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LATE ENHANCEMENT OF BRAIN-BEHAVIOR CORRELATIONS DURING RESPONSE INHIBITION

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Abstract—Previous neuroimaging studies of response inhibition have examined correlations between behavioral efficiency and brain activity, but the temporal stability of the correlations has largely been ignored. The present functional magnetic resonance imaging (fMRI) study demonstrates the temporal changes of the brain activity associated with performance efficiency that led to more robust brain-behavior correlations in a later part of the experimental sessions. Participants performed a stop-signal task requiring inhibition of inappropriate responses, where more efficient behavioral performance is reflected in a shorter stop-signal reaction time (SSRT). Among across-subject negative correlations between the brain activity and the SSRT, the majority of the negative correlations were observed in the second half of experimental sessions. In the cerebellar region that showed the greatest difference in correlations between the second and the first halves, the brain activity increased in efficient performers, whereas the brain activity decreased in poor performers. These results suggest the existence of multiple brain mechanisms that increase and decrease the brain activity depending on the behavioral efficiency of the performers. More practically, these results indicate that robust brain-behavior correlations can more effectively be detected in a later part of the experimental sessions.

Key words: stop-signal task, cognitive control, executive function, functional MRI, stop-signal reaction time.

INTRODUCTION

Inhibition of inappropriate responses has received intense attention of researchers using neuroimaging techniques. Prominent brain activity has reproducibly been observed in focal cortical and subcortical regions during successful response inhibition (Konishi et al., 1998, 1999; Garavan et al., 1999; de Zubicaray et al., 2000; Braver et al., 2001; Liddle et al., 2001; Menon et al., 2001; Rubia et al., 2001; Bunge et al., 2002; Durston et al., 2002a,b; Hester et al., 2004; Kelly et al., 2004; Matsubara et al., 2004; Brass et al., 2005; Aron and Poldrack, 2006; Li et al., 2006; Brass and Haggard, 2007; Leung and Cai, 2007; Sumner et al., 2007; Nakata et al., 2008; Zheng et al., 2008; Cai and Leung, 2009; Chambers et al., 2009; Chikazoe et al., 2009a,b; Duann et al., 2009; van Gaal et al., 2010; Jahfari et al., 2011; Cai et al., 2013). The contribution of the brain regions to response inhibition has been confirmed by TMS studies (Chambers et al., 2006). More recent neuroimaging studies have examined cross-subject correlation coefficients between brain activation and behavioral efficiency of response inhibition, and identified brain regions showing greater activity in more efficient individuals (Aron and Poldrack, 2006; Aron et al., 2007; Garavan et al., 2006; Li et al., 2006, 2008; Congdon et al., 2010; Rubia et al., 2010; Sharp et al., 2010; Boecker et al., 2011; Boehler et al., 2011; Ghahremani et al., 2012; Hirose et al., 2012). The identified regions include the right inferior frontal cortex (Aron and Poldrack, 2006; Aron et al., 2007; Congdon et al., 2010; Boecker et al., 2011), the subthalamic nucleus (Aron and Poldrack, 2006; Aron et al., 2007; Li et al., 2008), the left superior frontal cortex (Li et al., 2006; Hirose et al., 2012), the left precentral gyrus (Li et al., 2006; Congdon et al., 2010; Hirose et al., 2012), the anterior cingulate cortex (Li et al., 2006; Congdon et al., 2010; Rubia et al., 2010), the left and right insula (Boehler et al., 2011; Congdon et al., 2010), putamen (Congdon et al., 2010; Ghahremani et al., 2012), the left temporo-parietal junction (Congdon et al., 2010; Hirose et al., 2012; Ghahremani et al., 2012), the pre-supplementary motor area (Sharp et al., 2010; Boecker et al., 2011), the left inferior frontal cortex (Ghahremani et al., 2012; Hirose et al., 2012), the right superior frontal cortex (Ghahremani et al., 2012), and the cerebellum (Ghahremani et al., 2012). However,

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Abbreviations: fMRI, functional magnetic resonance imaging; SSD, stop-signal delay; SSRT, stop-signal reaction time.

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some of these studies include some degree of variability in terms of the anatomical location of the identified regions, and the effect size of the correlations appears relatively weak, compared to the well-known brain regions showing prominent activation during response inhibition.

One possibility of the variability and the weak effect may relate to the temporal instability of the correlations. The temporal changes in activity magnitude can occur even within the experimental sessions, as demonstrated by rapid activity decrease and increase through repetitive performance of cognitive tasks (Milham et al., 2003; Kelley et al., 2006). Thus, it seems reasonable to hypothesize that the short-term changes in correlations can occur due to the activity changes during response inhibition. In the current study, human participants performed a stop-signal task involving response inhibition during functional magnetic resonance imaging (fMRI) scanning. Correlations were examined between brain activity and a behavioral index reflecting the efficiency of response inhibition, called the stop-signal reaction time (SSRT) (Logan and Cowan, 1984; Rubia et al., 2001; Aron et al., 2003; Chikazoe et al., 2009b; Verbruggen et al., 2013). Temporal changes in the correlations were then explored across participants, and phenomenological mechanisms were sought that explain the temporal changes in correlations.

EXPERIMENTAL PROCEDURES

Participants

Written informed consent was obtained from 46 healthy right-handed subjects (26 males, 20 females; age range: 20–26), who were then scanned using experimental procedures approved by the institutional review board of the University of Tokyo School of Medicine. They had no prior experiences of performing the stop-signal task, and were administered to fMRI scan with instruction of the task, but without any practice.

Imaging procedures

The experiments were conducted using a 3.0T-MRI system. Localizer images were first collected to align the field of view centered on each subject's brain. T1-weighted structural images were then obtained for anatomical reference (76 2-mm slices; in-plane resolution: 1 × 1 mm). For functional imaging, a gradient echo echo-planar sequence was used (40 4-mm slices; TR = 3000 ms; TE = 50 ms; flip angle = 90 degree; field of view = 256 × 256 mm). Each functional run consisted of 64 whole-brain acquisitions. The first four functional images in each run were excluded from analysis to allow for the equilibration of longitudinal magnetization.

Behavioral procedures

Participants performed a stop-signal task with a common structure. The current stop-signal task is depicted in Fig. 1A. There were two types of trials, STOP and GO. At the beginning of the trial in both types, a gray circle was presented for 1.7 s. Then, in the GO trial, a green

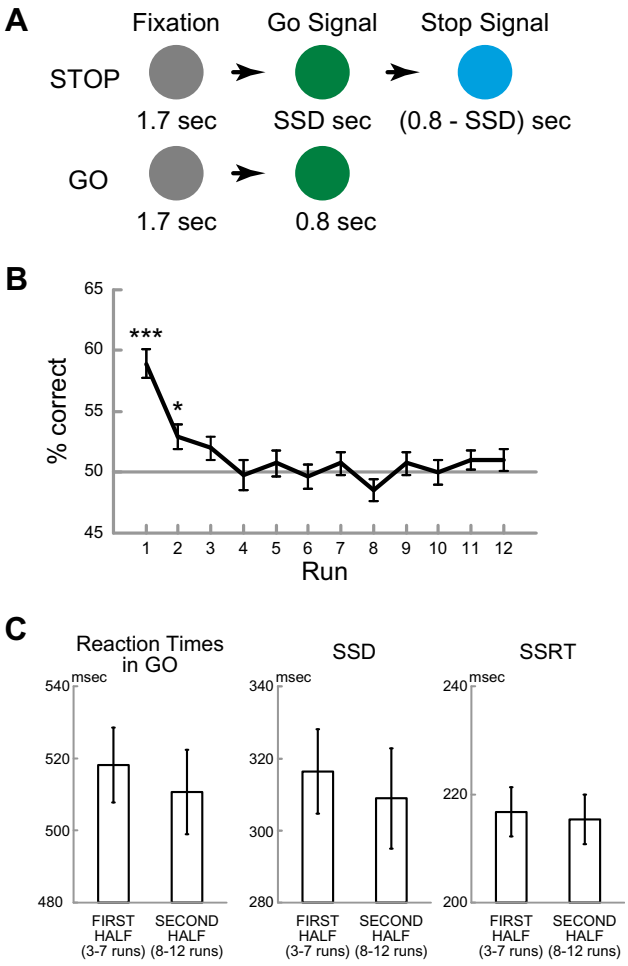

Fig. 1. (A) Participants performed a stop-signal task. In the STOP trial, a stop signal was presented after the presentation of Go signal for a short period (stop-signal delay: SSD). They were required to withhold a manual response that was triggered by the Go signal. On the other hand, in the GO trial, they made the manual response as quickly as possible. (B) Timecourse of accuracy for STOP trials. The horizontal and vertical axes indicate the number of functional runs and accuracy, respectively. The error bars indicate standard errors of mean across participants. $^{***}P < .001$; $^{*}P < .05$. (C) Reaction times in GO trials (left), SSD in STOP trials (middle), and SSRT (right) in the first half (from 3rd to 7th runs: FIRST) and second half (from 8th to 12th runs: SECOND) of the experimental sessions.

circle was presented for 0.8 s, and the participants were instructed to make a button press with the right thumb before the green circle disappeared. In the STOP trial, similar to the GO trial, a green circle was presented after the presentation of the gray stimulus. However, after a short period, the green circle was changed to a blue circle, and the participants were required to withhold the manual response that was once triggered by the presentation of the green circle. The duration of the presentation of the green circle is called stop-signal delay or SSD. Participants were instructed not to wait for the stop signals (blue circle) when go signal (green circle) was presented.

The SSD was updated on each STOP trial based on a tracking procedure, allowing us to maintain accuracy of the STOP trial at approximately 50% (Band et al., 2003). More specifically, if the subjects successfully