valuable (Ochse 1990). It has been essential to the development of human civilization and plays a crucial role in cultural life. Creativity has often been measured by divergent thinking (DT) tests psychometrically. DT pertains primarily to information retrieval and the call for a number of varied responses to a certain item (Guilford 1967). As summarized in Jung, Segall, et al. (2010), there are a number of cognitive processes that are important for creativity, such as flow (when a person is fully immersed in what he or she is doing; characterized by a feeling of energized focus, full involvement, and success in the process of the activity [Csikszentmihalyi 1997]), insight (the flash of recognition that solves a problem [Jung-Beeman et al. 2004]), perseverance in the face of social acceptance or resistance, such as that of personality variables, and also remote association of ideas. These and other cognitive processes contribute to the complex construct of creativity. As DT tests include a wide range of cognitive processes (Dietrich 2007), attempts ought to be undertaken to move beyond a reliance on DT tests to assess creativity in laboratory settings (Dietrich 2007). However, we focused on the DT test as a measure of creativity in this study

because, right now, DT tests dominate as a measure of creativity in this field (Dietrich 2007). DT has been proposed to be a key aspect of creativity (Guilford 1967) and a meta-analysis (Kim 2008) furthermore demonstrated that DT scores have a significantly stronger relationship with creative achievement than scores on intelligence tests do supporting the validity of DT as predictive of creative ability. To our knowledge, no other creative measures in laboratory settings have shown this level of validity. The major weak points of DT tests as described above are actually more or less common to comprehensive psychological tests of these kinds, such as “intelligence tests,” “processing speed tasks,” and “reading comprehension tasks.” For example, in the case of the processing speed task, the digit symbol test (Wechsler 1997), which is a typical test of processing speed, is considered to be affected by psychomotor speed, attention, perceptual organization, motor persistence, and visual short-term memory (Scheer and Sato 1989; Ellingsen et al. 2001). We should remember the weak points of these psychological tasks, for we believe it would take quite a lot of time to develop psychological tasks without these limitations.

One of the most consistent psychological findings regarding creativity is creativity's association with schizotypy and openness, as described below. Numerous studies reported a positive relationship between creativity and schizotypy (Fisher et al. 2004), and a positive relationship between creativity and openness (Dollinger et al. 2004; Carson et al. 2005; Miller and Tal 2007). Schizotypy refers to the personality trait of experiencing psychotic symptoms (Claridge 1997), which are also observed in normal populations (Johns and van Os 2001); the continuity of psychotic symptoms with normal experience has also been pointed out (Johns and van Os 2001). Furthermore, schizotypy may be conceptualized as a predisposition to schizophrenia at the level of personality organization not only among clinical populations but also normal populations (Meehl 1989; Vollema and Van Den Bosch 1995; van't Wout et al. 2004). Moreover, the abovementioned association between schizotypy and creativity as well as the association between creativity and openness is clearly observed in normal populations (Green and Williams 1999; Miller and Tal 2007; Jung, Grazioplene, et al. 2010). Openness is a personality trait that involves an active imagination, daydreaming, aesthetic sensitivity, preference for variety, and intellectual curiosity (McCrae 1987; Costa and McCrae 1992). Recently, Miller and Tal (2007) investigated associations among creativity, schizotypy, and openness. Consistent with vast numbers of previous studies, in their sample of college students, schizotypy correlated with creativity as well as openness and openness correlated with creativity. In their study, in a multiple regression model predicting creativity, the partial contribution of openness was statistically significant, while that of positive schizotypy was not. Their results may indicate that

the “schizotypy-creativity” link may be mediated by the personality trait of openness. Their results may suggest a path model where openness fully mediates the effect of schizotypy on creativity (i.e., schizotypy increases openness which, in turn, augments creativity) (Del Giudice et al. 2010) or 2 constructs may tap some of the same psychological processes (Del Giudice et al. 2010) that should not be partialled out. In either case, the natures of the associations among the 3 remain to be investigated. The strongly consistent findings from these studies are that there are associations between creativity and schizotypy as well as between creativity and openness. Other studies suggest a genetic association between psychosis and creativity. For example, the first-degree relatives and the offspring of people with schizophrenia tend to be more creative and enter more creative occupations than controls (Juda 1949; Karlsson 1970, 1984, 2001). Furthermore, the prevalent genotype of the neuregulin 1 gene that increases the risk of psychosis (Hall et al. 2006; Kéri et al. 2009) is associated with increased creativity (Kéri 2009).

Other cognitive components such as latent inhibition and deficits of selective attention may be associated with or may mediate the association between schizotypy and creativity. Latent inhibition is the capacity to screen from conscious awareness stimuli previously experienced as irrelevant. Previous studies revealed evidence that a heightened level of creativity is associated with attenuated latent inhibition (Carson et al. 2003; Fink, Slamar-Halbedl, et al. 2011), while attenuated latent inhibition has been generally associated with the tendency toward schizotypy (Carson et al. 2003). Accordingly, creative individuals do not tend to screen things out from conscious awareness that were previously experienced as irrelevant. This attenuated latent inhibition is assumed to be associated with selective attention deficits (Lubow 2005), while selective attention deficits have also been associated with heightened creativity (for summary, see Takeuchi, Taki, Hashizume, et al. 2011c). From these points, it can be said, “creative individuals appear to be characterized in part by the ability to perceive and describe what remains hidden from the view of others” (Carson et al. 2003).

Neuroimaging studies have shown the higher creativity is associated with brain connectivity and the functions of the frontal lobe. Schizotypes, who have enhanced creative thinking ability, increasingly recruit the right prefrontal cortex (PFC) during a DT test (Folley and Park 2005). Furthermore, our previous study of regional gray matter structures has shown the right PFC’s gray matter structure was associated with creativity as measured by DT (Takeuchi, Taki, Hashizume, et al. 2011c). On the other hand, in healthy subjects, a previous electroencephalogram (EEG) study (Jausovec 2000) reported that creative individuals showed higher interhemispheric and intrahemispheric EEG coherence (functional connectivity [FC]) during essay writing. In another EEG study (Jausovec N and Jausovec K 2000), a creative or divergent production problem (essay writing) caused noticeable intrahemispheric and interhemispheric cooperation, mainly between the far distant brain regions, compared with a nondivergent problem. The authors suggested that creative thinking seemed to require information transfer between different brain areas. In addition, when subjects hit upon more original ideas during a creative task, stronger task-related alpha synchronization was observed (Fink and Neubauer 2006). Furthermore, white matter structural integrity (structural connectivity), involving the corpus

callosum and the frontal lobe, was associated with creativity as measured by a DT test (Takeuchi et al. 2010b). These findings are consistent with integrative reviews that suggest the importance of brain connectivity for creativity (Heilman et al. 2003; Duch 2007; but see also Jung, Grazioplene, et al. 2010 for the negative association of creativity and the white matter structural integrity of inferior frontal areas). As a whole, the results of those studies indicate higher creativity may well be associated with brain connectivity and the functions of the frontal lobe. Structural connectivity underlies both FC during a task (Au Duong et al. 2005) and FC during rest (rFC) (Greicius et al. 2009; Honey et al. 2009). Therefore, considering the associations between creativity and structural connectivity and those between creativity and FC during a task, it can be reasoned that creativity is related to rFC.

Recently, rFC, which reflects temporal correlations between blood oxygen level-dependent (BOLD) signals in different brain regions during rest, has been widely used in functional magnetic resonance imaging (fMRI) studies. These temporal correlations suggest direct or indirect interactions between brain regions (Friston et al. 1993). Certain sets of regions show positively synchronized brain activity during rest (positive correlations between the brain activities of these regions) and form functional networks (Damoiseaux et al. 2006). One important finding obtained from a study of rFC is that there are 2 networks, the so called default mode network (DMN) and the task-positive network (TPN), whose brain activities during rest show spontaneous correlations within each network and anticorrelations between networks (Fox et al. 2005). Anticorrelations mean that when one network is activated, the other network is deactivated. The TPN consists of regions that are consistently activated during cognitive tasks, such as the lateral PFC (LPFC) and the inferior parietal lobe, and the DMN consists of regions that are consistently deactivated during cognitive tasks, such as the medial PFC (mPFC) and the posterior cingulate cortex (PCC) (Fox et al. 2005). Higher psychometric intelligence is associated with an higher correlation within the TPN (Song et al. 2008). On the other hand, relatives of schizophrenic persons show increased rFC within the DMN (Whitfield-Gabrieli et al. 2009).

In our previous studies, as described above, we investigated the characteristics of regional gray matter volume, white matter structural integrity, and functional activity during a working memory task that are shown by subjects with higher creativity measured by DT (Takeuchi et al. 2010a, 2010b; Takeuchi, Taki, Hashizume, et al. 2011c). Of note, the reduced task-induced deactivation (TID) in the precuneus, which is one of the key nodes of the DMN was associated with higher creativity. This was interpreted as reflection of the inefficient reallocation of cognitive resources in the creative subjects and this finding was also comparable to the finding of the reduced TID in the DMN in relatives of schizophrenic persons (Whitfield-Gabrieli et al. 2009). The interpretation of reduced TID in the DMN in the creative subjects is congruent with the abovementioned previously reported association between creativity and deficits of selective attention. However, despite these and a number of neuroimaging studies which investigated the functional activities of the brain during various creative tasks (e.g., Chávez-Eakle et al. 2007; Gibson et al. 2009) and the structural characteristics of the brains of creative subjects (Jung et al. 2009; Jung, Grazioplene, et al. 2010; Jung, Segall, et al. 2010), including the ones as described

above (for review, see Arden et al. 2010), the association between rFC and creativity has not been investigated. Using resting-state fMRI scans of the subjects whose fMRI data during a working memory task were analyzed in our study (Takeuchi, Taki, Hashizume, et al. 2011c), we investigated the correlations between creativity measured by a DT test (S-A creativity test) (Society\_For\_Creative\_Minds 1969) and the strength of rFC between the key node of the frontal lobe (the frontal lobe is associated with creativity, as described above) of the DMN, the mPFC, and regions elsewhere in the brain. The state of the DMN is of interest in investigating the neural basis of creativity for 3 reasons. First, the DMN is considered to be involved in daydreaming and self-reflection (Buckner et al. 2008). Creativity is associated with a personality of openness, which is characterized by much imagination, daydreaming, fantasy, and attentiveness to one's own feelings (McCrae 1987; Costa and McCrae 1992). Second, some recent previous studies of functional imaging studies of creative cognition reported that the regions of the DMN could be critically involved in creativity (Fink et al. 2010; Fink, Koschutnig, et al. 2011). Furthermore, the state of the DMN has been associated with schizotypy, which is associated with creativity (Fisher et al. 2004), as described above. Finally, the association between the activity of the DMN during rest, which is involved in cognitive processes at rest (Buckner et al. 2008), and creativity is intriguing because during the resting period one temporarily stops focusing on the problem being tackled. This cessation in focus has been suggested to facilitate creative insight and problem solving (Wallas 1926; Smith and Blankenship 1991; Ward 2003). Using the analysis of rFC, we are able 1) to know how brain regions interact with not only brain regions that are directly connected structurally but also with brain regions that are not structurally connected (the latter of which is impossible through studies on white matter structural integrity), 2) to investigate the state of the DMN during the cognitive processes involved at rest, and 3) to obtain new insights into the basis of creativity. Two hypotheses can be formed. One is subjects with higher creativity show decreased rFC within the DMN. This is because patient studies showed diseases or disorders with reduced TID in the DMN are generally associated with reduced rFC within the DMN (for review, see Broyd et al. 2009). And our unpublished study (H Takeuchi, Y Taki, R Nouchi, H Hashizume, Y Sassa, A Sekiguchi, Y Kotozaki, S Nakagawa, T Nagase, CM Miyauchi, R Kawashima, unpublished data) also showed reduced TID in the precuneus/PCC regions is associated with reduced rFC within between the mPFC and these precuneus/PCC regions. As described, creativity is associated with reduced TID in the DMN in the precuneus/PCC region. Thus, from this perspective, higher creativity is expected to be associated with reduced rFC between the mPFC and the precuneus/PCC region. The other hypothesis expects the opposite result and expects the association between higher creativity and increased rFC between the mPFC and the precuneus/PCC region. This hypothesis was based on the abovementioned observation that relatives of schizophrenic persons show increased rFC between the mPFC and the precuneus/PCC despite reduced TID in the DMN, while there is a strongly consistent association between creativity and schizotypy, as described above (note this reasoning is not affected whether creativity-schizotypy association is mediated by openness, diffused

attention, or other possible psychological mechanisms, as indicated above).

## Materials and Methods

### Subjects

One hundred and fifty-nine healthy right-handed individuals (90 men and 69 women) were participated in this study as part of our ongoing project to investigate the associations among brain imaging, cognitive functions, and aging (Takeuchi et al. 2010a, 2010b; Takeuchi, Taki, Hashizume, et al. 2011c; Takeuchi, Taki, Sassa, et al. 2011a; Taki et al. 2010). Data from 63 subjects among these 159 subjects were used in our previous studies to investigate the association between creativity and brain activity during a working memory task (Takeuchi, Taki, Hashizume, et al. 2011c) as well as the association between creativity and cerebral blood flow during rest (Takeuchi, Taki, Hashizume, et al. 2011a). Some of the subjects who took part in this study also became subjects of our intervention studies (psychological data and imaging data recorded before the intervention were used in this study) (Takeuchi, Taki, Hashizume, et al. 2011b; Takeuchi, Taki, Sassa, et al. 2011b). Psychological tests and MRI scans not described in this study were performed together with those described in this study. The mean age of subjects was 21.4 years (standard deviation [SD], 1.8). All subjects were university students or postgraduates. All subjects had normal vision and none had a history of neurological or psychiatric illness. Handedness was evaluated using the Edinburgh Handedness Inventory (Oldfield 1971).

### Creativity Assessment

The S-A creativity test (Society\_For\_Creative\_Minds 1969) was used to assess creativity. A detailed discussion of the psychometric properties of this instrument and how it was developed is found in the technical manual of this test (Society\_For\_Creative\_Minds 1969). The test is used to evaluate creativity through DT (Society\_For\_Creative\_Minds 1969), and it involves 3 types of tasks. The first task requires subjects to generate unique ways of using typical objects. The second task requires subjects to imagine desirable functions in ordinary objects. The third task requires subjects to imagine the consequences of "unimaginable things" happening. The S-A creativity test provides a total creativity score, which was used in this study, as well as scores for the following dimensions of the creative process: 1) Fluency—Fluency is measured by the number of relevant responses to questions and is related to the ability to produce and consider many alternatives. Fluency scores are determined by the total number of questions answered after excluding inappropriate responses or responses that are difficult to understand. 2) Flexibility—Flexibility is the ability to produce responses from a wide perspective. Flexibility scores are determined by the sum of the (total) number of category types that responses are assigned based on a criteria table or an almost equivalent judgment. 3) Originality—Originality is the ability to produce ideas that differ from those of others. Originality scoring is based on the sum of idea categories that are weighted based on a criteria table or an almost equivalent judgment. 4) Elaboration—Elaboration is the ability to produce detailed ideas (Society\_For\_Creative\_Minds 1969). Elaboration scores are determined by the sum of responses that are weighted based on a criteria table or an almost equivalent judgment. These 4 dimensions correspond to the same concepts as those of the Torrance tests of creative thinking (TTCT; Torrance 1966). Scoring of the tests was performed by the Tokyo Shinri Corporation. Please refer to our previous studies (Takeuchi et al. 2010a, 2010b) for more extensive details, including those on the psychometric properties of this test, sample answers to the questionnaire, and the manner in which the tests were scored.

The primary analysis was limited to the total creativity score and did not include the score for each dimension because this score was highly correlated with the total creativity score as well as with each other (all correlations between the scores of any 2 dimensions had simple correlation coefficients of >0.56). This is consistent with another group of rather similar DT tests (Heausler and Thompson 1988), TTCT (Torrance 1966). Heausler and Thompson (1988) concluded that the correlations among the subscales in TTCT were so high that

each subscale could not provide meaningfully different information. Treffinger (1985) warned that independent interpretations of TTCT subscores should be avoided. Consistent with this notion, a previous study (Chávez-Eakle et al. 2007) that investigated the association between regional cerebral flow (rCBF) and each dimension revealed that different creativity dimensions correlated with rCBF in similar regions. Thus, we believe that using only the total creativity score serves the purpose of this study. However, it is also true that sometimes the originality dimension of creativity displays psychometric characteristics distinct from those of other dimensions (Stavridou and Furnham 1996; Abraham et al. 2005). We therefore performed additional multiple regression analyses for each dimension as placing the scores from all 4 dimensions (which are strongly correlated) in a single multiple regression analysis was statistically inappropriate because of the problem of multicollinearity.

#### **Assessment of Psychometric Measures of General Intelligence**

Raven's Advanced Progressive Matrix (RAPM) (Raven 1993) has been the psychometric measure shown to be most correlated with general intelligence, making it the best measure of general intelligence. We used RAPM to assess intelligence and also to adjust for the effect general intelligence has on rFC. For more details of how RAPM was performed in our study, see our previous works (Takeuchi et al. 2010a, 2010b).

#### **Behavioral Data Analysis**

The behavioral data were analyzed using the statistic software SPSS 16.0 (SPSS Inc., Chicago, IL). Associations among demographic variables were analyzed using simple regression analyses. Results with a  $P < 0.05$  are statistically significant in these analyses.

#### **Image Acquisition and Analysis**

All MRI data acquisition was conducted with a 3-T Philips Intera Achieva scanner. Thirty-four transaxial gradient-echo images ( $64 \times 64$  matrix, time repetition [TR] = 2000 ms, time echo [TE] = 30 ms, flip angle =  $70^\circ$ , field of view [FOV] = 24 cm, 3.75 mm slice thickness) covering the entire brain were acquired using an echo planar sequence. For this scan, 160 functional volumes were obtained, while subjects were resting. During the resting-state scanning, the subjects were instructed to keep still with their eyes closed, as motionless as possible and not to sleep and not to think about anything in particular, as has been done similarly (Greicius et al. 2003; Damoiseaux et al. 2006). Furthermore, diffusion-weighted data were acquired using a spin-echo echo-planar imaging (EPI) sequence (TR = 10293 ms, TE = 55 ms, FOV = 22.4 cm,  $2 \times 2 \times 2$  mm<sup>3</sup> voxels, 60 slices). The diffusion weighting was isotropically distributed along 32 directions ( $b$  value = 1000 s/mm<sup>2</sup>). Additionally, a data set with no diffusion weighting ( $b$  value = 0 s/mm<sup>2</sup>) ( $b = 0$  image) was acquired. The total scan time was 7 min 17 s. The  $b = 0$  image in the DTI was used for spatial normalization of the EPI data. These scans as well as other scans used in another study (Takeuchi, Taki, Hashizume, et al. 2011c) were in most of the case, taken within the same session.

#### **Preprocessing and Individual-Level Functional Imaging Data Analysis**

Preprocessing and data analysis were performed using Statistical Parametric Mapping software (SPM5; Wellcome Department of Cognitive Neurology, London, UK) and implemented in Matlab (Mathworks Inc., Natick, MA). Prior to the analysis, the BOLD images were corrected for slice timing and realigned and resliced to the mean image of the series. Then, the BOLD images were skull stripped by masking the images using the threshold of a given signal intensity from the spatially smoothed (using 8 mm full-width at half-maximum [FWHM]) BOLD images and coregistered to a skull-stripped  $b = 0$  image of diffusion tensor imaging (created using a similar method to the one used for making skull-stripped BOLD images). The images were then spatially normalized into a skull-stripped  $b = 0$  image template, which was made from the data obtained in our scanner (for the creation of this template, see Takeuchi et al. 2010b) using the  $b = 0$  image to give

images with  $2 \times 2 \times 2$  mm voxels. These normalized procedures were performed as they were to the fMRI scans during a N-back task in our previous study (for detail, see Takeuchi, Taki, Hashizume, et al. 2011c). Finally, the images were smoothed (4 mm FWHM). As described in our previous study (Takeuchi, Taki, Hashizume, et al. 2011c), we did not use  $T_1$ -weighted structural images for coregistration because visual inspections suggested that the process of coregistering the BOLD images acquired in our studies to the  $T_1$ -weighted structural images used in our laboratory often failed. This failure could be attributed to differences in the 2 images caused by distortions of the BOLD images. The normalization procedures used  $b = 0$  images for the following reasons. First, the process of coregistering the BOLD images acquired in our studies to the  $b = 0$  images is reliable according to visual inspection of all images. This might be because both images were obtained using an EPI sequence and have similar characteristics, including distortion (Reber et al. 1998). Second,  $b = 0$  images have clearer anatomical characteristics (compared with BOLD images), which allows for precise normalization procedures. Third, the structure of the orbitofrontal cortex (OFC) is typically lost in the BOLD images acquired using a 3-T scanner (Stenger 2006) (although, it should be noted that certain methods of scanning such as optimization of the imaging slice orientation can reduce occurrence of image distortions and signal losses caused by susceptibility gradients near air/tissue interfaces [Deichmann et al. 2003]). In a few cases, direct normalization of the BOLD images to SPM5's EPI template distorted the structures around OFC to compensate for the loss of OFC in the BOLD images acquired in our study. On the other hand,  $b = 0$  images apparently have relatively more of these structures around OFC according to visual inspection. Therefore,  $b = 0$  images prevent the type of distortion observed in BOLD images and allow for better normalization procedures. However, since  $b = 0$  and BOLD images in the same subjects have similar characteristic, these images probably also match well in coregistration, despite the difference in the structures around OFC.

Individual-level statistical analyses were performed using a general linear model. We removed low-frequency fluctuations using a high-pass filter cutoff value of 128 s (or 1/128 Hz). Slow signal drifts with a period longer than this which are probably not based on brain activities will be removed by this value. On the other hand, we did not use a low-pass filter. And serial correlations in the BOLD signal were accounted for by a first-degree autoregressive correction (instead of being removed by a low-pass filter). The use of autoregressive model over the use of low-pass filter has been recommended when the signals of the model frequently changes through time series such as in rapid presentation event-related designs (Della-Maggiore et al. 2002). Several sources of spurious variances along with their temporal derivatives were then regressed out by putting these variances into regressors: 1) 6 parameters obtained by rigid body correction of head motion, 2) the whole-brain signal averaged over a whole-brain mask. This regression procedure removes fluctuations unlikely to be involved in specific regional correlations. Regressing out the global signal shifts the distribution of correlation coefficients, ensuring that they are approximately centered around zero in such a manner that their sum is less than or equal to zero. This method of data cleaning has been criticized as "artificially" creating anticorrelations (Murphy et al. 2009), though, a recent study suggested that anticorrelations observed in resting-state connectivity are not an artifact introduced by global signal regression and might have biological origins (Chai et al. 2012). However, more importantly, regardless of the recent controversy about regressing out the whole-brain signal, we believe that for the purposes of this study, it was important to regress out the global signal because of the following reasons. First, global signal correlation is observed partly because the brain is globally activated (Schölvinck et al. 2010). In this case, when these global brain activities are not regressed out, FC between 2 brain regions would show correlation of activity due to global brain activity as well as region- or network-specific activity synchronization. Our underlying assumption is that we would observe correlations due to network- or region-specific activity synchronization and not those due to region or network irrelevant global brain activity. Furthermore, in this study, no significant results related to anticorrelation were observed. Thus, the controversy over whether the magnitude of

correlations is a plus or minus in anticorrelated networks does not affect the current results and subsequent discussions. Correlation maps were produced by extracting the BOLD time course from a seed region then computing the correlation coefficient between that time course and the time course from all other brain voxels. The seed region in this study was a 6 mm radius sphere centered on a focus. For the current study, we examined correlations associated with the key node of the DMN (the mPFC). The peak voxel of the mPFC ( $x, y, z = -1, 47, -4$ ) was defined, as was performed in previous literature (Fox et al. 2005). The seed region included 123 voxels.

For the FC analysis, contrast images representing rFC with the mPFC were estimated for each subject after preprocessing. Data were subject to a random-effects analysis, which allowed inferences derived from this subject sample to be generalized to the population. To study the effect of individual difference in creativity measured by a DT test on rFC, we entered the first-level contrast images into a second-level regression analysis.

### Group-Level Statistical Analysis

At the group-level analysis, we tested for a relationship between individual creativity measured by a DT test and rFC with the ROI. In the whole-brain analysis, we used a multiple linear regression analysis to look for areas where rFC with the ROI was significantly related to individual creativity as measured by the DT test (total creativity score from the S-A creativity test). The effects of sex, age, and the score of RAPM were included as regressors of no interest. In additional whole-brain multiple regression analyses, we tested for a relationship between each dimension of creativity (fluency, flexibility, originality, and elaboration) and rFC with mPFC separately. These additional analyses included multiple linear regression analyses, which were performed to determine areas where rFC with ROI (mPFC) was significantly related to each dimension of creativity (the score for each dimension in the S-A creativity test). In these 4 additional analyses, each multiple regression analysis had 4 covariates (the score for each dimension in the S-A creativity test, age, sex, and the RAPM score). Refer to the Creativity Assessment of the Materials and Methods for an explanation of why we did not add the scores for the 4 dimensions in a single multiple regression analysis.

Next, we tested for a relationship between individual general intelligence measured by the RAPM score and rFC with mPFC to determine whether the association between creativity and rFC with ROI and that between general intelligence and rFC with ROI were identical. Whole-brain analysis included multiple linear regression analysis, which was performed to determine areas where rFC with mPFC was significantly associated with individual general intelligence as measured by the RAPM score. The effects of sex, age, and the total creativity score from the S-A creativity test were included as regressors of no interest.

We then tested for a relationship between individual creativity measured by a DT test and rFC with ROI to determine whether creativity is also associated with rFC in networks other than DMN. For this purpose, we investigated the network involving the bilateral dorsolateral prefrontal cortices (DLPFCs) (Fox et al. 2005). In these analyses, 2 seed ROIs (the left and right DLPFC) were included, and the seed regions were constructed in the same manner as in a previous study (Song et al. 2008). Subsequent individual- and group-level analyses were performed in the same manner as the analysis of rFC with mPFC.

Next, we investigated whether the relationship between rFC with mPFC and creativity differed between sexes (i.e., whether interaction between sex and creativity affects rFC with mPFC). In whole-brain analysis, we used voxelwise analysis of covariance (ANCOVA) in which sex difference was a group factor (using the full factorial option of SPM5). In this analysis, age, the RAPM score, and the total creativity score from the S-A creativity test were covariates. All of these covariates were modeled so that each covariate's unique relationship with rFC with mPFC could be observed for each sex (using the interactions option in SPM5), which facilitated investigation of any effect of the interaction between sex and the covariates for rFC with mPFC. These effects were assessed using  $t$ -contrasts.

A multiple comparison correction was performed using the voxel-level familywise error (FWE) approach at the whole-brain level.

## Results

### Behavioral Data

Table 1 shows the average, the SD, and the range of scores from the S-A creativity test, the RAPM score, and age in our sample. None of the psychological or epidemiological measures (the RAPM score, sex, and age) correlated significantly with the total S-A creativity test score.

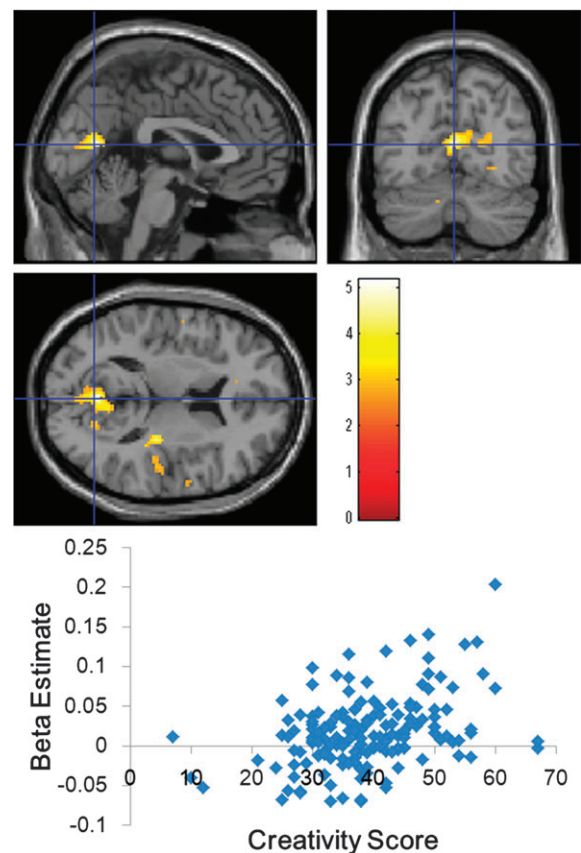
### Correlation of the Strength of rFC with the mPFC and Creativity across Sexes

We examined areas showing an association between the DT test (S-A creativity test) score, which reflects creativity, and the

**Table 1**

Average, SD, and range of scores from the S-A creativity test, Raven's advanced progressive matrices score, and age in our sample

	Average	SD	Range
S-A creativity test score	38.8	9.83	7-67
Raven's advanced progressive matrices score	28.2	3.66	18-36
Age	21.4	1.80	18-27



**Figure 1.** Regions of correlation between the strength of rFC with the mPFC and creativity test scores (the results are shown with a threshold of  $P < 0.005$  uncorrected for visualization purposes). Regions of correlation are overlaid on a single subject  $T_1$  image of SPM5. As seen, creativity was significantly and positively correlated with the strength of rFC between the mPFC and the posterior cingulate gyrus. Below is a scatter plot of the relationships involving rFC between the mPFC and the PCC (0, -68, 12) and creativity test scores.

strength of rFC with the mPFC. After controlling for the age, sex, and score of RAPM, a multiple regression analysis revealed that the total score of the S-A creativity test was significantly and positively correlated with the strength of rFC between the mPFC and the PCC ( $x, y, x = 0, -68, 12, t = 5.16, P = 0.038$  corrected for multiple comparisons at voxel-level FWE at the whole-brain level; Fig. 1). There were no regions of significant negative correlation between the strength of rFC with the mPFC and the total score of the S-A creativity test.

Moreover, we examined areas showing an association between each dimension of creativity (fluency, flexibility, originality, and elaboration) and the strength of rFC with mPFC. We performed 4 separate whole-brain multiple regression analyses that included the score for each dimension, age, sex, and the RAPM score as covariates. No significant associations were observed in any of these analyses ( $P > 0.05$  corrected for multiple comparisons at voxel-level FWE at the whole-brain level). Furthermore, in all analyses, similar tendencies for an association between each of the dimensions and the strength of rFC between mPFC and PCC were observed (statistical values and coordinates of the peak voxel in this region from the 4 analyses were as follows:  $x, y, x = -2, -66, 10, t = 3.75$  in the analysis of fluency;  $x, y, x = 0, -66, 12, t = 4.17$  in the analysis of flexibility;  $x, y, x = 0, -68, 12, t = 4.41$  in the analysis of originality; and  $x, y, x = 0, -68, 12, t = 4.73$  in the analysis of elaboration). Given these results, associations between certain dimensions of creativity and rFC with mPFC remain unclear.

#### **Correlation of the Strength of rFC with the mPFC and General Intelligence**

We also tested for a relationship between individual general intelligence as measured by RAPM and rFC with mPFC to determine whether the association between creativity and rFC with ROI and that between general intelligence and rFC with ROI were identical. After controlling for age, sex, and the total creativity score from the S-A creativity test, multiple regression analysis revealed no significant correlations between the RAPM score and the strength of rFC with mPFC in any of the regions. A tendency toward a positive correlation between the creativity and the magnitude of rFC between mPFC and a region in PCC ( $x, y, z = -22, -66, 28, t = 3.30, 6$  voxels;  $P < 0.001$ , uncorrected). However, this result was not significant but also far from no (0) correlations. In addition, the peak was a little bit distant from the peak of the association between creativity and rFC between mPFC and PCC. Thus, these results do not suggest any clear conclusions. It should be noted that this study involved a college cohort, and therefore, the psychometric measures of intelligence were concentrated at a rather high level, which might have substantially weakened the sensitivity of the analysis because of the resulting lower variability in general intelligence. However, as noted in the Discussion, focusing on a study population with a higher level of intelligence is important for investigating the neural basis of creativity as in samples with lower level of intelligence, creativity, and intelligence tend to correlate more strongly (Sternberg 2005), although this might make it difficult to compare the results of neural correlates of creativity and those of psychometric intelligence. This is a common characteristic of college-based study populations (e.g., Jung, Segall, et al. 2010). Thus, results related to general intelligence should be taken with caution, especially these are whole-brain analyses, and in whole-brain analyses, negative findings usually do not have much meaning.

#### **Correlation of the Strength of rFC with the Bilateral DLPFCs and Creativity**

We examined areas showing an association between the DT test (S-A creativity test) score, which reflects creativity, and the strength of rFC with the bilateral DLPFCs to determine whether creativity was also associated with rFC in networks other than DMN. After controlling for age, sex, and the RAPM score, multiple regression analysis revealed no significant correlations between the total S-A creativity test score and the strength of rFC with the left DLPFC in any of the regions. Moreover, no significant correlations were observed in the analysis of rFC with the right DLPFC.

#### **Effects of Interaction between Sex and Creativity on the Strength of rFC with mPFC**

The ANCOVA using data from both sexes revealed no significant effects of the interaction between the total S-A creativity test score and sex on the strength of rFC with mPFC.

#### **Discussion**

To our knowledge, this is the first study to investigate the association between individual creativity measured by a DT test and rFC. Our findings showed that higher creativity is associated with increased rFC between the mPFC and the PCC, the key nodes of the DMN. The result is completely opposite from our first hypothesis and what is generally expected from the association between higher creativity and reduced TID in this region (Takeuchi, Taki, Hashizume, et al. 2011c) as reduced TID in the DMN is generally associated with decreased rFC in the DMN as described in the Introduction. However, the result conforms to our second hypothesis and is similar to the pattern seen in relatives of schizophrenia as described in the Introduction. The results may suggest that higher creativity is achieved through increased interaction in this network and combination of ideas represented in different regions in this network. These results may be also congruent with the recent functional imaging studies of creative cognition reported that the regions of the DMN could be critically involved in creativity (Fink et al. 2010; Fink, Koschutnig, et al. 2011).

The pattern of rFC and TID that is associated with higher creativity presented in this study and our previous study (Takeuchi, Taki, Hashizume, et al. 2011c) is partly similar to and partly distinct from the pattern of rFC and TID that is associated with general cognitive abilities. Increased rFC between the mPFC and other nodes in the DMN (the precuneus), which was associated with higher creativity, is common to rFC patterns that are associated with better working memory performance (Hampson et al. 2006). Conversely, decreased rFC between the mPFC and the precuneus is associated with Alzheimer's disease's amyloid deposition (Sheline et al. 2009). Thus, increased rFC within the DMN is a reflection of the integrity of the network and may lead to higher cognitive abilities. On the other hand, reduced TID in the DMN is the opposite pattern that is associated with higher working memory performance (Sambataro et al. 2010) and common to the pattern that is associated with Alzheimer's disease. From the perspective of rFC and TID, the neural correlates of creativity as measured by the DT test are, at least in part, clearly distinct from those of general cognitive abilities.

Our findings of increased FC in subjects with higher creativity measured by DT are consistent with literature about

creativity that indicated the importance of brain connectivity in creativity and revealed further detail about this finding. The importance of increased FC in creativity has been shown by previous EEG studies (Jausovec 2000; Jausovec N and Jausovec K 2000; Fink and Neubauer 2006) as described in detail in the Introduction. Our white matter structural study of creativity (Takeuchi et al. 2010b) also showed the importance of structural connectivity for creativity measured by DT. Together with the view of integrative reviews of creativity (Heilman et al. 2003; Duch 2007), these findings have shown the importance of brain connectivity for creativity. Our findings are consistent with this view and further revealed how the precise interactions between the key nodes of the DMN are associated with creativity, which has not been revealed by previous studies of brain connectivity, as described above.

Previously reported increased structural connectivity involving the frontal lobe in subjects with higher creativity measured by DT may underlie increased rFC with the mPFC in subjects with higher creativity measured by DT. Our previous diffusion tensor imaging study revealed that white matter structural integrity involving extensive areas of the frontal lobe, including the white matter regions adjacent to the mPFC, positively correlated with creativity measured by a DT test (Takeuchi et al. 2010b). Furthermore, structural connectivity underlies increased FC between brain regions (Greicius et al. 2009), and it has been implicated that higher individual white matter integrity underlies stronger FC (Au Duong et al. 2005). Considering these points, the observed increase in rFC with the mPFC in subjects with higher creativity as measured by a DT test may be partly underlain by previously reported increases in white matter structural integrity in subjects with higher creativity.

There is at least one limitation in this study as was the case with our previous studies (Jung, Segall, et al. 2010; Takeuchi et al. 2010a, 2010b). We used young healthy subjects with a high level of education. Limited sampling of the full range of intellectual ability is a common hazard when sampling from college cohorts. Whether our findings would also hold across the full range of population samples and normal distribution must be determined with larger and more representative samples. Though our interpretations have a certain limitation as was the case in our previous structural studies on creativity (Takeuchi et al. 2010a, 2010b), focusing on highly intelligent subjects was certainly warranted for the purpose of this study, given the correlation between intelligence and creativity among subjects with normal and inferior intelligence (Sternberg 2005).

In summary, the present results showed that creativity, as measured by a DT test, is associated with increased rFC between the mPFC and the PCC, which are the key nodes of the DMN. Traditionally, it has been suggested that brain connectivity is important for higher creativity and recent structural studies confirm that idea. Our current finding is consistent with this view and further revealed the functional interaction between the nodes of the DMN is associated with creativity. Also the increased rFC within the DMN is completely opposite from that is generally expected from the association between higher creativity and reduced TID in this region (Takeuchi, Taki, Hashizume, et al. 2011c). This is because patient studies showed diseases or disorders with reduced TID in the DMN are generally associated with reduced rFC within the DMN (for review, see Broyd et al. 2009). Furthermore, our

unpublished study (H Takeuchi, Y Taki, R Nouchi, H Hashizume, Y Sassa, A Sekiguchi, Y Kotozaki, S Nakagawa, T Nagase, CM Miyauchi, R Kawashima, unpublished data) also showed reduced TID in the precuneus/PCC regions is associated with reduced rFC between the mPFC and these precuneus/PCC regions. Finally, subjects with higher working memory performance, which have opposing characteristic with subjects with higher creativity in certain aspects (for summary, see Takeuchi, Taki, Hashizume, et al. 2011c), show increased rFC within the DMN (Hampson et al. 2006) and increased TID in the DMN (Sambataro et al. 2010). However, on the contrary, the combination of increased rFC within DMN and reduced TID in DMN, which is observed in creative subjects, is also observed in the relatives of schizophrenia patients (Whitfield-Gabrieli et al. 2009). These findings are comparable to those of numerous previous studies that have shown associations between schizotypy and creativity, including those observed in normal populations.

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