



Linking inter-individual differences in the conflict adaptation effect to spontaneous brain activity



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ABSTRACT

Conflict adaptation has been widely researched in normal and clinical populations. There are large individual differences in conflict adaptation, and it has been linked to the schizotypal trait. However, no study to date has examined how individual differences in spontaneous brain activity are related to behavioral conflict adaptation (performance). Resting-state functional magnetic resonance imaging (RS-fMRI) is a promising tool to investigate this issue. The present study evaluated the regional homogeneity (ReHo) of RS-fMRI signals in order to explore the neural basis of individual differences in conflict adaptation across two independent samples comprising a total of 67 normal subjects. A partial correlation analysis was carried out to examine the relationship between ReHo and behavioral conflict adaptation, while controlling for reaction time, standard deviation and flanker interference effects. This analysis was conducted on 39 subjects' data (sample 1); the results showed significant positive correlations in the left dorsolateral prefrontal cortex (DLPFC) and left ventrolateral prefrontal cortex. We then conducted a test-validation procedure on the remaining 28 subjects' data (sample 2) to examine the reliability of the results. Regions of interest were defined based on the correlation results. Regression analysis showed that variability in ReHo values in the DLPFC accounted for 48% of the individual differences in the conflict adaptation effect in sample 2. The present findings provide further support for the importance of the DLPFC in the conflict adaptation process. More importantly, we demonstrated that ReHo of RS-fMRI signals in the DLPFC can predict behavioral performance in conflict adaptation, which provides potential biomarkers for the early detection of cognitive control deterioration.

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Introduction

It is important for people to control thoughts and behaviors. However, individuals vary greatly in their control ability. For example, some people can control the impulse to smoke, whereas others cannot suppress their craving, despite being aware of the hazards of cigarettes. From the viewpoint of cognitive psychology, such variation represents individual differences in cognitive control. The main function of cognitive control is to accomplish goal-directed behaviors by monitoring interference or response conflict, and dynamically adjusting performance (Botvinick et al., 2001; Egner, 2011). Such dynamic adjustments can be studied via the “conflict adaptation effect” (Egner, 2007; Gratton et al., 1992; Tang et al., 2013), which is frequently observed in congruency tasks, such as the Eriksen flanker task (Eriksen and Eriksen, 1974).

In the flanker task, participants are required to respond to target stimuli while ignoring flanking stimuli that may suggest the same

response as the target (congruent trial, C) or an opposite response to the target (incongruent trial, I). Subjects typically respond more slowly to incongruent than to congruent trials, and the performance difference in terms of incongruent minus congruent trial reaction times (RTs) is a classic flanker interference effect. The conflict adaptation effect refers to the tendency in which the interference effect following an incongruent trial (II-IC) is smaller than that following a congruent trial (CI-CC) (Egner, 2007; Gratton et al., 1992; Tang et al., 2013). Task-based functional magnetic resonance imaging (fMRI) has been used to study the underlying neural basis of conflict adaptation. This has revealed strong links to the prefrontal cortex, especially the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (DLPFC). The ACC appears to be associated with the function of conflict monitoring (Botvinick et al., 2001, 2004; MacDonald et al., 2000), while the DLPFC is involved in attempts to resolve conflict by transiently amplifying neural representations of task-relevant information and/or suppressing the processing of irrelevant information (Biswal et al., 1995; Egner and Hirsch, 2005a; Posner and Dehaene, 1994; Zhang et al., 2012).

However, there are large individual differences in conflict adaptation. These differences have been used to explore specific cognitive

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and neural dysfunction in psychiatric patients (Kerns et al., 2005; Melcher et al., 2008). For example, a negative correlation has been found between the conflict adaptation effect and the schizotypal trait (Voelter et al., 2012). Examination of individual differences in conflict adaptation in normal subjects is helpful for understanding dysfunction (Egner, 2011), particularly for investigations of the neural markers of the schizotypal trait. However, only one study has examined individual variability in conflict adaptation and linked it with the functional activation of the ventrolateral prefrontal cortex (VLPFC) (Egner, 2011). To our knowledge, no study to date has used resting-state fMRI (RS-fMRI) to examine the intrinsic neural basis of inter-individual differences in conflict adaptation. Therefore, the present study attempted to explore the conflict adaptation effect using RS-fMRI.

RS-fMRI is a relatively new method that can be used to explore the intrinsic functional architecture of the brain based on measurements of spontaneous low-frequency fluctuations in the blood oxygenation level dependent signal (Biswal, 2012; Fox and Raichle, 2007; Raichle, 2010). This technique is useful for the examination of regional interactions that occur when a subject is not performing an explicit task (Fox et al., 2005). Numerous studies have shown that resting-state functional connectivity (RSFC) between brain regions is associated with individual differences in the performance of several different cognitive tasks (e.g., working memory task, Eriksen flanker task) (Hampson et al., 2006; Kelly et al., 2008; Seeley et al., 2007) in normal subjects. However, RSFC analysis can only provide information about synchronization between spatially distinct brain regions (Mennes et al., 2011). The results of studies that used a task-based fMRI method are representative of the local brain activations elicited by a certain task. More information may be provided by directly comparing the regional properties of intrinsic brain dynamics with existing task-based fMRI results. Regional properties can be analyzed using a regional homogeneity (ReHo) approach, which evaluates the temporal homogeneity of the time series of a given voxel compared to that of its nearest neighbors (Zang et al., 2004). It is a data-driven method, which does not require a priori selection of regions of interest (ROIs), so it can identify non-anticipated or transient task-related components (Zang et al., 2004). Studies have demonstrated that ReHo analyses can also be used to investigate the neural basis of individual differences in behavioral performance (Tian et al., 2012; Wang et al., 2011). For instance, Tian et al. (2012) found that the ReHo of RS-fMRI signals could predict subjects' performance in a stop signal task. This finding implies that the regional properties of intrinsic brain dynamics can be used to predict subjects' behavioral performance in cognitive tasks.

In the present study, we attempted to investigate the functional basis of individual differences in conflict adaptation by measuring the ReHo of RS-fMRI signals. The conflict adaptation effect was investigated via a letter flanker task which employed a 2×2 within-subject design, in which previous trial types (C, I) and current trial types (C, I) were the factors. The magnitude of the conflict adaptation effect was evaluated for each subject using the full previous \times current trial interference interaction term ([CI-CC]-[II-IC]) in the flanker task (Egner, 2011). Researchers have suggested that ReHo variation might reflect individual differences in cognition and behavior (Jiang et al., under review). In addition, studies have shown that "voxels within a functional brain area were more temporally homogeneous when this area was involved in a specific task" (Zang et al., 2004). Moreover, Smith et al. (2009) have shown that task-related activation of brain networks is mirrored in resting-state brain activity. Therefore, we speculated that voxels in regions subserving conflict adaptation (e.g., the ACC and/or DLPFC) might be more temporally homogeneous in the resting-state activity of individuals who presented greater conflict adaptation effects. That is to say, ReHo values in these regions should be significantly correlated with the conflict adaptation effect.

We incorporated a test-validation procedure to ensure the reliability of our findings (Berkman and Falk, 2013). Specifically, we collected behavioral and fMRI data from two independent samples. For sample 1,

we performed a brain-behavior correlation analysis to identify the regions associated with individual differences in conflict adaptation. Once we had identified the ROIs, we extracted the ReHo values of the ROIs from sample 2 and then performed a multiple linear regression analysis to explore the predictive capability of ReHo values in these ROIs for behavioral variability.

Materials and methods

Subjects

Sample 1 consisted of 39 undergraduates (17 women) aged 20–24 years (mean age of 21.1 years) from Southwest University in China. Two additional subjects were enrolled, but their data were excluded from analysis because of excessive head motion (which exceeded 2 mm in transition or 2° in rotation).

Sample 2 consisted of 28 undergraduates (13 women) aged 18–23 years (mean age of 20.7 years) from the same population. Two additional subjects were enrolled, but their data were excluded because of excessive head motion (which exceeded 2 mm in transition or 2° in rotation).

This study was approved by the institutional review board (IRB) at Southwest University, China. We had obtained appropriate ethics committee approval for the research reported. All of the subjects were right-handed, and had normal or corrected-to-normal vision. None of the subjects had any current or past neurological or psychiatric illness. Subjects gave written informed consent after the nature of the study had been explained and understood.

Experimental procedure

Firstly, each subject underwent a brief resting-state scan during which they were instructed to relax with their eyes closed. Subjects then completed a letter flanker task, which was presented using E-Prime software (Psychological Software Tools, Pittsburgh, PA, USA). In each trial, a line of five letters was presented: the central one was the target, and the remaining letters were the flankers. Four letters (S, H, N and P) were employed in the task, and each letter could be a target or a flanker. In the congruent trials, the flankers were identical to the target (for example, NNNNN), and in the incongruent trials, the flankers were mapped onto a different response hand to the target stimulus (for example, SSNSS). Participants were instructed to press the key corresponding to the central letter. Responses were made using one of four different fingers (left middle finger, left index finger, right index finger and right middle finger). The four responses corresponding to each letter were counterbalanced across the subjects. Specifically, for half of the subjects, S was mapped onto the left middle finger (D key), H was mapped onto the left index finger (F key), N was mapped onto the right index finger (J key) and P was mapped onto the right middle finger (K key). For the other half of the subjects, S, H, N and P were mapped onto the right middle finger (K key), the right index finger (J key), the left index finger (F key) and the left middle finger (D key) respectively.

The flanker task consisted of three blocks and each block comprised 97 trials. Stimuli were presented in a pseudorandom order in which the numbers of CC, CI, IC, and II trial sequences were counterbalanced. In order to control for repetition priming (Mayr et al., 2003) and "partial repetition" effects (Hommel, 2004), target and flanker stimuli were always alternated across trials. The order of a trial was as follows. After a 300-ms fixation display, the letter array was presented in the center of the screen for 200 ms. Then, a blank screen was presented for 1500 ms, during which period participants were instructed to press the corresponding key as quickly and as accurately as possible. After another blank screen, lasting for 1000 ms, the next trial started.

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