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Degree centrality and fractional amplitude of low-frequency oscillations associated with Stroop interference

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ABSTRACT

Stroop paradigms are commonly used as an index of attention deficits and a tool for investigating functions of the frontal lobes and other associated structures. Here we investigated the correlation between resting-state functional magnetic imaging (fMRI) measures [degree centrality (DC)/fractional amplitude of low frequency fluctuations (fALFFs)] and Stroop interference. We examined this relationship in the brains of 958 healthy young adults. DC reflects the number of instantaneous functional connections between a region and the rest of the brain within the entire connectivity matrix of the brain (connectome), and thus how much of the node influences the entire brain areas, while fALFF is an indicator of the intensity of regional brain spontaneous activity. Reduced Stroop interference was associated with larger DC in the left lateral prefrontal cortex, left IFJ, and left inferior parietal lobule as well as larger fALFF in the areas of the dorsal attention network and the precuneus. These findings suggest that Stroop performance is reflected in resting state functional properties of these areas and the network. In addition, default brain activity of the dorsal attention network and precuneus as well as higher cognitive processes represented there, and default stronger global influence of the areas critical in executive functioning underlie better Stroop performance.

Introduction

As described in our previous study (Takeuchi et al., 2012b), the Stroop task (Stroop, 1935) is one of the most widely used paradigms in psychology and clinical medicine (MacLeod, 1991). During Stroop paradigms, subjects experience cognitive interference when they resolve interferences such as identifying the ink color of a printed word while ignoring the word's identity (Stroop, 1935). The Stroop task is now commonly used and considered to be an index of attention deficit and an index of functions of the frontal lobes and their associated structures (MacLeod and MacDonald, 2000).

More than 20 functional activation studies investigated brain activation during Stroop paradigms and identified consistently activated structures during this paradigm (Nee et al., 2007): (a) the anterior cingulate cortex (ACC; MacLeod and MacDonald, 2000), (b) the right inferior frontal junction (IFJ), which is located in the vicinity of the junction of the inferior frontal sulcus and the inferior precentral sulcus, and (c) dorsolateral prefrontal cortex (DLPFC). In our previous study (Takeuchi et al., 2012b), we revealed that regional gray matter volume (rGMV) of ACC and other regions and regional white matter volume (rWMV) of the extensive bilateral white matter areas, which mainly spread in the dorsal part of the frontal lobe, are associated with individual Stroop interference. Through these task-free brain imaging methods, it was demonstrated that ACC contributes to Stroop performance and the involvement of regions that have been implicated in response inhibition and attention in Stroop performance.

On the other hand, resting-state functional connectivity (RSFC) has been widely used in functional magnetic resonance imaging (fMRI) studies. It is well known that RSFC underlies cognitive differences between individuals (Song et al., 2008; Takeuchi et al., 2012a; Wei et al., 2013). Potential associations between RSFC and Stroop performance

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have also been investigated. For example, it was revealed that the greater RSFC within the networks, referred to as the default mode network and the salience network, was associated with Stroop performance in cognitively normal older adults (Duchek et al., 2013). Recently, global brain connectivity through degree centrality (DC) can be measured by resting state functional magnetic resonance imaging (rsfMRI) (Buckner et al., 2009). This graph-based measurement of network organization reflects the number of instantaneous functional connections between a region and the rest of the brain within the entire connectivity matrix of the brain (connectome), and thus how much of the node influences the entire brain areas and in integrating information across functionally segregated brain regions (Hagmann et al., 2008). On the other hand, these cognitive control and information integration may well be important functions for Stroop paradigms (Maddox et al., 2010). Further, fractional amplitude of low-frequency fluctuation (fALFF) has been developed to indicate the magnitude of neural activity during rest (Chao-Gan and Yu-Feng, 2010; Zang et al., 2007; Zou et al., 2008). The fALFF approach is an improvement on ALFF and has better sensitivity and specificity in detecting spontaneous brain activities (Zou et al., 2008). Recent studies have begun revealing the physiological bases behind these measures. For example, it has been shown that the amount of regional blood supply each individual has underlies the individual differences in DC (Liang et al., 2013). Furthermore, the brain's metabolic demands are associated with its degree of connectivity and are also largely accounted for by the amplitude of brain activity (Tomasi et al., 2013). Further, repetition rate of visual stimuli induces changes in fALFF like it does to BOLD signal change, further supporting the notion that fALFF reflects the strength of intrinsic brain activity (Li et al., 2011). These measures have widely been used to detect the neural changes in clinical patients (Ren et al., 2013; Wang et al., 2014). But what individual differences lie in regional differences of these measures underlie is still largely unknown. A recent study revealed that ALFF is associated with the precuneus and the medial part of left superior frontal gyrus based on the performance of the Attention Network Test (Xu et al., 2014). This task combines cued response time (RT) and the flanker tasks (Fan et al., 2005). It involves conflict resolution like the Stroop task; however, the neural bases of the flanker task may be partly overlapping but have rather distinct neural bases (Nee et al., 2007). In addition, the Attention Network Test and Stroop task have distinct psychological properties (Vandenbossche et al., 2012).

Although the Stroop task has received considerable attention, no study has investigated whether DC/fALFF underlie individual differences in Stroop task (or interference) performance. The purpose of this study was to investigate the association between DC/fALFF and Stroop interference.

Areas that are activated through cognitive tasks and rsfMRI properties sometimes appear to differ (Hampson et al., 2006); thus, to build hypotheses, we relied on a few available published studies on ALFF and DC. As for fALFF, the previous studies on ALFF and the paradigms that are relevant to Stroop tasks; namely, the Attention Network Test and working memory, both showed an association of performance with ALFF in the precuneus (Xu et al., 2014; Zou et al., 2013). Both these paradigms involve executive control (Fan et al., 2005; Owen et al., 2005). This region has also been identified as being consistently activated during Stroop paradigms (Laird et al., 2005). In addition, although ALFF is strongly associated with metabolic rate (Tomasi et al., 2013), the precuneus shows the highest metabolic rate (Cavanna and Trimble, 2006) and a decline in metabolic rate in this area has been associated with cognitive decline in the elderly (Buckner et al., 2005). Thus, we hypothesized that the precuneus is the strongest candidate, of the fALFF correlates with Stroop performance. As for DC, the only published relevant study showed that working memory performance and general intelligence are associated with DC in DLPFC (Cole et al., 2012). This area is also involved with cognitive control, which plays a critical role in working memory and Stroop performance and is consistently activated with these 2 paradigms (Cole et al., 2012; Laird et al., 2005; MacDonald et al., 2000; Owen et al., 2005). Furthermore, while DLPFC is associated with top-down cognitive control over other cognitive processes (MacDonald et al., 2000), it is also involved in the control of activation in a number of other areas (Miller and Cohen, 2001). DC in the DLPFC is thought to represent the influence of this area over other areas and may be particularly relevant to the control process for this area (Cole et al., 2012). Thus, we hypothesized that DLPFC is the strongest candidate of DC correlates of Stroop performance. However, the areas that are activated during the tasks may be less relevant to rsfMRI measures as described above; areas whose activities are specifically critical to the execution of Stroop tasks, such as ACC and IFJ (Laird et al., 2005; Nee et al., 2007), may also be associated with these fALFF/DC measures and are less viable candidates. As described, fALFF and DC can provide unique information such as global influence and magnitude of intrinsic activity. Compared with the VBM method that we previously employed, the rsfMRI measures also are considered to reflect cognitive and neural mechanisms ongoing at rest (Takeuchi et al., 2012a) and may be more relevant to the default state attention and vigilant state. Although fALFF and rGMV may reflect the neural properties of one particular area, they have different characteristics and offer a different topology (Ren et al., 2013). And fALFF and DC are shown to be altered in a number of clinical disorders. Thus, revealing whether and how they are associated with representative attention measures is an important neuroscientific topic.

Methods

Subjects

The present study, which is a part of an ongoing project to investigate the association between brain imaging, cognitive function, and aging, included 958 healthy, right-handed individuals (531 men and 427 women). In our previous study, data from 63 subjects enrolled in the present study were used to investigate the association between Stroop interference and gray and white matter structures together with the data from 55 other subjects (Takeuchi et al., 2012b). Psychological tests and MRI scans that are not described in this article were performed in this experiment/project together with the psychological tests and MRI scans that are described in this article. The mean age of the subjects was 20.8 years [standard deviation (SD), 1.8]. All subjects were university students or postgraduates with normal vision and no history of neurological or psychiatric illness. Handedness was evaluated using the Edinburgh Handedness Inventory (Oldfield, 1971). Written informed consent was obtained from each subject for their participation in this project. All study procedures were approved by the Ethics Committee of Tohoku University.

Similar to most of the studies of this kind, we did not control the menstrual cycle of the female participants. Thus, the present associations in females are those of the average among the various stages of the menstrual cycle. The sensitivity of our findings may be reduced if menstrual cycles affect cognitive performance and resting state fMRI measures that are associated with cognitive performance in a different manner.

Subjects were instructed to get sufficient sleep, maintain their conditions, eat sufficient breakfast, and to consume their normal amounts of caffeinated foods and drinks in the day of cognitive tests and MRI scans. In addition, subjects were instructed to avoid alcohol the night before the assessment. As for mediation, routinely taking certain drugs such as antipsychotics was a study exclusion criterion. However, daily drugs such as anti-allergy drugs were not prohibited.

Stroop task (matching type)

For the Stroop task, we used Hakoda's version (Hakoda and Sasaki, 1990), which is a Japanese test and matching-type that we have used previously (Takeuchi et al., 2012b). As described in our previous study

(Takeuchi et al., 2012b), unlike the oral naming-type Stroop tasks, in the matching-type Stroop task (writing), subjects had to choose and write down as many appropriate answers as possible from five options. This type of task is rather close to the button-pressing matching-type Stroop tasks used in neuroimaging studies (e.g., Langenecker et al., 2004), and it enables the measurement of subjects' performance correctly. The task consists of two control tasks (Word–Color task, Color–Word task), a reverse Stroop task, and a Stroop task.

In the Word–Color task, a color name (e.g., "blue") is presented in the leftmost column. In addition, five columns are painted with five different colors and subjects have to check the column whose color corresponds to the color name in the leftmost column. In the Color–Word task, the leftmost column is painted with a color, and five other columns contain color names. The subjects have to check the column with the word corresponding to the name of the color painted in the leftmost column. In the reverse Stroop task, in the leftmost column, a color name is printed in another color (e.g., "blue" is printed in green) and five other columns are painted in five different colors. The subjects have to check the column whose color corresponds to the color name in the leftmost column. In the Stroop task, in the leftmost column, a color name is printed in another color (e.g., "blue" is printed in green) and five other columns contain color names. The subjects have to check the column with the word corresponding to the name of the color in which the word in the leftmost column is printed. During each task, the subjects were instructed to complete as many tasks as possible in 1 min. Each recorded task was preceded by a practice task that consisted of 10 problems (maximum) in 10 s. Four tasks were performed in a fixed order, but the order of the task did not affect the performance of each task (Hakoda and Sasaki, 1990). Performance of the four tasks has high test–retest reliability ($r = 0.695$–0.824) (Hakoda and Sasaki, 1990).

The two independent measures, reverse Stroop interference rate and Stroop interference rate, are calculated as follows:

Reverse Stroop interference = (correct answers on the Word–Color task − correct answers on the reverse Stroop task)/(correct answers on the Word–Color task) × 100.

Stroop interference = (correct answers on the Color–Word task − correct answers on the Stroop task)/(correct answers on the Color–Word task) × 100.

Reverse Stroop interference means the slowing of an output when subjects have to provide the meaning of a word when there is a conflict between the meaning of the word and its printed color.

While Stroop interference is observed in both oral naming- and matching-type Stroop tasks, reverse Stroop interference is observed only in matching-type Stroop tasks (Flowers, 1975; Pritchatt, 1968). Stroop interference and reverse Stroop interference rates, which are both measured by Hakoda's version, are high in patients with schizophrenia (Sasaki et al., 1993). In contrast, while the Stroop interference rate shows an age-related increase after subjects reach their early 20s, the reverse Stroop interference rate shows an age-related decrease (Sasaki and Hakoda, 1985).

Data from five subjects, who misunderstood the rules of the tasks involved in calculation of reverse Stroop interference rate, as well as data from 3 subjects who misunderstood the rules of the tasks involved in calculation of Stroop interference rate were not included in the analyses involving those tasks. There were no quantitative indices used to assess subject understanding of the task. However, if they misunderstood the rules of the task itself, they would give only a few correct responses in this task and their misunderstanding would become obvious.

Assessment of psychometric measures of general intelligence

Raven's Advanced Progressive Matrix (Raven, 1998) is a measurement that is most correlated with general intelligence and is considered to be the best measurement of general intelligence (Raven, 1998). Raven's Advanced Progressive Matrix was used to assess intelligence and adjust for the effect of general intelligence on resting-state fMRI measures (Song et al., 2008), because this test is thought to be the best measure of general intelligence. More detailed information about how this test was performed in our study is described in previous studies (Takeuchi et al., 2010a,b).

Image acquisition

All MRI data acquisition was conducted with a 3-T Philips Achieva scanner. As in our previous study (Takeuchi et al., 2012a), 34 transaxial gradient-echo images (64 × 64 matrix, TR = 2000 ms, TE = 30 ms, flip angle = 70°, FOV = 24 cm, slice thickness = 3.75 mm) covering the entire brain were acquired using an echo planar sequence for resting state fMRI analyses. 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 (Damoiseaux et al., 2006; Greicius et al., 2003).

To avoid motions, pads and magic tapes were used and subjects were given thorough instructions to prevent motion during the scan and explanations as to why motions are not preferable as well as the instruction that excessive motion would lead to the re-scan.

We did not exclude any subject from the analyses based on excessive motion during the scan. The subjects were young adults and the scan did not last long. Furthermore, the maximum movement from the original point in each direction was <3.75 mm (voxel size of one voxel, Table 1).

Pre-processing of functional imaging data

Preprocessing of imaging data was performed using SPM8 implemented in Matlab and SPM8's extension software DPARSF (Data Processing Assistant for Resting-state fMRI).

For each subject, the first image of a series of BOLD images was skull stripped by masking the images using the threshold of a given signal intensity from the spatially smoothed (using 8 mm FWHM) BOLD images. This skin–skull-stripping procedure was performed so that these parts were not treated as the outer edge of the brain parenchyma in the preprocessing procedures. Furthermore, the skull-stripped BOLD image was coregistered to a previously created custom made skull-stripped EPI template (Takeuchi et al., 2014b). The series of BOLD images for each session for each subject were slice timing corrected and realigned using DPARSF. The series of BOLD images for each subject were segmented and normalized using the previously described method (Takeuchi et al., 2014b) that modified the diffeomorphic anatomical

Table 1
The average, range, and SD of age, Raven's Advanced Progressive Matrix score, reverse Stroop interference rate, Stroop interference rate, volume level framewise displacement, and maximum movement from the origin in each direction among the subjects of this study.

Measure	Mean	Range	SD
Age	20.7	18–27	1.8
Raven's Advanced Progressive Matrix	28.5	15–36	3.8
Reverse Stroop interference rate (%)	14.8	−34.0–60.7	9.4
Stroop interference rate (%)	6.7	−25.0–46.0	8.8
Volumewise framewise displacement[a]	0.1647	0.1021–0.4133	0.0414
Maximum motion from the origin in the *x* direction (mm)	0.2767	0.1087–0.9185	0.1119
Maximum motion from the origin in the *y* direction (mm)	0.1486	0.0344–1.572	0.1311
Maximum motion from the origin in the *z* direction (mm)	0.3852	0.0739–3.568	0.3431

[a] Framewise displacement calculated by the method of Power et al. (2012).

registration through exponentiated lie algebra (DARTEL) (Ashburner, 2007) to give images with 3.75 × 3.75 × 3.75 mm^3 voxels. A detailed description of the procedures is presented in the Supplemental Methods. In this process, a custom template was also created (Takeuchi et al., 2014b), and the whole brain mask, which consists of voxels that show gray matter tissue probability + white matter tissue probability + cerebrospinal fluid (CSF) tissue probability, >0.1, the mask of the areas that are likely to be white matter (white matter tissue probability >0.99, to avoid contamination of signals from white matter), the mask of the areas that are strongly likely to be CSF (CSF tissue probability >0.99, to avoid the contamination of signals from other tissues) were created from the custom template.

The basis for not using T1-weighted structural images for the abovementioned normalization procedure has been previously described (Takeuchi et al., 2014b). This is merely because the shape of these images is apparently different from that of BOLD images (see extensive explanations for this problem, Takeuchi et al., 2011a). Moreover, coregistration of 3 T MRI BOLD images to T1-weighted structural images does not allow accurate segmentation, normalization, and signal extractions that take advantage of DARTEL-based procedures, as long as it relies on linear registration, because the two images are morphologically different.

The normalized series of BOLD images were processed by DPARSF for individual level analysis. First, 26 nuisance covariates including the mean timecourse of signals from the voxels within the white matter mask, the mean timecourse of signals from the voxels within the CSF mask, and Friston 24 motion parameters. The Friston 24-parameter model (i.e., six head motion parameters, six head motion parameters one time point before, and the 12 corresponding squared items) (Friston et al., 1996b) was used to regress out head motion effects. Recent work indicates that regressing out Friston 24-parameters is more effective than other movement correction methods, such as correction for rigid-body using six parameters, derivative 12 parameters, voxel-specific 12 regressors (Chao-Gan et al., 2013). To further rule out the residual effect of motion on rsfMRI measures, volume-level mean framewise displacement was computed and used at the second-level analyses as covariates (Power et al., 2012).

There is a fierce recent controversy regarding whether the mean timecourse of whole brain should be regressed out in the rsfMRI analysis (Takeuchi et al., 2012a). Regressing out the mean timecourse of whole brain may have merits (Chao-Gan et al., 2013) as well as weaknesses (Murphy et al., 2009). Considering this controversy, for fALFF, we performed both analyses of images in which mean timecourse of whole brain is regressed out and analyses of images in which mean timecourse of whole brain is not regressed out. For DC, we did not regress out the mean timecourse of whole brain because it partly reflects global brain activity (Schölvinck et al., 2010), and conceptually, regressing out mean timecourse of whole brain is particularly problematic for calculating DC, which is the correlation between one voxel and the rest of the whole brain. However, just to be sure, we checked how the results of this study were when mean timecourse of whole brain is regressed out in individual analyses. There were neither significant results nor tendencies (at the level of $P < 0.1$, corrected) for association between Stroop interference and DC when the mean timecourse of whole brain is regressed out at the first level of analysis. The remaining procedures for group level multiple regression analyses were performed as described below.

The processed images were spatially smoothed with 8-mm FWHM, and the resultant images were masked with the whole brain mask that was created as described above.

Individual-level functional imaging data analysis for DC/fALFF

The fALFF analyses were performed using the DPARSF software as previously described similarly (Han et al., 2011; Wang et al., 2011). The time series of each voxel was transformed into the frequency domain, and the power spectrum was obtained. Because the power of a given frequency is proportional to the square of the amplitude of that frequency component, the square root was calculated at each frequency of the power spectrum, and the average square root was then obtained across 0.01–0.08 Hz at each voxel. This average square root was taken as ALFF. For fALFF, as described previously (Chao-Gan and Yu-Feng, 2010; Wang et al., 2012), a ratio of the power of each frequency at a low frequency range to that of the entire frequency range (fALFF) was computed. Specifically, after preprocessing, the time series for each voxel was transformed into the frequency domain without band-pass filtering. The square root was calculated at each frequency of the power spectrum. The sum of the amplitudes across 0.01–0.08 Hz was divided by that of the entire frequency range.

After preprocessing, the fMRI data were temporally band-pass filtered ($0.01 < f < 0.08$ Hz) to reduce low frequency drift and high frequency. Furthermore, weighted DC measures were calculated using DPARSF, as previously described similarly (Wang et al., 2014). In brief, Pearson correlation coefficients were first computed between the time series of all pairs of gray matter voxels, leading to a whole-brain functional connectivity matrix for each individual. We calculated that in the areas of gray matter signal >.2 in the aforementioned gray matter template is consistent with previous studies (Wang et al., 2014). Individual correlation matrices were transformed into a Z-score matrix using Fisher's r-to-z transformation to improve normality. We further computed weighted DC strength of a voxel as the sum of the connections (Z-values) between a given voxel and all other voxels. As has been performed elsewhere (Buckner et al., 2009), we conservatively restricted our analysis to positive correlations above a threshold of $r = 0.25$. A relatively higher threshold was chosen to eliminate counting the voxels with weak correlations attributable to signal noise. Changing the threshold to $r = 0.20$ or $r = 0.30$ changed little the mean betas of the clusters of significant association between DC and Stroop interference, which were reported in the Results section. Finally, standardized weighted DC maps were acquired by subtracting the mean value within the abovementioned gray matter mask, and then dividing by the standard deviation of whole gray matter mask (Yan et al., 2013). Voxels with higher DC values reflect the sum of the connections for a given voxel and all other voxels, and are thus indicative of their central roles in transferring information across brain regions. z-Standardization was performed only for DC measures. A previous study suggested the importance of application of z-standardization to rsfMRI measures to mitigate the association between motion and rsfMRI measures. However, such effects of z-standardization were not statistically clear in the case of fALFF when other methods to mitigate the effects of motion were also performed (see Supplemental Fig. S7 of Chao-Gan et al., 2013).

Second-level statistical analysis

We performed four multiple regression analyses to test the relationship between the two types of Stroop interference (reverse Stroop interference or Stroop interference) and two types of resting-state fMRI measures (DC/fALFF). We performed separate multiple regression analyses for reverse Stroop interference and Stroop interference because the two interferences may partly have been of the same fundamental nature and correcting one interference with the other in multiple regression analysis may have been inappropriate. Biological Parametrical Mapping (Casanova et al., 2007) implemented in SPM5 allowed the use of these voxel-wise multiple regression analyses by including images representing regional values as covariates. The analyses were performed using this software. Analyses were performed with sex, age, Raven's Advanced Progressive Matrix score, volume-level mean framewise displacement that is calculated according to the previous study (Power et al., 2012) and performance of the control task for each interference (number of correct answers on the Word–Color task for the analysis of reverse Stroop interference and the number of correct answers on the Color–Word task for the analysis of Stroop interference)

the signal intensities of preprocessed regional gray matter density (rGMD) at each voxel (for details of the inducement of this measure, see Takeuchi et al., 2014b), as additional covariates. The movement related parameter was used due to the concern for the effect of movement during the scan on resting-state fMRI measures (Fair et al., 2012). Control task performance was included as a covariate to correct the effects of task execution speed on Stroop interference. For example, if lower (simple) task execution speed itself allows one to deal with the Stroop task relatively easily (or make it more difficult to deal with Stroop effects), then we would like to remove the effects.

Regions of significance were inferred using cluster-level statistics (Friston et al., 1996a). Only clusters with a $P < 0.05$ after correcting for multiple comparisons (controlling for family-wise error) at the cluster size with a voxel-level cluster-determining threshold of $P < 0.0025$, uncorrected in the T contrasts, were considered statistically significant in this analysis.

We did not consider it to be theoretically accurate (or at least necessary) to correct for the effects of the mood states of anxiety and depression in the abovementioned multiple regression analyses. Our rationale for this decision was that if certain moods affect cognitive functions and brain resting state activities, then such moods are important and essential sources of association between cognitive functions and resting state activity. And fALFF/DC correlates of Stroop performance that are affected by moods or other factors were also included in our analytic aims for this study. However, we did capture data on mood state profiles (McNair et al., 1992) in this project (for details, see Takeuchi et al., 2013). Such data were available for 939 subjects. Even if these measures are included in the multiple regression analyses, inclusion of mood state of anxiety and depression on the day of the experiment had little effect on the strength of the association found for fALFF/DC. If these factors are included in the multiple regression analytical models in this study, the mean beta values of the association between Stroop interference and fALFF/DC of the significant clusters that were identified in the Results section either slightly increase or are almost unchanged in every case. These results suggest that the effects of the mood states of anxiety and depression experienced on the day of the experiment did not affect the present findings.

We did not report any results on the sex-specific effects of the association between Stroop interference and rsfMRI measures in this study because there were not any hypotheses or backgrounds with which to evaluate this association. However, for the interest of readers, we tested the interaction effects between Stroop interference and sex on fALFF/DC and found no significant interactions. We followed the method from a previous study for the construction of the models and contrast (for details, see Takeuchi et al., 2014b). In brief, in these test of interaction effects, we used the function of ANCOVA in SPM8, since BPM cannot be used to model the interaction effects in ANCOVA. Covariates and methods of correction for multiple comparisons were the same as those for the other multiple regression analyses in this study except for sex, which was a group factor in ANCOVA, and rGMD at each voxel, since BPM could not be used.

Investigation of the specificity of fALFF/DC correlates of Stroop performance when compared with those of verbal working memory performance

Although the purpose of this study was to investigate fALFF/DC associated with Stroop performance, it is interesting and informative to see the specificity and overlaps of the resting-state fMRI correlates of Stroop performance when compared with resting-state fMRI correlates of other cognitive control or attention-related cognitive measures. This is because functional activation paradigms have demonstrated that Stroop paradigms demonstrate activation that are partly overlapped with and partly distinct from other cognitive control or attention-related cognitive paradigms (Derrfuss et al., 2004, 2005; Liu et al., 2004; Verbruggen et al., 2004).

For this purpose, we compared the specificity of DC/fALFF correlates of Stroop performance with DC/fALFF correlates of a verbal working memory task. For measuring verbal working memory, we used a computerized visual digit span task (for details of methods, see Takeuchi et al., 2011a). We performed a multiple regression analysis that included age, sex, volume-level mean framewise displacement in the resting-state fMRI session, and the verbal working memory task as independent variables. The same statistical threshold as those used in the analyses of Stroop interference was used. Further, we performed small volume correction (SVC) using voxel level correction for multiple comparisons using family wise error (FWE) among the significant clusters of correlates of Stroop interference in corresponding image types.

Investigation of the correlation of fALFF/DC with Stroop performance in anatomically defined, confined regions of interest in multiple samples

Next, we separated the samples into 2 groups by alternating assignment based on sequential study ID (478 subjects and 477 subjects) and performed the regions of interest approach on these two samples. The rationale for this exercise was to confirm the consistency of our hypotheses.

For fALFF, in accordance with our hypothesis as described in the Introduction, we tested if Stroop interference correlates with fALFF in the precuneus. The statistical design was the same as was described in the Second-level statistical analysis section. The mask of the precuneus for the region of interest analysis was constructed using the image of the precuneus with the Talairach Daemon option (Lancaster et al., 2000) of the WFU PickAtlas Tool (http://www.fmri.wfubmc.edu/cms/software#PickAtlas) (Maldjian et al., 2003, 2004).

For DC, in accordance with our hypothesis as described in the Introduction, we tested if Stroop interference correlates with DC in the bilateral DLPFCs. ROIs for bilateral DLPFCs were constructed in accordance with our previous studies and those from other laboratories (Song et al., 2008; Takeuchi et al., 2012a, 2014b).

For these areas with strong a priori hypotheses, the statistical significance level was set at $P < 0.05$, with a small volume correction (SVC) for multiple comparisons (family-wise error) in the regions of interest. This analysis corresponds to a form of region of interest analysis that is well established (Poldrack, 2007).

Results

Behavioral data

Average, SD, minimum and maximum of age, Raven's Advanced Progressive Matrix score, reverse Stroop interference rate, Stroop interference rate, and motion related parameters were presented in Table 1. The distribution of reverse Stroop interference and Stroop interference in our sample is provided in Table 2.

Correlation between fALFF and Stroop interference

After controlling for age, sex, Raven's Advanced Progressive Matrix score, framewise displacement during the resting-state fMRI session and performance on the Color–Word task, multiple regression analysis revealed that the Stroop interference rate was significantly and negatively correlated with fALFF (when global signal is regressed out in individual analyses) in the anatomical cluster around the caudal part of the DLPFC, the area around the left Rolandic operculum, areas in the left superior occipital lobule and the left inferior occipital lobule, areas in the precuneus, and the area in the right inferior parietal lobule (Fig. 1, Table 3). The tendencies were seen across wide-spread areas of the dorsal attention network (Luo et al., 2010) regardless of the hemispheres (Supplemental Fig. 1).

The analyses with the same covariates revealed that Stroop interference rate was not significantly correlated with fALFF

Table 2
Distribution of reverse Stroop interference and Stroop interference in our sample.

	$x \leq -20$	$-20 < x \leq -10$	$-10 < x \leq 0$	$0 < x \leq 10$	$10 < x \leq 20$	$20 < x \leq 30$	$30 < x \leq 40$	$40 < x \leq 50$	$50 < x$
Reverse Stroop interference (%)	3	8	28	240	451	166	43	11	3
Stroop interference (%)	5	21	198	436	233	52	8	2	0

(when global signal is not regressed out in individual analyses). Though, the tendencies were seen in similar areas.

Correlation between degree centrality and Stroop interference

After controlling for age, sex, Raven's Advanced Progressive Matrix score, framewise displacement during the resting-state fMRI session and performance on the Color–Word task, multiple regression analysis revealed that Stroop interference rate was significantly and negatively correlated with degree centrality (when global signal is not regressed out in individual analyses) in the anatomical cluster that spread across the left dorsolateral prefrontal cortex and the left ventrolateral cluster, the area around the left inferior frontal junction and the area in the left inferior parietal lobule (Fig. 2, Table 4). The same tendencies were seen in the right homologue areas, too (Supplemental Fig. 2).

Correlation between fALFF/degree centrality and reverse Stroop interference

After controlling for age, sex, Raven's Advanced Progressive Matrix score, framewise displacement during resting-state fMRI session and performance on the Word–Color task, multiple regression analysis revealed that the reverse Stroop interference rate was not significantly correlated with fALFF nor degree centrality regardless of global signal is regressed out or not. This lack of associations between individual differences and reverse Stroop interference is consistent with our previous study (Takeuchi et al., 2012b).

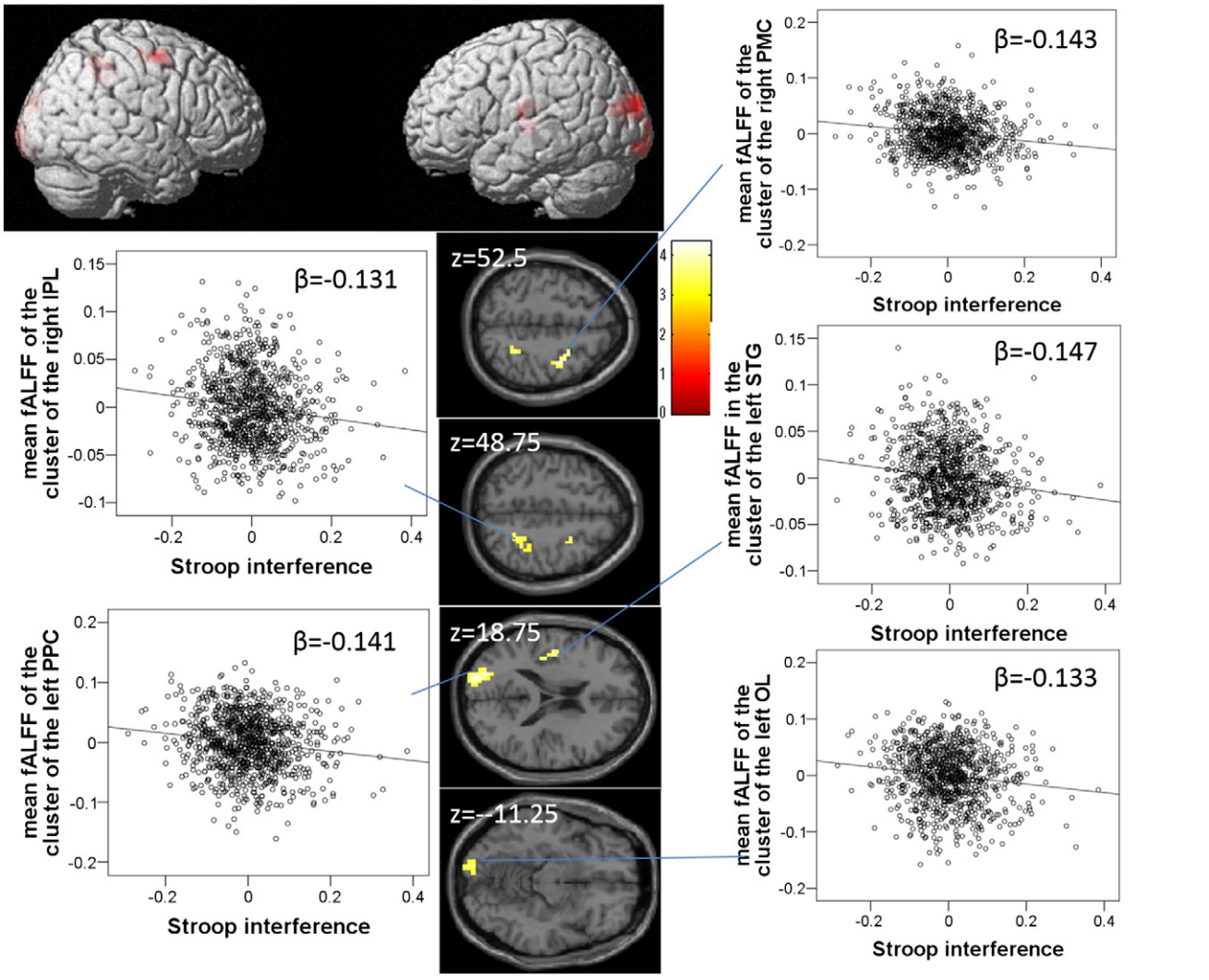

Fig. 1. Regions of correlation between Stroop interference and fractional amplitude of low frequency fluctuations (fALFFs) when global signal is regressed out. Results are shown with $P < 0.05$, corrected for multiple comparisons at the cluster-level using false discovery rate (FDR) with an underlying voxel-level of $P < 0.001$, uncorrected. Regions of significant negative correlations between Stroop interference and fALFF are seen in various regions of the dorsal attention network. Panels show residual plots with trend lines depicting the correlations between residuals in the multiple regression analyses, with the mean fALFF in the significant clusters as dependent variables, and Stroop interference and other confounding factors as independent variables.

Table 3
Brain regions with significant negative correlations between fractional amplitude of low frequency fluctuations (fALFFs) when global signal is regressed out and the Stroop interference rate.

	Area		x	y	z	T score	Raw cluster size (mm^3)	Corrected P value (cluster, FDR)
1	Middle frontal gyrus/preccentral gyrus	R	37.5	−3.75	56.25	4.34	1371	0.047
2	Rolanding operculum/insula	L	−41.25	−11.25	15	4.34	1582	0.047
3	Superior occipital lobule/precuneus	L	−18.75	−93.75	22.5	4.19	3639	0.001
4	Inferior parietal lobule/precuneus	R	26.25	−48.75	52.5	3.71	1529	0.047
5	Inferior occipital lobule/superior occipital lobule	L	−15	−97.5	−11.25	3.63	1424	0.047

Investigation of the specificity of the fALFF/degree centrality correlates of Stroop performance when compared with those of verbal working memory performance

To investigate the specificity of the fALFF/degree centrality correlates of Stroop performance when compared with those of verbal working memory performance, we investigated fALFF/degree centrality correlates of verbal working memory performance. After controlling for age, sex, and framewise displacement during the resting-state fMRI session, verbal working memory performance did not correlate with degree centrality or fALFF regardless of whether global signal is regressed out or not. We then investigated whether verbal working memory performance correlated with fALFF (when global signal is regressed out in individual analyses) within the areas of the significant clusters of negative correlations between Stroop interference and fALFF as well as whether verbal working memory performance correlated with degree centrality (when global signal is not regressed out in individual analyses) within the areas of significant clusters of negative correlations between Stroop interference and degree centrality ($P < 0.05$, corrected for multiple comparisons at voxel-level FWE, SVC). No significant results were found in these analyses.

Investigation of the correlation of fALFF/DC with Stroop performance in anatomically defined confined regions of interest in multiple samples

As for fALFF, in the first sample, a multiple regression analysis revealed that the Stroop interference rate was significantly and negatively correlated with fALFF when the global signal is regressed out in individual analyses in the precuneus (x, y, z = 26.25, −71.24, and 18.75, respectively; t = 4.04; and P = 0.039 with correction for FWE at the voxel level within the precuneus). In the second sample, a multiple regression analysis revealed that there were no significant correlations between Stroop interference rate and fALFF when the global signal is regressed out in individual analyses. However, when SVC was analyzed within the area of the significant negative correlations in the first sample, there was a significant negative correlation (x, y, z = 26.25, −71.25, and 18.75, respectively; t = 2.27; and P = 0.012 when corrected for FWE at the voxel level within the precuneus).

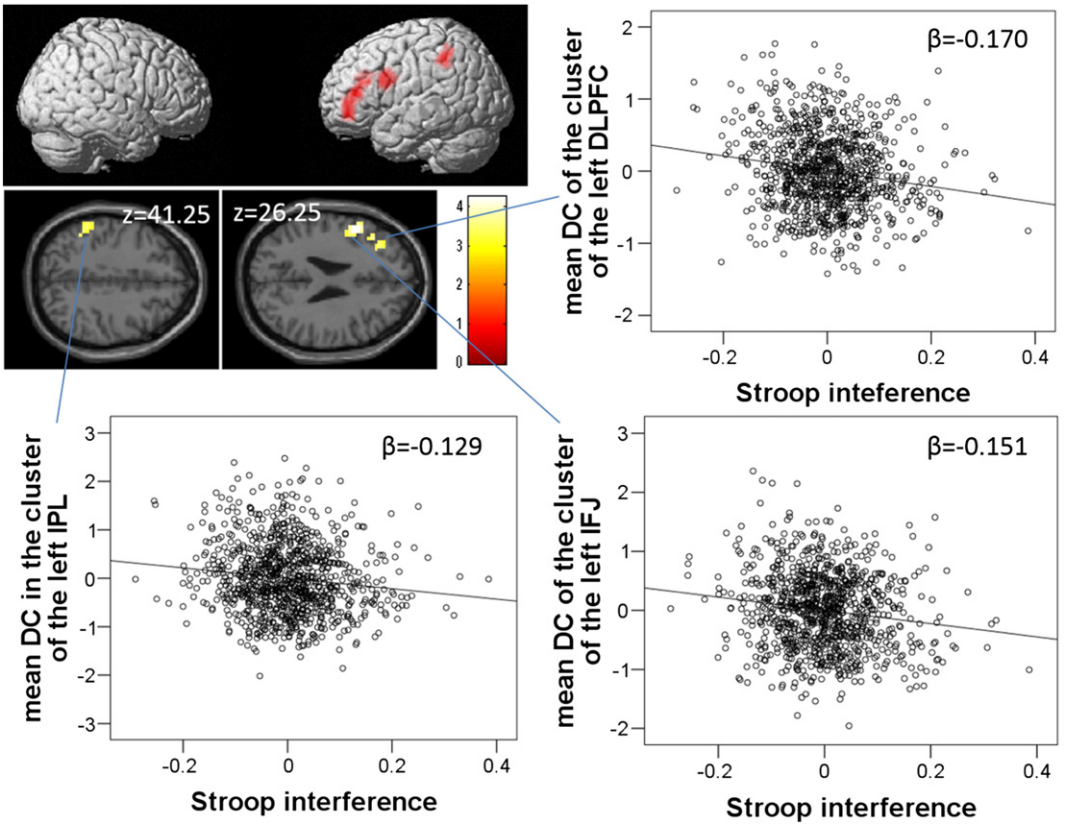

Fig. 2. Regions of correlation between Stroop interference and degree centrality when global signal is not regressed out. Results are shown with $P < 0.05$, corrected for multiple comparisons at the cluster-level using false discovery rate (FDR) with an underlying voxel-level of $P < 0.001$, uncorrected. Regions of significant negative correlation between Stroop interference and degree centrality are seen in the anatomical cluster involving the left dorsolateral prefrontal cortex and the left ventral lateral prefrontal cortex, the area in the left inferior frontal junction, and the area in the inferior parietal lobule. Panels show residual plots with trend lines depicting the correlations between residuals in the multiple regression analyses, with mean degree centrality in the significant clusters as dependent variables, and Stroop interference and other confounding factors as independent variables.

Table 4
Brain regions with significant negative correlations between degree centrality when global signal is not regressed out and the Stroop interference rate.

	Area		x	y	z	T score	Raw cluster size (mm^3)	Corrected *P* value (cluster, FDR)
6	Inferior frontal gyrus	L	−52.5	11.25	26.25	4.25	2479	0.005
7	Inferior frontal gyrus/middle frontal gyrus	L	−45	37.5	11.25	3.98	5326	<0.001
8	Inferior parietal lobule	L	−52.5	−45	48.75	3.64	1740	0.016

Analyses using the same covariates revealed that the Stroop interference rate was not significantly correlated with fALFF in either sample when the global signal is not regressed out in individual analyses. When the entire sample was used in the analysis, SVC in the precuneus revealed a significant negative correlation between the Stroop interference rate and fALFF when the global signal was regressed out in individual analyses ($x, y, z = 26.25, -71.25$, and 18.75, respectively; $t = 4.26$; and $P = 0.014$ when corrected for FWE at the voxel level within the precuneus) (Fig. 3).

As for DC, in the first sample, a multiple regression analysis revealed that the Stroop interference rate was significantly and negatively correlated with DC in the left DLPFC ($x, y, z = -45$, 45, and 11.25, respectively; $t = 3.12$; and $P = 0.023$ when corrected for FWE at the voxel level within the left DLPFC) and in the right DLPFC ($x, y, z = 45$, 41.25, and 30, respectively; $t = 3.64$; and $P = 0.004$ when corrected for FWE at the voxel level within the right DLPFC). In the second sample, a multiple regression analysis revealed that the Stroop interference rate was again significantly and negatively correlated with DC in the left DLPFC ($x, y, z = -48.75$, 30, and 22.75, respectively; $t = 3.54$; and $P = 0.005$ when corrected for FWE at the voxel level within the left DLPFC) and in the right DLPFC ($x, y, z = 56.25$, 22.50, and 26.25, respectively; $t = 3.64$; and $P = 0.004$ when corrected for FWE at the voxel level within the right DLPFC). When the whole sample was used in the analysis, SVC in the left DLPFC revealed a significant negative correlation between the Stroop interference rate and DC in the left DLPFC ($x, y, z = -45$, 45, and 11.25, respectively; $t = 3.47$; and $P = 0.007$ when corrected for FWE at the voxel level within the left DLPFC) (Fig. 4) and in the right DLPFC ($x, y, z = 56.25$, 22.5, and 26.25, respectively; $t = 3.63$; and $P = 0.007$ when corrected for FWE at the voxel level within the right DLPFC) (Fig. 4).

Discussion

Here we investigated the association between fALFF/DC and Stroop interference. Partially consistent with our hypothesis, the whole brain analysis revealed that reduced Stroop interference was associated with a larger DC in the left lateral prefrontal cortex, left IFJ, and left inferior parietal lobule. The region of interest analyses toward the areas of a strong a priori hypothesis revealed the consistent association between reduced Stroop interference and DC in the bilateral DLPFCs. On the other hand, the whole brain analysis revealed larger fALFF (when global signal is regressed out in individual analyses) in the right premotor cortex, left Rolandic operculum, left superior occipital lobule, left inferior occipital lobule, precuneus, and area in the right inferior parietal lobule. These were mostly not parts in the areas of our hypothesis, but rather mostly parts of the dorsal attention network during rest as described below. The region of interest analyses toward the areas of a strong a priori hypothesis revealed a consistent association between reduced Stroop interference and fALFF in the right precuneus. In contrast to previously reported Stroop paradigms (Nee et al., 2007), we could not obtain significant findings in the ACC in any of the analyses. But there were certain tendencies (Supplemental Fig. 1) and thus, due to the nature of the difficulty of the interpretation of lack of significant correlation in the whole brain analyses, we do not draw any conclusions from here. The verbal working memory performance did not show tendency of correlation in these areas in the similar manner and the findings seem somewhat specific to resolution of cognitive interference.

Present significant results of DC may be interpreted as ability to resolve cognitive interference is positively associated with the conditions that areas that play central roles in executive functions are functionally associated with the areas across the brain. Stroop interference rate was significantly and negatively correlated with degree centrality (when global signal is not regressed out in individual analyses) in the areas of the left dorsolateral prefrontal cortex, the left ventrolateral cluster, the left inferior frontal junction and in the left inferior parietal lobule. All of these regions are consistently activated by different types of Stroop tasks (Laird et al., 2005) and play central roles in certain executive functions. IFJ has distinctive roles from other lateral frontal regions (Brass et al., 2005). IFJ is strongly and consistently involved in task-switching paradigms, set-shifting paradigms, and Stroop paradigms (interference resolution) (Brass et al., 2005; Derrfuss et al., 2005). Thus, this region is probably consistently involved in cognition during

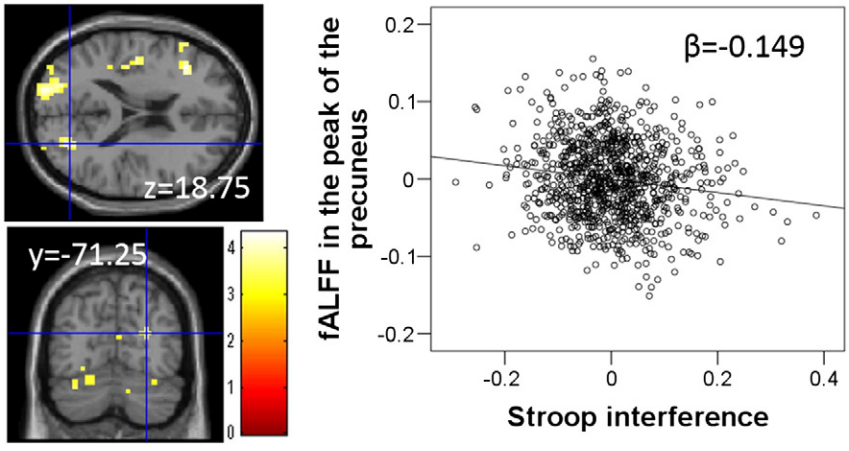

Fig. 3. A region of correlation between Stroop interference and fractional amplitude of low frequency fluctuations (fALFFs) when global signal is regressed out. Results are shown with $P < 0.005$, uncorrected for the visualization purpose. The significant region of negative correlations between Stroop interference and fALFF is seen in the right precuneus. The panel shows residual plots with the trend line depicting the correlations between residuals in the multiple regression analyses, with fALFF in the peak voxel as a dependent variable, and Stroop interference and other confounding factors as independent variables.

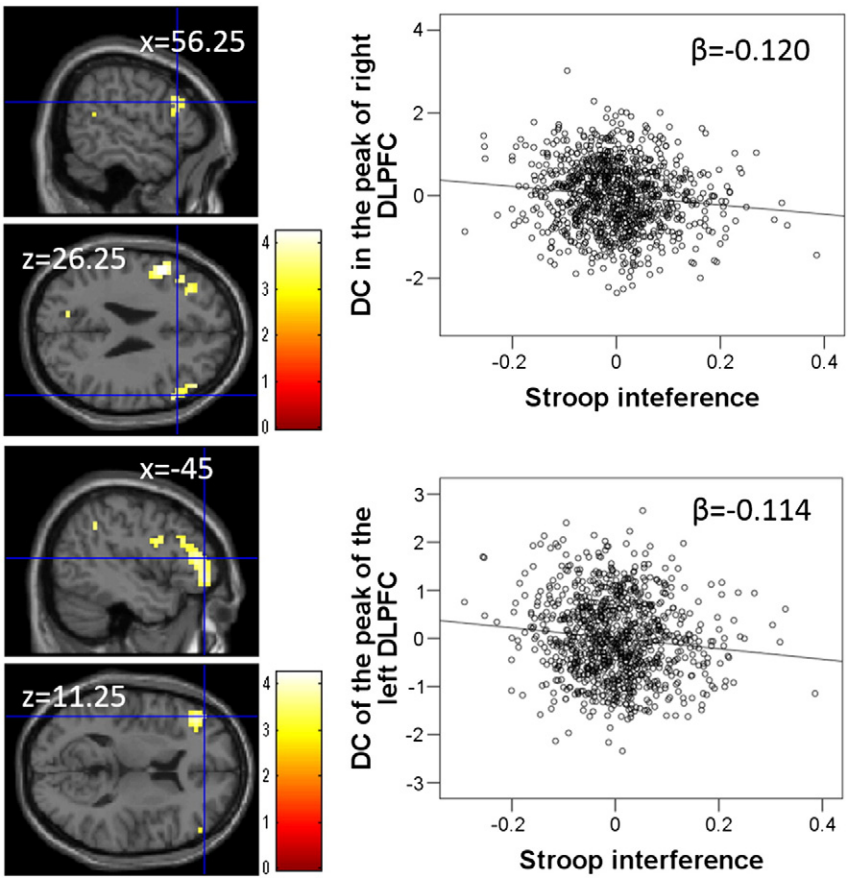

Fig. 4. Regions of correlations between Stroop interference and degree centrality when global signal is not regressed out. Results are shown with $P < 0.005$, uncorrected for the visualization purpose. The significant regions of negative correlations between Stroop interference and degree centrality are seen in the bilateral DLPFCs. Panels show residual plots with the trend line depicting the correlations between residuals in the multiple regression analyses, with the degree centrality in the peak voxel as dependent variables, and Stroop interference and other confounding factors as independent variables.

these paradigms such as resolution, mediation, and control of different and distinct information flows. And the regions around the inferior parietal lobule are activated in response to all types of executive functions (Wager and Smith, 2003). Further the DLPFC plays a key role in top-down executive control system and the DLPFC and areas in the ventral lateral prefrontal cortex plays a key role in the manipulation of information in the mind (Van Veen and Carter, 2002; Wager and Smith, 2003). Thus, we weakly speculate that perhaps, in subjects with lower Stroop interference, areas over the entire brain are functionally strongly connected with those systems and efficient task execution may become possible.

The present significant results for fALFF in the precuneus may be interpreted as resolving cognitive interference or achieving a better attentional state resulting in greater intrinsic activity in this area. As described in the Introduction, previous studies of ALFF have also shown associations between cognitive abilities related to attention or executive control with ALFF in a similar area (Xu et al., 2014; Zou et al., 2013). This area gathers externally and internally generated information from a wide range of areas and is believed to generate and be involved in higher order mental activity (Cavanna and Trimble, 2006). These activities include cognitive processes that operate strongly at rest, such as self-processing operations and perhaps self-consciousness, as well as visuospatial imagery. Moreover, this area has the highest metabolic rate in the region (Cavanna and Trimble, 2006) and a wide range of the neurological and psychiatric disorders that are characterized by cognitive deficits show declines in fALFF in this area (Cha et al., 2015; Shen et al., 2014; Turner et al., 2013). Considering these factors, reduced fALFF may reflect deficits in the cognitive processes as described above and may be a better indicator of the basic cognitive ability such as attentional integrity, which Stroop performance is believed to represent (MacLeod and MacDonald, 2000).

Other present significant results of fALFF may be interpreted as ability to resolve cognitive interference is positively associated with intrinsic activity of the dorsal attention network at default state. Significant negative correlation between Stroop interference and fALFF (when global signal is regressed out in individual analyses) in the anatomical cluster around the caudal part of the dorsolateral prefrontal cortex DLPFC, the area around the left Rolandic operculum, areas in the left superior occipital lobule and the left inferior occipital lobule, and the area in the right inferior parietal lobule. These regions are mostly included in the part of the dorsal attention network that is formed at rest (Luo et al., 2010). Further, the distribution of the negative correlation between Stroop interference and fALFF at the results at the threshold of $P < 0.01$, uncorrected is well matched with the areas of the dorsal attention network that is formed at rest (Luo et al., 2010). As fALFF can be considered to reflect magnitude of intrinsic brain activity (Chao-Gan and Yu-Feng, 2010; Zang et al., 2007), the present result of fALFF can be considered that the ability to resolve cognitive interference is associated with higher intrinsic activity of the dorsal attention network at default state. Further, the dorsal attention network is involved in the top-down control of attention or selection of stimuli (Corbetta and Shulman, 2002). Thus, we weakly speculate that perhaps, in subjects with lower Stroop interference the top-down control system is highly active even at default state, and can control attention and select the information in a top-down manner easily when necessary and through the function, they can solve cognitive interference easily.

As described in Methods, we believe regressing out global signals in calculation of DC does not make much sense. On the other hand, in this study, fALFF was associated with Stroop interference only when global signal is regressed out in individual analyses. This may be because since global signal reflects partly global brain activity and partly motion related factors (Schölvinck et al., 2010) and by removing these factors, the analyses may become sensitive to network or region specific brain activities (Chao-Gan et al., 2013).

Previously, researchers revealed the differences of fALFF/DC in psychiatric and neurological diseases as summarized below and the important step of this study is we revealed the source of individual differences of the measure related to attention and executive functions in a huge sample. Patients with schizophrenia, who are typically known for deficits in executive functions (Sasaki et al., 1993), show reduced ALFFs in the frontal and parietal areas (Ren et al., 2013) and reduced DC in the lateral frontal and parietal areas (Wang et al., 2014). Patients with mild cognitive impairment who are typically known for executive deficits (Traykov et al., 2007) show reduced fALFF in various areas including the lateral prefrontal cortex (Han et al., 2011) and reduced degree centrality in various areas including the lateral prefrontal cortex (Wang et al., 2013). Some studies investigated if these resting state measures correlated with cognitive functions (Mennes et al., 2011) and traits (Kunisato et al., 2011). But more and more studies reveal it requires a larger sample size in the whole brain analysis to reveal the robust correlates of individual differences. This study used a huge sample size and revealed robust correlates of attention and executive function-related measures in the areas involved in attention and executive functions. These findings suggest that fALFF/DC measures can be used to investigate individual differences. Further, the present findings may suggest that differences of these DC/fALFF measures in the abovementioned psychiatric and neurological diseases may underlie their executive deficits.

The previously reported increased rWMV in the dorsal part of the bilateral frontal lobe in subjects with lower Stroop interference may underlie increased DC in subjects with superior Stroop interference performance. Our previous structural study revealed that rWMV in the bilateral areas that extend along the dorsal part of the frontal lobe to the anterior part of the parietal cortex negatively correlates with Stroop interference rate (Takeuchi et al., 2012b). There is a relatively strong influence of genetic factors on psychometric intelligence and white matter volume, and these genetic factors appear to contribute to the association between psychometric intelligence and white matter volume (Posthuma et al., 2002). Furthermore, psychometric intelligence and RSFC are also correlated (Song et al., 2008) and there is a strong influence of genetic factors on RSFC (Posthuma et al., 2005). Thus, the same physiological factors may underlie rWMV and functional connectivity. The number of axon collateral spines and increased myelination are two of the factors that are thought to underlie increased white matter volume (Takeuchi et al., 2011b), and these may facilitate neural transmission in the area and may form increased functional connectivity. Alternatively, the increase in white matter fibers connecting to different brain regions may underlie the increased RSFC between different areas. Partly consistent with the notion that white matter structure underlies RSFC, a wide range of psychiatric diseases are characterized by white matter deficits and reduced white matter volume (Fields, 2008), and these diseases are also generally characterized by reduced RSFC (Broyd et al., 2009). Considering DC is the sum of the RSFC of the node and rest of the areas, wide spread increase of rWMV in subjects with superior Stroop performance may contribute to their higher DC.

Consistent with our previous structural study on Stroop interference, no significant associations were found between reverse Stroop interference and DC/fALFF. As described extensively in our previous study (Takeuchi et al., 2012b), this could be due to a number of reasons. First, it could have resulted from a lack of statistical power in the analysis of the reverse Stroop interference rate due to slightly lower test–retest reliabilities of the tasks used when calculating the reverse Stroop interference rate (Word–Color task and reverse Stroop task). Second, the lack of correlation could have resulted from the complex nature of the matching-type reverse Stroop interference rate. Reduced selective attention ability (non-preferable cognitive function) as well as facilitated visual processing (preferable cognitive function) may cause greater reverse Stroop interference (Hakoda and Sasaki, 1986), and there may have been substantial individual differences in these two cognitive functions among the subjects of this study. Furthermore, contrary to the matching-type Stroop interference rate and other cognitive functions, the matching-type reverse Stroop interference rate shows an age-related decrease (Sasaki and Hakoda, 1985). Similarly, our previous study showed that working memory using mental calculations increases reverse Stroop interference (Takeuchi et al., 2011c). However, reverse Stroop interference and Stroop interference rates both show increases in patients with schizophrenia (Sasaki et al., 1993).

In this study, we recruited 959 subjects, but the observed results are only marginally significant. It has been indicated that whole brain analyses tend to substantially overestimate the effect size in significant areas (Vul et al., 2009). Thus, the true effect size of the association between Stroop performance and rsfMRI measures may be very small. In comparison with previous studies, it is important to consider that this possibility does not mean that previous studies' true effect sizes are likely to be bigger than that identified in the present study. Vul et al. (2009) provide details on how this problem occurs even when true effects exist. It has also been shown that statistical power is typically very low in the field of neuroscience (Button et al., 2013). The consequences of this reality include overestimates of effect size and low reproducibility of results without whole brain analyses (Button et al., 2013). Even when single studies show a remarkable effect size, especially under low statistical power, the true effect size can be very small, as reported by (e.g., Murphy et al., 2012); thus, the importance of a large sample size has been stressed (Button et al., 2013). We believe that it was very important to use a relatively large sample size and that it increased the reliability of our results. The possible list of sources of a small effect size can be widely variable. One possibility is that the executive functions that are measured by Stroop tasks and properties of intrinsic activities have only minor relationships. However, at the same time, this does not necessarily prove that the effect size of the association between cognitive functions, which Stroop performance aimed to measure, and the properties of intrinsic brain activities are small. Another possibility is the low reliability of the resting state fMRI measures (Braun et al., 2012). Yet other possibility is partly related to the second possibility, in that even when the executive functions and intrinsic brain activities are strongly associated, differences in the conditions of subjects, normalization of brain images, random factors such as temperature, noise in the scanner, or the subject's specific thoughts in the scanner may, for solely random reasons, impact the association between the rsfMRI measures and intrinsic activities and potentially undermine the strength of the association between Stroop performance and rsfMRI measures. Therefore, we believe that these analyses cannot be used to truly reveal how strongly individual cognitive functions that cognitive measures are trying to measure, and individual neural properties that rsfMRI measures are trying to measure, associate.

This study had a few limitations that are common to our and other previous studies. First, as discussed in our previous studies (Takeuchi et al., 2011a), we used young healthy subjects with high educational backgrounds. Limited sampling of intellectual abilities is a common hazard when sampling from college cohorts (Jung et al., 2010; Song et al., 2008; Takeuchi et al., 2011a). On the other hand, our findings contrasted to the previous findings showing DC is associated with working memory performance as well as general intelligence using a small sample size ($N = 121$) (Cole et al., 2012), as well as fALFF and working memory performance ($N = 41$) (Zou et al., 2013). There may be a number of reasons for this discrepancy and one of them is this sample characteristics and our sample may not be sensitive to the individual differences of general cognitive abilities (Cole et al., 2012). The cohorts in these two studies

had a relatively larger age range, including middle age. Individual differences in cognitive abilities that are caused by the aging process instead of individual differences within young adults may be important factors that caused the previously observed associations between brain and working memory performance in the studies mentioned above. Whether our findings would hold across the full range of population samples and normal distributions must be determined with larger and more representative samples. Another possibility is the difference in the assigned task. The two studies mentioned above both used an N-back task to measure working memory performance, whereas we used a digit span task. N-back tasks require an upload of memory and have rather unique psychological characteristics compared with that of other working memory tasks (Kane et al., 2007). Second, as described in our previous study (Takeuchi et al., 2012b), in addition to the Stroop tasks used in this study, there are other types of Stroop tasks such as the counting Stroop task (Bush et al., 1998) and emotional Stroop task (Williams et al., 1996) as well as other response styles such as oral naming types. However, in the case of the (non-reverse) Stroop task, the difference in the psychological nature or associated brain regions in the matching and oral naming types is unknown, unlike the reverse Stroop effect (Hakoda and Sasaki, 1990). DC/fALFF associated with Stroop interference different from that used in the present study is yet to be investigated. In this study, we gathered 160 volumes for rsfMRI scans and it took about 5 min. Most of the recent rsfMRI cans have been done between 3 min and 11 min and our length was not the longer one (Birn et al., 2013). And it has been shown that reliability of rsfMRI measures increase substantially when scan length is increased from 5 min to 13 min (Birn et al., 2013). So, while the large number of sample size is the strength of this study, accuracy of each individual's data is assumed to have space to improve and this may be a limitation of this study. As for limitations of measures of fALFF/DC, fALFF has been claimed to indicate the magnitude of neural activity during rest (Chao-Gan and Yu-Feng, 2010; Zang et al., 2007; Zou et al., 2008). DC has also been claimed to reflect how much of the node influences the entire brain area and in integrating information across functionally segregated brain regions (Hagmann et al., 2008) or the degree to which the node functions as a cortical hub (Buckner et al., 2009). fALFF is also consistently shown to correlate well with the metabolic demand of the area (Tomasi et al., 2013). However, whether these measures truly and specifically reflect what they are claimed to reflect remains to be investigated. At the macro-level, most MRI measures have interrelations (Hugenschmidt et al., 2008; Takeuchi et al., 2014a) and macro-level MRI measures are suggested to reflect diverse micro-level brain processes (e.g., Jones et al., 2013). Like most MRI measures, research involving these measures started from the inducement and calculation, but their biological meaning remains to be verified in future studies.

In conclusion, the ability to resolve Stroop interference which was used as an index for attention integrity and executive functioning was associated with the higher magnitude of resting state brain activity in the precuneus and the areas of the dorsal attention network and higher functional connection with the global areas with the areas that play critical roles in executive functioning. These findings suggest that Stroop performance is reflected in resting state functional properties of these areas and the network. Further, the lack of correlation between fALFF/DC measures and working memory performance suggests that the observed findings is specific to Stroop performance and perhaps, there are certain cognitive differences that can relate to fALFF/DC and those that can't.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2015.06.058.

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