Neuroscience 263 (2014) 181–192

SPONTANEOUS NEURONAL ACTIVITY PREDICTS INTERSUBJECT VARIATIONS IN EXECUTIVE CONTROL OF ATTENTION

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Abstract—Executive control of attention regulates our thoughts, emotion and behavior. Individual differences in executive control are associated with task-related differences in brain activity. But it is unknown whether attentional differences depend on endogenous (resting state) brain activity and to what extent regional fluctuations and functional connectivity contribute to individual variations in executive control processing. Here, we explored the potential contribution of intrinsic brain activity to executive control by using resting-state functional magnetic resonance imaging (fMRI). Using the amplitude of low-frequency fluctuations (ALFF) as an index of spontaneous brain activity, we found that ALFF in the right precuneus (PCUN) and the medial part of left superior frontal gyrus (msFC) was significantly correlated with the efficiency of executive control processing. Crucially, the strengths of functional connectivity between the right PCUN/left msFC and distributed brain regions, including the left fusiform gyrus, right inferior frontal gyrus, left superior frontal gyrus and right precentral gyrus, were correlated with individual differences in executive performance. Together, the ALFF and functional connectivity accounted for 67% of the variability in behavioral performance. Moreover, the strength of functional connectivity between specific regions could predict more individual variability in executive control performance than regionally specific fluctuations. In conclusion, our findings suggest that spontaneous brain activity may reflect or underpin executive control of attention. It will provide new insights into the origins of inter-individual variability in human executive control processing.

Key words: resting-state fMRI, ALFF, functional connectivity, executive control.

INTRODUCTION

Executive control of attention is involved in the regulation of thoughts, emotions and responses. It is associated with activity in a neural network comprising the anterior cingulate and prefrontal cortices (Dosenbach and Petersen, 2009). Functionally, it overlaps with the more general domain of executive functions, which accomplish a set of processes involved in planning and executing goal-directed actions, such as working memory, task switching, inhibitory control and conflict monitoring. These cognitive processes are required when it is necessary to retain information in mind, integrate information and resolve conflict between different stimuli or responses (Diamond, 2013). Combining cued response time (RT) and the flanker tasks, the Attention Network Test (ANT) provides one means of characterizing individual differences in the efficiency of executive control processing (Fan et al., 2003a, 2005). It has been used in numerous researches involved in the normal population (Fan et al., 2005) as well as patients with neuropsychiatric disorders, such as attention deficit hyperactivity disorder (ADHD) (Bush, 2010), schizophrenia (Urbanek et al., 2009) and Alzheimer's disease (Fernandez-Duque and Black, 2006).

Previous studies have explored the relationships between human brain activity and individual variations in cognitive behavior. The differences in behavioral performance have been demonstrated to be attributed to individual variability in task-related factors, such as attention or anticipation (Ress et al., 2000; Sapir et al., 2005). Individual differences in executive control are associated with task-related differences in brain activity (Fan et al., 2005). In the resting state, both the regional fluctuations and functional integration exert great influence in predicting the cognitive variations. The amplitudes of the local low oscillations in the midline cingulate regions can predict not only the speed and consistency of performance but also the magnitude of

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Abbreviations: ALFF, amplitude of low-frequency fluctuations; ADHD, attention deficit hyperactivity disorder; ANT, Attention Network Test; BOLD, blood oxygen level-dependent; dACC, dorsal anterior cingulate cortex; DMN, default mode network; FA, flip angle; fALFF, fractional ALFF; FFG, fusiform gyrus; fMRI, functional magnetic resonance imaging; FOV, field of view; LFF, low-frequency fluctuations; msFC, medial part of left superior frontal gyrus; PCUN, precuneus; ROI, regions of interest; RSFC, resting-state functional connectivity; RT, response time; SFG, superior frontal gyrus; TR, repetition time; TE, echo time.

0306-4522/13 $36.00
http://dx.doi.org/10.1016/j.neuroscience.2014.01.020

the behavioral congruency effect in the Eriksen task (Mennes et al., 2011b). Moreover, the individual differences in resting-state functional connectivity (RSFC) can predict the blood oxygen level-dependent (BOLD) activity induced by the Flanker task (Mennes et al., 2010). However, the relationship between individual differences in intrinsic brain activity and executive control is currently unknown. In addition, whether the regional amplitude or integration of neuronal fluctuations could predict intersubject variations of executive control remains elusive.

Imaging studies have found that low-frequency fluctuations (LFF) (0.01–0.1 Hz) in the BOLD signal provide an important window on spontaneous neuronal fluctuations and associated mental activity (Fox et al., 2006; Raichle and Mintun, 2006; Raichle, 2010). The amplitude of LFFs (ALFF) reflects the intensity of neurophysiological fluctuations, and distinct ALFF patterns have been found in visual, auditory and sensorimotor cortices (Kiviniemi et al., 2003). Patients with cognitive disorders show abnormal ALFF in cortical regions underpinning the cognitive function (Zang et al., 2007; Chen et al., 2012; Liu et al., 2012). Importantly, the ALFFs of healthy individuals in the resting state are correlated with task-evoked BOLD responses (Fox et al., 2006; Zou et al., 2012) and behavioral performance (Fox et al., 2007; Liu et al., 2011; Scholvinck et al., 2012). Furthermore, functional interactions between distinct regions may play a crucial role in cognitive processing, which makes functional connectivity particularly interesting as a predictor of cognitive abilities (van den Heuvel and Hulshoff Pol, 2010). For resting-state functional magnetic resonance imaging (fMRI), there is a high level of RSFC between brain regions engaged in the same higher order cognitive tasks (see (van den Heuvel and Hulshoff Pol, 2010) for a review). Significantly, the strength of functional connectivity is correlated with intersubject variability in cognitive processing ability (conceptual ability) (Wei et al., 2012), performance improvements (Lewis et al., 2009) and personality traits (Di Martino et al., 2009). Therefore, the regional amplitude and integrated pattern of the LFFs appear to represent the key aspects of cognitive function.

To test whether individual differences in behavioral performance on executive control tasks are associated with spontaneous brain activity at rest, and to characterize the extent to which intrinsic brain activity (regional fluctuations and functional connectivity) could predict cognitive performance, we investigated the role of spontaneous brain activity in executive control using resting-state fMRI. First, we identified the potential brain areas that accounted for individual behavioral variability using a regression analysis between participants' executive control performance and regional ALFF. We then calculated the functional connectivity between these regions and remaining brain voxels to identify the brain network in which the regions were embedded at the within subject level. Finally, we quantified the relative abilities of regional ALFF and interregional functional connectivity to predict individual differences in the performance of executive control task. We hypothesized that functional connectivity measures might have greater predictive validity – given the distributed nature of executive control processing; despite the fact that the regional measures (ALFF) were chosen explicitly to account for intersubject variations in attentional performance.

EXPERIMENTAL PROCEDURES

Participants

Fifty-eight healthy humans (27 females; 17.4 ± 1.4 years old; range, 15–20 years old) participated in the study. Inclusion criteria were: (1) right-handed measured with Edinburgh Inventory (Oldfield, 1971); (2) no history of any neurological, psychiatric or cognitive symptoms, and no abnormalities observed in conventional brain MRI. The study was approved by the Human Research Ethics Committee of the Shandong University School of Medicine. Written informed consent was obtained from all participants.

Experimental paradigm

A version of ANT devised by Fan et al. (2005) was adopted as the behavioral measure for this study. The resting-state fMRI scans were acquired before participants completed the ANT task. Briefly, participants were instructed to press a button as quickly and accurately as possible to decide whether an arrow was pointing left or right. The target was flanked on either side by two arrows; either pointing in the same direction (congruent condition), or in the opposite direction (incongruent condition). The target and flankers were presented until the participant made a response or 2000 ms elapsed. A cue (an asterisk) was presented for 200 ms before the appearance of the target. There were three cue conditions: no cue (baseline), center cue (at the fixation point for alerting) and spatial cue (at the target location for alerting plus orienting).

In total, six blocks of trials were presented in a predetermined counterbalanced order, each block lasting 5 min 42 s and consisting of 36 trials plus two buffer trials in the beginning. In each block, there were six trial types – three cue conditions (non, center and spatial) by two target conditions (congruent and incongruent). All participants were trained before testing. Stimulus presentation and behavioral response collection were performed using E-Prime (Psychology Software Tools, Pittsburgh, PA, USA).

Data acquisition

All participants were scanned using a 3.0-Tesla GE Signa scanner (General Electric Medical Systems, Milwaukee, WI, USA) before the behavioral test. Foam pads and earplugs were used to reduce head motion and scanner noise. Participants were instructed to keep their eyes closed, relax their minds and think of nothing in particular without falling asleep. Functional images were