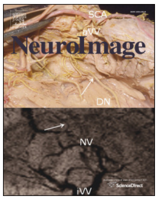
NeuroImage xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

NeuroImage

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



Watch out! Medial frontal cortex is activated by cues signaling potential changes in response demands

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ARTICLE INFO

Article history:
Received 3 December 2014
Accepted 7 April 2015
Available online xxxx

Keywords:
Anterior cingulate cortex
Performance monitoring
Task switching
Independent components analysis
Robust estimation
ERN

ABSTRACT

The human medial frontal cortex and especially the anterior cingulate cortex (ACC) have been implicated in several aspects of performance monitoring. We examined event-related EEG during a general process of controlling attention by using a novel paradigm to elicit a medial frontal negativity (MFN) to stimuli that indicate potential changes in future response demands. Independent components analysis revealed that the latent factors that accounted for MFN activity to such changes also accounted for activity associated with the error-related negativity and the NoGo inhibitory N2. Given that the medial frontal activation to these changes varied reliably across subjects simply as a function of potential need to alter responses in the absence of error commission and response inhibition, we propose that the underlying basis for medial frontal activation in situations demanding ongoing monitoring of performance involves an increase in attention control, a factor common to all MFN paradigms.

Introduction

One of the core cognitive functions of the human medial frontal cortex, in particular the anterior cingulate cortex (ACC), has been variably attributed to error detection (Gehring et al., 1993; Miltner et al., 1993), response-conflict monitoring (van Veen et al., 2001), reinforcement/associative learning (Holroyd and Coles, 2008; Holroyd and Yeung, 2012; Holroyd and Coles, 2002), deviation from expectancy (Oliveira et al., 2007), inhibitory control (Falkenstein et al., 1999), and the prediction of timing of action outcomes (Alexander and Brown, 2011). This range of models is due to the proliferation of paradigms that elicit a particular event-related potential (ERP) component, collectively referred to as medial frontal negativities (MFNs), which are thought to reflect activation of ACC and surrounding medial frontal sources. Functionally isolating and describing MFN effects such as the error-related negativity (ERN) and NoGo inhibitory N2 (N2) is complicated with respect to underlying neurophysiology, and tempered further by group-level statistics focused on mixed source projections in the EEG. We present evidence across single subjects that several MFNs are indeed functionally complicated, but can parsimoniously be attributed to the general process of controlling attention even in the absence of errors, response conflicts, reinforcement/associative learning, or inhibitory control. This general function can be shown to account for medial frontal activation that is typically associated with these paradigm-specific processes that result in the MFN.

Single-unit ACC recordings in rats suggest that functional relationships in neuronal assemblies serve as a basis for successful behavioral adaptation such that error commission reflects a lack of organization in firing patterns (Lapish et al., 2008). Extending this interpretation, Bryden et al. (2011) concluded that neurons in the rat ACC are not only sensitive to commission and reward-prediction errors, but that they also become active when there is an increased demand for attentional resources such as those needed for the learning of new response contingencies or during unexpected shifts in target value. Indeed, the firing of neurons in the ACC is impacted by changes in task demands, such as task-switching (Johnston et al., 2007) and the presentation of events that inform optimal stimulus–response strategies (Hyafil et al., 2009; Quilodran et al., 2008). Some researchers have documented that phasic theta oscillations in the primate ACC increase during both the preparatory and remedial stages of stimulus–response selections (Womelsdorf et al., 2010), further suggesting that the ACC is involved in establishing and modulating behavioral strategies (Isomura et al., 2003).

In humans, activity in the ACC has been shown to increase when response conflicts are introduced (Hsieh and Wu, 2011; Liston et al., 2006) and when stimulus–response rules are reversed (Schroder et al., 2012). Others report that ACC activity, as reflected in a class of ERPs involving a MFN (Randall and Smith, 2011) and in blood–oxygen-level dependent (BOLD) responses (Aarts et al., 2008), is associated with changes in

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http://dx.doi.org/10.1016/j.neuroimage.2015.04.021
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Please cite this article as: van Noordt, S.J.R., et al., Watch out! Medial frontal cortex is activated by cues signaling potential changes in response demands, NeuroImage (2015), http://dx.doi.org/10.1016/j.neuroimage.2015.04.021

expectation and attention allocation in the pursuit of establishing appropriate response sets (Luks et al., 2002; Swainson et al., 2003). This includes biasing attention toward relevant stimuli in order to minimize behavioral interference in the presence of distracting information (Weissman et al., 2005). The ACC's role in the dynamic online control of behavior is further reflected by data showing that phasic responses in the ACC are greater when task demands require moment-to-moment adjustments in behavior compared to when response strategies need to be maintained (Wilk et al., 2012).

Indeed, the medial frontal cortex is sensitive to cognitive load (Davis et al., 2005) and lesion studies involving both humans and rats show that medial frontal regions are important for the optimization of ongoing behavior (Bissonette et al., 2013; Newman et al., 2014; Sheth et al., 2012; Srinivasan et al., 2013). Several models focusing on error processing, response conflict, reinforcement learning, expectation violation, action-outcome predictions and evaluation (Jahn et al., 2014) explain well some empirical findings, but medial frontal activity is not necessarily specific to factors described in current models. For example, Grinband et al. (2011a, 2011b) show that medial frontal activity is modulated by time on task, irrespective of error likelihood or conflict stemming from competing response options. Others have reported that, compared to easier trials, simply showing individuals a preview of an upcoming trial that is relatively more difficult elicits a MFN similar to those observed during error commission and inhibitory control (Oliveira et al., 2014). Furthermore, functional connectivity within caudal and anterior regions of the ACC and between the ACC and frontal regions (dorsolateral prefrontal cortex, frontal operculum) is increased in cued inhibitory control conditions of a Go–NoGo task (Schulz et al., 2011), suggesting that the ACC, along with other brain regions, is involved in the coordination of those processes related to preparing and/or biasing the selection of appropriate responses.

Taken together, these data indicate that the role of the medial frontal cortex, including the ACC, in performance monitoring is not specific to error commission, response conflict monitoring, or reinforcement learning but might be better understood by focusing on what is constant across these various paradigms. A general theme regarding medial frontal activation during performance monitoring is that the ACC and surrounding medial frontal cortex are sensitive to events that signal the need for changes in attentional and behavioral control. However, current data do not address the issue of whether the MFNs elicited in the various paradigms result from a common underlying generator and functional basis, or the degree to which these effects are reliable across subjects.

We present here data from a new paradigm demonstrating that an MFN ERP component is elicited when individuals are alerted to potential changes in response demands, and that this activation also describes MFN activity associated with the traditional ERN and response-inhibition NoGo N2. Importantly the MFN associated with stimuli signaling such a change in the response demands was not tied to processes based on error detection, response conflict, inhibition, reinforcement learning, or feedback evaluation and yet still accounted for the MFN resulting from some of these paradigms. Therefore, we propose that this basic function associated with the attention system reflects the underlying basis for medial frontal activation in situations that demand the dynamic ongoing monitoring of performance.

Methods

Participants

Twelve young adults ($M_{\text{age}} = 27$ years, $SD = 4.35$ years; 5 female, 7 male) participated in the present study, the majority of whom were university students ($n = 10$). Participants were free from any neurological or psychiatric conditions, and had self-reported normal or corrected-to-normal vision. Participation was voluntary and was not influenced by monetary compensation.

Task

Our novel task was similar to traditional NoGo paradigms in that the overall goal was to respond as quickly as possible to target Go stimuli and withhold responses to infrequent NoGo stimuli. The Go and NoGo stimuli were centered plus signs that were either black or white, counterbalanced across participants. The novel part of this task is that the Go and NoGo stimuli appear inside a square border, the color of which signaled the current context. The context border was always on the screen and changed color every 1 to 8 trials at the time of a Go stimulus onset. The context border indicated one of two situations: The “Certain” context indicated that the participant was in a run of trials consisting of only Go trials; the “Possible” context indicated that the run consisted of both Go and NoGo trials. Thus, participants knew whether or not there was a possibility of encountering NoGo trials and could use this information to adjust their response strategy accordingly. Each context was associated with a pair of colors, counterbalanced across participants. As an example, for half of the counterbalanced sessions a black or white border color indicated that there would be no NoGo trials (Certain run), but while the border was either red or blue a NoGo trial could occur on any trial (Possible run). Border color changes only occurred on Go trials. So, a border color change from black to white would indicate no change of context, but a border color change from black to red would indicate a change in context, say, from Certain to Possible. Thus, the border color changes were of four types: from Certain to Certain (CC), from Certain to Possible (CP), from Possible to Certain (PC), and from Possible to Possible (PP). Introducing these context cues allows us to assess whether changing expectations for Go versus NoGo trials is reflected in medial frontal activation. The task therefore consisted of seven types of trials all together; four Go trials with a border color change (CC, CP, PC, and PP), two Go trials without a border change (Go in Certain context, Go in Possible context) and NoGo trials. Participants were given all the details regarding task dynamics and trial types, and could use this information to strategize behavior across contexts. See Fig. 1 for a summary of the various Go and context cue trial types.

Go and NoGo stimuli were presented for 50 ms and were followed by a 2-second response window, with an ITI selected randomly between 400 and 900 ms after the response. The task was performed in 4 blocks, approximately 12 min each, separated by short breaks. Participants completed a total of 2640 trials, which were broken down into the following trial types: 1776 Go trials without border color changes (888 × two response contexts: Certain and Possible), 576 with border color changes (144 × four types: CC, CP, PC and PP), and 288 NoGo trials.

Electrophysiological recordings and data reduction

Electrophysiological recordings were done using a 128-channel BioSemi Active Two system. The zero-reference principal voltage values (each site quantified relative to the driven right leg and common mode sense loop) were digitized at a rate of 512 Hz. Coordinates for the electrode montages were digitized for each subject using the Polhemus3 System® Fastrak. In addition to the 128 electrodes mounted in the cap, six external sensors were applied symmetrically on the zygomatic processes, outer canthi, and inferior orbital bones, as well as one sensor at the nasion.

Offline, automated pre-processing and bootstrap testing was done using EEGLab (Delorme and Makeig, 2004) with custom in-house code created in MATLab 2010b and executed in Octave 3.6.3 on the Shared Hierarchical Academic Research Computing Network (SHARCNet). The data were systematically processed for the removal of bad channels and periods of non-stationarity based on correlation distributions between neighboring channels (see Desjardins and Segalowitz, 2013, for an expanded description of these methods). On average there were 12 channels removed ($SD = 6.54$, ranging from 5 to 28), before implementing independent components analysis (ICA).

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