International Journal of Psychophysiology 93 (2014) 371–380

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Age-related spatiotemporal reorganization during response inhibition

Xiangfei Hong [a,b], Junfeng Sun [a], Jesse J. Bengson [b], Shanbao Tong [a,*]

[a] School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai 200240, China
[b] Center for Mind and Brain, University of California-Davis, Davis CA 95618, USA

ARTICLE INFO

Article history:
Received 19 March 2014
Received in revised form 22 May 2014
Accepted 27 May 2014
Available online 4 June 2014

Keywords:
Aging
Event-related potentials
Go/NoGo
Response inhibition
Source localization

ABSTRACT

As a key high-level cognitive function in human beings, response inhibition is crucial for adaptive behavior. Previous neuroimaging studies have shown that older individuals exhibit greater neural activation than younger individuals during response inhibition tasks. This finding has been interpreted within a neural compensation framework, in which additional neural resources are recruited in response to age-related cognitive decline. Although this interpretation has received empirical support, the precise event-related temporal course of this age-related compensatory neural response remains unexplored. In the present study, we conducted source analysis on inhibition-related ERP components (i.e., N2 and P3) that were recorded while healthy younger and older adults participated in a visual Go/NoGo task. We found that older adults showed increased source current densities of the N2 and P3 components than younger adults, which support previous hemodynamic findings. Further, such age-related differences in neural activation were successfully separated between the N2 and P3 periods by source localization analysis. Interestingly, the increased activations in older adults were primarily localized to the right precentral and postcentral gyri during the N2 period, which shifted to the right dorsolateral prefrontal cortex and the right inferior frontal gyrus during the P3 period. Taken together, our results clearly illustrate the spatiotemporal dynamics of age-related functional brain reorganization, and further specify the exact temporal course at the millisecond scale by which age-related compensatory neural responses occur during response inhibition.

1. Introduction

The ability to inhibit a prepotent tendency in reaction to changing task demands is a core cognitive function of human beings. Go/NoGo and Stop-Signal paradigms have been widely used in combination with neuroimaging techniques in order to investigate the neural mechanisms associated with response inhibition. In a typical Go/NoGo task, a overt or covert response (i.e., button press or silent counting) is made to one stimulus type (Go) and withheld to another (NoGo). Difference waves of event-related potentials (ERPs) between correctly performed NoGo-trials and Go-trials (NoGo minus Go) consistently reveal a frontocentral negative component around 200–400 ms post-stimulus onset (N2), followed by a frontocentral positive component around 300–600 ms post-stimulus onset (P3) (Albert et al., 2013; Eimer, 1993; Falkenstein, 2006; Falkenstein et al., 1999; Kok, 1986; Pfefferbaum and Ford, 1988). In the Stop-Signal task, where subjects perform a speeded choice and occasionally receive a stop signal that instructs them to withhold a response, the ERP difference waves between correctly performed Stop-trials and Go-trials (Stop minus Go) also show prominent N2 and P3 components (Huster et al., 2010; Kok et al., 2004; Ramautar et al., 2006).

In spite of years of research, the precise functional significance of these two components is still under debate. Early studies interpreted both N2 and P3 components as neural markers of response inhibition (Eimer, 1993; Falkenstein et al., 1999; Jodo and Kayama, 1992). However, the relationship between N2 and response inhibition has been questioned by recent studies, which proposes that P3 primarily reflects inhibitory process, whereas N2 seems to reflect "response conflict monitoring" rather than "response inhibition" (Albert et al., 2013; Donkers and van Boxtel, 2004; Enriquez-Geppert et al., 2010; Falkenstein, 2006; Nieuwenhuis et al., 2003). Along with these findings, functional magnetic resonance imaging (fMRI) and ERP source localization studies have suggested that response inhibition is subserved by a distributed brain network, including superior frontal gyrus, middle frontal gyrus, medial frontal gyrus, inferior frontal gyrus, precentral gyrus, anterior cingulate, insula, precuneus and inferior parietal lobule (Albert et al., 2013; Huster et al., 2010; Liddle et al., 2001; Rubia et al., 2001; Simmonds et al., 2008; Swick et al., 2011; Zheng et al., 2008). Interestingly, ERP source localization studies reported anterior frontal regions and central regions as the primary neural generators for N2 and P3

* Corresponding author at: Shanghai Jiao Tong University, Dongchuan Road 800, Shanghai 200240, China. Tel.: +86 21 34205138; fax: +86 21 34204717.
E-mail address: stong@sjtu.edu.cn (S. Tong).

http://dx.doi.org/10.1016/j.ijpsycho.2014.05.013
0167-8760/

respectively, indicating a neuroanatomical segregation, which also supported the functional dissociation of these two components (Huster et al., 2010; Kok et al., 2004; Lavric et al., 2004; Nieuwenhuis et al., 2003).

Neuroimaging studies using fMRI or near-infrared spectroscopy (NIRS) have shown that older adults had greater brain activations than younger adults when performing the Go/NoGo task (summarized in Table 1), and these hyper-activations in the older brain were interpreted within a neural compensation framework (Heilbronner and Munte, 2013; Langenecker and Nielson, 2003; Nielson et al., 2002). However, due to the low temporal resolution, neither fMRI nor NIRS can characterize the precise time course of this age-related functional reorganization (Table 1) at the scale of milliseconds. Thus, the within-trial temporal and anatomical evolution of how older individuals exhibit a compensatory inhibition-related neural response during N2 and P3 periods is still unclear.

We examined this question in a visual Go/NoGo paradigm. Subjects were required to direct their attention to the cued (left or right) visual field, discriminate the forthcoming target at the attended location, and respond to one type of target (Go) but withhold response to another (NoGo). We recorded behavioral performances and scalp electroencephalography (EEG) from both younger and older adults during the experiments. Scalp ERP and source localization analyses were carried out to investigate the spatiotemporal brain activations during response inhibition. We expected to observe the delayed latencies of N2 and P3 components due to normal aging. Also, we expected that older adults would show increased brain activations than younger adults during N2 and P3 periods. Finally, since the N2 and P3 components were suggested to be neuroanatomically segregated and functionally dissociated, we hypothesized that the spatiotemporal pattern of such age-related hyper-activations might differ between N2 and P3 periods. The confirmation of these hypotheses would enrich our understanding of the complicated neural processes involved in response inhibition, as well as the temporal course of functional brain reorganization during normal aging.

2. Material and methods

2.1. Participants

Twenty-three healthy younger students from Shanghai Jiao Tong University (mean age: 21.4 years; range: 18–25 years; 7 females; all right-handed) and eighteen healthy older adults from a neighboring community (mean age: 61 years; range: 50–70 years; 11 females; all right-handed) were recruited in this study. There was no significant difference of gender ratios between the two groups (Fisher's Exact Test, $p > 0.05$). Each participant had 9 years of minimum school education (mean ± standard deviation; younger: 14.1 ± 1.7 years vs. older: 11.1 ± 2.7 years; $t_{(27.040)} = 4.223$, $p < 0.001$). All participants reported normal or corrected-to-normal vision, and no history of neurological or psychiatric disorders. All older participants were evaluated to be cognitively healthy based on the Mini-Mental Status Examination (MMSE; mean: 28; range: 26–29), which is consistent with prior aging studies (Langenecker and Nielson, 2003; Nagamatsu et al., 2011; Nielson et al., 2002). Each participant gave a written informed consent prior to the experiment. The experimental protocol complied with the Declaration of Helsinki and was approved by the institutional ethical committee.

2.2. Stimuli and procedures

A commercially available software (E-Prime 2.0, Psychology Software Tools, Inc., Sharpsburg, USA) was used to present stimuli and record responses. All stimuli were presented on a 19 inch LCD display (Dell: P190SB) 60 cm in front of the participant. A black central crosshair (1.38° by 1.38° visual angle) and two black location marks (2.39° by 2.39° visual angle, 9.05° from the vertical meridian, 7.2° below the horizontal meridian) were presented on a white background on the display. Subjects were instructed to always maintain fixation on the central crosshair in each trial. Trial sequences and timing are illustrated in Fig. 1. In each trial, a spatial cue (black arrow pointing left or right, 2.24° by 1.62° visual angle) was first presented in the central for 200 ms, directing the subject to covertly attend either the lower-left or lower-right square with equal probability, and totally ignore the other location. After a random cue-target interval (CTI, 1000–1200 ms from cue offset to target onset), a target (1.67° by 1.67° visual angle) was presented for 200 ms inside either the attended or ignored square with equal probability. The target was either the letter "x" or plus sign, which was randomized across trials with equal probability. Subjects were required to discriminate the target at the attended location, and respond to the plus sign (Go-target) while refrain from responding to the letter "x" (NoGo-target). Response was made by pressing a button of the response box with the right index finger as quickly and accurately as possible. Correctly responded Go-targets with response time between 200 and 1800 ms were considered as valid trials. A fixed delay of 2600 ms was presented between the target offset and the onset of next trial.

Each block consisted of 60 trials for about 5 min, with a 2–3 min break between two successive blocks. Subjects were first given the experimental instructions, and trained for at least one block to get familiar with the task. For each experiment, there were 8 blocks in the younger group, and 6 blocks in the older group, given that older adults were more likely to develop visual fatigue during the experiment. In total, 480 and 360 trials were recorded for each younger and older adult respectively.

2.3. EEG recording

EEG data were continuously recorded during the experiment using BrainAmp MR Plus amplifier and EasyCap™ (Brain Products GmbH, Gilching, Germany) from 30 scalp locations (Fp1, Fp2, F3, F4, F7, F8, Fz, FC1, FC2, FC5, FC6, C3, C4, Cz, T7, T8, CP1, CP2, CP5, CP6, P3, P4, P7, P8, Pz, O1, O2, Oz, TP9, TP10). The electrodes TP9 and TP10 refer to inferior temporal locations over the left and right mastoids, respectively. FCz

Table 1
A summary of significantly increased brain activations (corrected $p < 0.05$) in older adults than younger adults during response inhibition in the literature based on hemodynamic approaches (L: left hemisphere; R: right hemisphere).

Study	Method	NoGo stimuli	Lobe	Brain structure	Hemisphere
(Heilbronner and Munte, 2013)	NIRS	Fixed	Frontal	Precentral gyrus	R
				Middle frontal gyrus	R
			Parietal	Postcentral gyrus	R
(Nielson et al., 2002) and (Langenecker and Nielson, 2003) for a replication	fMRI	Varied	Frontal	Middle frontal gyrus	L, R
				Inferior frontal gyrus	L
				Medial frontal gyrus	R
			Parietal	Inferior parietal lobule	L
			Subcortical	Claustrum	L
				Putamen	L