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RESEARCH PAPER

Structural Integrity in the Genu of Corpus Callosum Predicts Conflict-induced Functional Connectivity Between Medial Frontal Cortex and Right Posterior Parietal Cortex

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Abstract—Studies using the flanker task have reported that response conflict is detected by the medial frontal cortex (MFC). As a conflict alert system, the MFC shows enhanced functional communication with task-related regions. Previous studies have revealed individual differences in functional connectivity during cognitive task performance. However, the mechanisms underlying these individual differences remain unclear. In the current study, electroencephalography (EEG) was recorded while 30 subjects performed a flanker task that was modified to exclude feature integration and contingency learning. The diffusion tensor imaging (DTI) data were collected the day before the EEG session. FCz-P3/4 theta phase synchronization was used to measure functional connectivity between the MFC and posterior parietal cortex (PPC). Hierarchical regression analyses were used to assess the relationship between MFC-PPC conflict-induced theta phase synchronization and white matter integrity in significant regions derived from tract-based spatial statistics (TBSS) analysis. As expected, MFC-PPC theta phase synchronization was significantly enhanced during conflict, suggesting a conflict-induced functional connectivity. However, these findings were only found in the right hemisphere, which may be related to the asymmetrical role of the bilateral PPC in response conflict processing. Furthermore, hierarchical regression analyses revealed that 44% of individual variability in FCz-P4 conflict-induced theta phase synchronization could be explained by variations in axial diffusivity (AD) in the genu of the corpus callosum (gCC). These results demonstrated that structural integrity in the gCC predicts conflict-induced functional connectivity between the MFC and right PPC.

Key words: functional connectivity, structural connectivity, individual difference, phase synchronization.

INTRODUCTION

Conflict processing is the ability of humans to appropriately adjust behavior according to the environment and goal demands. Convergent evidence suggests that conflict processing is accomplished by collaboration between anatomically distributed cortical regions, including the medial frontal cortex (MFC), lateral prefrontal cortex (LPFC), posterior parietal cortex (PPC), and other cortical regions (Ridderinkhof et al., 2004; Liston et al., 2006). Collaboration between the MFC and other regions indicates that there may be a neural oscillatory mechanism underlying functional communication among them.

Phase synchronization is proposed to be a mechanism of neural communication that enables the long-scale functional connectivity (Varela et al., 2001; Fell and Axmacher, 2011). Recently, researchers have examined the role of mid-frontal theta activity (4.5–8 Hz) in conflict processing (Cavanagh and Frank, 2014). Several studies have suggested that theta phase synchronization signals the need for control to regions

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Abbreviations: AD, axial diffusivity; CSD, current-source-density; DTI, diffusion tensor imaging; EEG, electroencephalography; EOG, electrooculogram; gCC, genu of the corpus callosum; ITI, inter-trial interval; LPFC, lateral prefrontal cortex; MFC, medial frontal cortex; PPC, posterior parietal cortex; RTs, reaction time; TBSS, tract-based spatial statistics.

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responsible for control, such as the LPFC (Cavanagh et al., 2009; Cohen and van Gaal, 2013). These findings support the conflict monitoring theory which suggest that the MFC operates in a hub-like manner, monitoring ongoing conflict and enhancing functional communication with task-related regions (Botvinick et al., 2001; Cohen, 2014). In contrast to the role of the LPFC in representing and maintaining context information (MacDonald et al., 2000), the PPC, especially in the right hemisphere, participates in activating all competing stimulus–response mapping (Coulthard et al., 2008). This suggests the possibility that functional connectivity between the MFC and PPC may become enhanced during high-conflict conditions.

In recent years, differences in functional connectivity between two groups (e.g., patients and healthy controls) are extensively reported in neuroimaging studies (de Kwaasteniet et al., 2013). It is widely believed that functional connectivity between large-scale regions is restricted by the anatomy of the brain (Honey et al., 2009; Chu et al., 2015; Harris and Gordon, 2015). Several recent studies reported individual differences in functional connectivity during cognitive tasks, resting state, and even across rest and task states (Smith et al., 2009; Cole et al., 2014; Finn et al., 2015). However, the mechanisms underlying these individual differences remain unclear. The development of multimodal combination studies in neuroimaging provides a new methodology for examining the neuroanatomical processes underlying individual differences in functional connectivity (Cohen, 2011). A lesion study of Babiloni et al. (2008) reported that subjects with the larger white matter vascular lesions exhibited higher parietal-frontal resting electroencephalography (EEG) oscillation coupling. Associations between functional and structural connectivity were also observed in healthy subjects. Cohen (2011) combined diffusion tensor imaging (DTI) with error theta phase synchronization, reporting that the degree of fronto-medial error synchronization was positively correlated with tract strength in fibers underlying error-related theta activity. These findings indicated that the individual variability in the EEG functional connectivity may be related to individual differences in the white matter tracts.

In the present study, functional connectivity between the MFC and bilateral PPC was investigated by theta phase synchronization between FCz and P3/P4. DTI enables detail quantification of white matter microstructural characteristics (Piantoni et al., 2013). The current study had two major aims. First, we tested the hypothesis that MFC-PPC theta phase synchronization would be significantly enhanced during conflict conditions and varied across subjects. Second, we wished to clarify the relationship between individual differences in white matter integrity and MFC-PPC conflict-induced functional connectivity by testing, in a hierarchical regression model, whether white matter integrity could be used to predict MFC-PPC conflict-induced theta phase synchronization. Using combined EEG-DTI, the current study revealed that white matter tract integrity partially predicted conflict-induced functional connectivity between the MFC and right PPC.

EXPERIMENTAL PROCEDURES

Subjects

Thirty subjects (all right-handed, 16 females) aged from 18 to 27 (mean 23 years, SD: 1.84) were enrolled from the Xidian University in China through a bulletin board. All subjects underwent a physical examination and questionnaires to exclude those with current or chronic illness, addiction (including excessive alcohol, nicotine, drugs and caffeine users), neurological or psychiatric diseases, or a family history of neurological and psychiatric diseases. All participants had normal or corrected-to-normal vision and were experienced in using computer keyboards. The research program and all the experimental procedures were reviewed and approved by the local ethics committee for human subject studies and implemented according to the Helsinki Declaration. Each participant signed an informed consent before the experiment and received compensation for the time spent on the experiment.

Task

A modified flanker task without feature integration or contingency learning was used to exclude the effects of these two potential confounds (Duthoo et al., 2014). An array of five Arabic numerals was presented in the center of the screen, consisting of a target digit with two flanker digits on both sides (1, 2, 3 or 4). The flanker digits were either the same as or different from the target digit, giving congruent (C, e.g., 111111) or incongruent (I, e.g., 11311) trials. Participants responded to the target by pressing the corresponding key on the keyboard as required (Press the 1 and 2 keys with the left middle and the index finger, and 3 and 4 keys with the right and middle fingers) and ignored the bilateral flanker digits. Both speed and accuracy were emphasized. Each of the four possible conditions, congruent followed by incongruent (CI), incongruent followed by incongruent (II), incongruent followed by congruent (IC) and congruent followed by congruent (CC) accounted for one-quarter of the total trials to avoid the contingency learning confound. To avoid the feature integration confound, both flanker and target digits changed across two consecutive trials. Previous studies showed that conflict effect was modulated by the stimulus onset asynchrony (SOA) between targets and flankers. The asynchrony between the onsets of flanker and target digits yields an increased conflict effect compared to simultaneous onset of flanker and target (Wendt et al., 2014). This also interpreted by some authors as an important determinant of congruency sequence effect (Weissman et al., 2015). Moreover, the present study is part of the entire researches of our team on conflict processing. Without prejudice to the purpose of the present study, we chose the asynchrony between the onset of flanker and target digits to ensure comparability between studies. In all trials, flanker digits preceded the target digit by 250 ms, then both remained on the screen for 400 ms followed by an 800-ms blank screen. Participants were required to respond in a maximum responding time of 1200 ms. To control for expectancy effects, the

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