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To stop or not to stop: A high spatio-temporal resolution study of response inhibition using MEG

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Abstract. Event-related potential studies in healthy adults and children have shown that stimuli signaling the need to stop elicit a robust, right-frontal-maximal N2 that is strongly reduced in children with attention-deficit hyperactivity disorder. To further investigate the mechanisms of normal response inhibition, the Stop Signal Task was applied to 12 healthy young adults using whole-head magnetoencephalography. The evoked magnetic response to Successful Stops showed an earlier and greater amplitude N2-like peak (mean = 167 ms) relative to Failed Stops. Such success-related modulation had a scalp distribution over frontomedial scalp. Dipole source analysis using BESA and a five-dipole fMRI-constrained solution identified a dACC source as a major contributor to the success-related N2-like modulation, while right DLPFC appears to contribute to differences in early preparatory or orienting mechanisms. © 2007 Published by Elsevier B.V.

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1. Introduction

A deficit in inhibitory control is thought to be at the core of the cognitive syndrome in attention-deficit hyperactivity disorder (ADHD). A task tapping into response inhibition is the Stop Signal Task (SST), which is a choice-reaction task with a twist: participants are instructed to inhibit a prepotent response when an infrequent Stop signal is presented.

In previous event-related potential (ERP) studies of the SST, two ERP waves have been associated to inhibitory control, a right inferior frontal NoGo-N2 [1], and a midline frontocentral

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NoGo-P3 [2]. Both waves were found to be reduced in amplitude in ADHD children [1,2]. Furthermore, the NoGo-N2 wave was greater in amplitude for Success than Fail Stops in healthy adults [3] and children [4], but such modulation was absent in ADHD children [4], consistent with a crucial role in early triggering of the inhibitory process and its successful implementation [1,2]. The scalp topography of the No-GoN2 suggested a brain source in right dorsolateral prefrontal cortex (DLPFC), consistent with fMRI studies of GoNogo tasks [5,6]. However, a recent fMRI study of the SST in ADHD and healthy children failed to report significant group differences in right DLPFC activity for either Success of Fail Stops, the only group difference being reduced dorsal Anterior Cingulate (dACC) activation during Fail Stops [7].

Aim of the present study was to clarify the inconsistency of ERP and fMRI findings of the SST, by using a technique with higher spatio-temporal resolution, magnetoencephalography (MEG), to better characterize the temporal dynamics of activity in the network of brain regions during the unfolding of the SST in healthy participants, and provide a foundation for future investigations in ADHD subjects.

2. Methods

2.1. Subjects

Twelve individuals with normal or corrected to normal vision gave written informed consent to participate in the study. One was excluded because of excessive head motion during recording, leaving eleven subjects (5 females) with a mean age of 28 years (S.D. = 5.3).

2.2. Task and stimuli

A visual version of the SST was used [1–4,6]. Subjects were instructed to respond to the letters A or B (150 ms) with a left or right hand button. They were also told to withdraw responding when they saw a letter S (stop signal) following the A or B. Intertrial interval was 1–3 s. A 50-ms stepwise correction was implemented, allowing online adjustments of performance by balancing the number of success and fail stop trials by increments or decrements of the Go–Stop delay.

2.3. Data collection and signal preprocessing

Data were collected from a 151-channel OMEGA (CTF Systems) axial gradiometer system at the Down Syndrome Research Foundation (Burnaby, BC, Canada). Recordings were high-pass filtered at 0.1 Hz and low-pass filtered at 30 Hz and digitized at 600 Hz. MEG epochs contaminated by ocular artifacts were removed from the analysis. Trials were selectively averaged for Go hits, Success Stops and Fail Stops (1000 ms epoch, 100 ms baseline) time-locked to Stop signal, then grand averaged across subjects. Inspection of the grand average waveforms for Success and Fail trials, and of the success minus fail difference wave, and of the related scalp topographical maps in different time windows showed N200-like and P3a-like ERF components peaking at 211 ± 26 ms and 274 ± 23 ms over lateral frontotemporal and medial frontal regions, respectively. Differences between Success and Fail Inhibitions (SI, FI) were greatest in the 100–220 ms range, peaking at 167 ms after the Stop Signal. For statistical

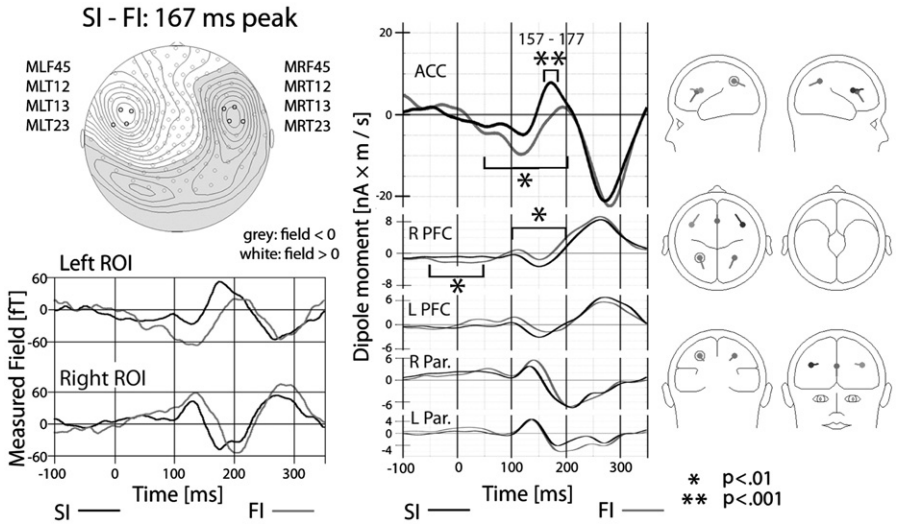

Fig. 1. **Left** – Top: Grand average scalp topography of the SI vs. FI difference wave at 167 ms. Focal source and sink are over R and L mediofrontal scalp. Bottom: Grand average ERFs for SI and FI trials for the left and right ROI sensors, showing earlier and greater amplitude Fields for SI than FI responses. **Right** – Dipole moments for SI and FI trials for the five source waveforms. Asterisks show time interval where SI and FI were statistically different. Note ACC peak at 167 ms, with significant success modulation.

analysis of the SI vs. FI effects, two frontocentral regions of interest (ROIs) were created by collapsing four neighbor sensors (indicated below).

2.4. Source analysis

We used Brain Electrical Source Analysis (BESA) software to estimate the brain sources associated to SI and FI trials (−100 to 350 ms). We used a 5-dipole solution with the location constrained by event-related fMRI regional activations during the SST [7]. Dipole locations were fixed across subjects, with the orientation left to vary. One dipole was placed in dACC, and two symmetric pairs in dorsolateral prefrontal cortex (PFC) and parietal cortex (Par) [see Fig. 1, right].

3. Results

3.1. Scalp data

Comparing SI with FI trials, the average magnitude for a 20-ms window around the 167 ms peak was significantly more negative for the right ROI ($p < .0007$) and more positive for the left ROI ($p < .001$).

3.2. Source waveforms

The 5-dipole solution accounted for 72% of the variance in the window (peak residual variance = 15.3% at 167 ms), with most of the variance due to the ACC dipole. Source

waveforms for the five dipoles were computed for each subject, and sample-by-sample *t*-tests between SI and FI trials were carried out. Average time courses for the 5 source waveforms indicated a possible order of activation in the five regions. ACC showed a first peak around 120 ms, followed by a peak at 167 ms and a later peak at 274 ms (the latter two similar to the peaks observed at the scalp). PFC sources showed smaller peaks at 140 ms and 270 ms. Parietal sources showed peaks at 140 ms and around 200 ms. Differences between SI and FI were present around stimulus onset (−50 to 50 ms) and between 100 and 200 ms (peaking at 140 ms) for the R PFC source, and between 50 and 200 ms for the dACC source (peaking at 167 ms). The latter peak corresponded to the scalp recorded success-related modulation.

4. Discussion

Previous ERP studies of the SST have identified the timing on the evoked response to stimuli signaling the need to stop (the NoGo-N2 and NoGo-P3), but failed to provide spatial localization of such effects [1–4]. In contrast, fMRI studies of the SST identify regional activations but lacked temporal information [5].

The present MEG study characterizes for the first time both the timing and the localization of brain activations during the unfolding of the Stop Signal Task. Success Stops elicited an earlier and significantly greater amplitude Nogo-N2, peaking at 167 ms over frontomedial scalp, with a more dorsal and anterior topography than the later N200 peak to the Fail stops (anterior temporal scalp). BESA Source dipole analysis identified the main source of the Success-related N2 modulation in dACC.

Activity in right prefrontal cortex appeared to contribute to the difference in processing between success and fail stops, albeit at a lesser degree. Its timing, however, was different from that of the dACC dipole, with an early difference present around Stop signal onset (−50 to 50) likely reflecting a difference in preparatory or orienting mechanisms for SI and FI trials, previously reported in an ERP study [1], and a second time window (100–200 ms) which appeared to precede the 167 ms dACC peak.

This study provides a foundation for future MEG studies investigating the mechanisms of impaired inhibitory control in ADHD.

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