



Sex differences in neurophysiological responses are modulated by attentional aspects of impulse control



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ABSTRACT

The amplitudes of the N2 and P3 components of event-related potentials (ERPs) may be influenced by personality traits such as impulsivity, and male/female differences may also have an effect. However, few studies have assessed the interaction between personality traits and the sex of the subject in these components. Therefore, in this study we evaluated sex differences in the amplitudes of the N2 and P3 ERP components during a continuous performance task, and their relation to impulse control. Twenty-seven healthy participants were asked to perform an AX-type continuous performance task, also known as a Go/Nogo task, during electroencephalographic recording. Participants then completed the Barratt impulsiveness scale (version 11; BIS-11), and the effortful control (EC) scale to self-report personality measures related to impulse control. We found that in the Nogo condition, males showed significantly larger N2 amplitudes than females in the frontal area. Interestingly, Nogo-N2 amplitudes were positively correlated with BIS-attentional subscale scores, but were negatively correlated with EC-attentional subscale scores, and both correlations were observed only in males. These results suggest that attentional aspects of impulse control modulate Nogo-N2 amplitude only in males. This modulatory effect may be related to a sex-specific inhibitory control mechanism acting during early stimulus evaluation.

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1. Introduction

Event-related potentials (ERPs) measure neural activity associated with executive functions (Kam, Dominelli, & Carlson, 2012). Previous research has revealed individual differences in some components of ERPs related to executive functions, and personality traits are one of the factors underlying this variability (Hansenne, 1999; Hansenne et al., 2000; Kam et al., 2012; Nijs, Franken, & Smulders, 2007). Response inhibition, considered a component of executive function, is necessary for control of prepotent responses under conditions of changing situational demands. Differences in response inhibition characteristic of individuals are captured by personality traits such as trait impulsivity, which is a lack of response inhibition at the behavioral level. A behavioral task called the continuous performance task (CPT), also known as “AX-CPT”

(Fallgatter, Brandeis, & Strik, 1997) uses Go/Nogo tests to assess response inhibition. Lack of response inhibition is quantified as the number of premature responses in behavioral performance tasks such as the Go/Nogo task and as ERPs at the neurophysiological level. In such a paradigm, subjects are asked to respond to the target stimulus in the Go condition and to withhold responses to the non-target stimulus in the Nogo condition. Two distinct ERP components have been associated with neurocognitive activity in the Go/Nogo task, which have been labeled N2 and P3. Specifically, the amplitudes and latencies of the ERP N2 and P3 components during the Go/Nogo task are thought to be related to trait impulsivity (Kam et al., 2012; Ruchow, Groen, Kiefer, Buchheim, et al., 2008; Ruchow, Groen, Kiefer, Hermle, et al., 2008).

Traditionally, it has been suggested that N2 and P3 amplitude differences are associated with inhibition of the prepotent response on Nogo trials (Falkenstein, Hoormann, & Hohnsbein, 1999; Pandey et al., 2012). A large number of reports have focused on the role of anterior N2 amplitudes in cognitive control (e.g., Falkenstein et al., 1999; Folstein & Van Petten, 2008; Nieuwenhuis, Yeung, van den Wildenberg, & Ridderinkhof, 2003). N2 refers to the second negative peak in the averaged ERP waveform, found between 200 and 350 ms after stimulus onset at frontocentral sites (Folstein & Van Petten, 2008). On the other hand, P3

Abbreviations: ACC, Anterior cingulate cortex; ADHD, attention-deficit/hyperactivity disorder; ANOVA, analysis of variance; BIS, Barratt impulsiveness scale; CPT, continuous performance task; EC, effortful control; ERP, event-related potential; fMRI, functional magnetic resonance imaging; sLORETA, standardized low-resolution electromagnetic tomography; MNI, Montreal Neurological Institute.

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is sensitive to stimulus probability and task-relevant stimulus information, peaking 300–600 ms after stimulus onset at fronto-central/centroparietal sites (Bokura, Yamaguchi, & Kobayashi, 2001). Recently, P3 amplitude has been proposed as a possible psychophysiological marker for impulsivity (Nijs et al., 2007). Interestingly, both of these ERP components extracted during the Nogo condition of the Go/Nogo task (i.e., Nogo-N2 and Nogo-P3) have been associated with response inhibition (Ruchow, Groen, Kiefer, Hermle, et al., 2008). Nogo-N2 is a negative deflection with its maximum over frontal sites, peaking between 250 and 350 ms after stimulus onset, and has a larger amplitude than the corresponding deflection in the Go condition (Ruchow, Groen, Kiefer, Hermle, et al., 2008). Nogo-P3 is a positive deflection with its maximum at frontocentral sites. Nogo-N2 is assumed to reflect inhibition or revision of the motor plan prior to execution, whereas Nogo-P3 is associated with motor inhibition or the monitoring of the outcome of inhibition (Falkenstein et al., 1999; Sehlmeier et al., 2010).

In experiments with visually presented stimuli, Nogo stimuli typically elicit an enhanced N2 amplitude relative to the Go stimuli, which has been suggested to reflect response inhibition (Fox, Michie, Wynne, & Maybery, 2000). This phenomenon has been called “N2 enhancement” or “the N2 effect”, and is thought to be an index of individual differences in response inhibition (Nieuwenhuis et al., 2003). However, the role of Nogo-N2 is still controversial, and it is unclear whether it is related to inhibition mechanisms that suppress an incorrect response (Falkenstein et al., 1999; Ruchow, Groen, Kiefer, Hermle, et al., 2008), or to conflict detection (Nieuwenhuis et al., 2003; Ruchow, Groen, Kiefer, Hermle, et al., 2008). At the anatomical level, response inhibition and cognitive control have been associated with activity in the anterior cingulate cortex (ACC) and the frontal brain area (Sehlmeier et al., 2010). In particular, it has been suggested that the ACC may play an important role in monitoring for the occurrence of conflict during response selection (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Carter et al., 1998; Nieuwenhuis et al., 2003). Previous ERP studies in which the Nogo-N2 was localized by source analysis have consistently reported source models near the frontal midline, which is in accordance with a generator in the ACC (Bekker, Kenemans, & Verbaten, 2005). Bokura et al. (2001) found that the N2 component was seen only in the Nogo condition, and that its source was localized in the right lateral orbitofrontal and cingulate cortices. Nieuwenhuis et al. (2003) showed that Nogo-N2 was localized in the ACC during a Go/Nogo task in which the relative frequency of Go versus Nogo stimuli was varied. They suggested that Nogo-N2 is an electrophysiological correlate of conflict between the Go and Nogo response representations that is detected in the ACC.

Several self-reported measures of the ability to control impulses have been widely used to investigate the association of impulse control with these ERP components. One of these measures is the Barratt impulsiveness scale (version 11; BIS-11) (Patton, Stanford, & Barratt, 1995), which comprises three related but dissociable facets (non-plan, motor, and attentional). Previous research has shown that N2 and P3 components are related to trait impulsivity as measured by the BIS-11, and that each facet is differentially related to these components (Kam et al., 2012). Another measure is the effortful control (EC) scale that measures executive attention, essentially capturing the opposite of the trait impulsivity measured by BIS-11. The EC also includes three components: attentional, inhibitory, and activation control (Rothbart, Ahadi, & Evans, 2000; Rothbart, Ahadi, Hershey, & Fisher, 2001). EC is defined as the ability to inhibit a dominant response in order to perform a subdominant response and/or to facilitate efficient executive attention. Temperament-related differences in EC have been related to attentional control (Rueda, Rothbart, McCandliss,

Saccomanno, & Posner, 2005). Individuals with high EC showed larger N2 amplitude on executive attentional control, as revealed by a visual Flanker task and an auditory Simon task (Kanske & Kotz, 2012). Buss, Dennis, Brooker, and Sippel (2011) demonstrated that in children, larger N2 amplitudes in response to incongruent versus congruent flankers were associated with less efficient executive attention and lower temperamental EC. However, until recently, few studies have recorded ERPs and studied executive attention related to EC (Samyn, Wiersema, Bijttebier, & Roeyers, 2014).

An additional important factor of trait impulsivity is the sex of the subject: in general, males are more impulsive than females. Objective behavioral measures provide some evidence for sex differences in trait impulsivity. In fact, there is evidence suggesting that males may be less able to control inappropriate behaviors than females (Li, Huang, Constable, & Sinha, 2006; Yuan, He, Qinglin, Chen, & Li, 2008). Poor impulse control is associated with behavioral problems such as attention-deficit/hyperactivity disorder (ADHD), which is more prevalent in males (Kessler et al., 2005). Furthermore, males are generally thought to exhibit higher rates of drug use and abuse. In relation to drug abuse, a review article on sex differences summarized the data on behavioral impulsivity as indicating that impulsivity consists of two distinct components: impulsive action (i.e., difficulty inhibiting a prepotent response) and impulsive choice (i.e., difficulty delaying gratification) (Weafer & de Wit, 2014). Concerning impulsive action, on which our study focused, they concluded that human studies have provided inconsistent evidence for sex being significant. However, this could be because sex differences vary depending on the task. In CPT and Go/Nogo tasks, when impulsive action is measured as inhibitory failures, males show greater impulsivity. In stop-signal tasks, when stimulus presentation is adjusted to maintain a 50% inhibition rate, females require more time to inhibit a prepotent response (Weafer & de Wit, 2014). A meta-analytic study found that sex differences in general measures of impulsivity, although statistically significant, were small in magnitude (Cross, Copping, & Campbell, 2011). They also found a small female advantage in EC. However, no sex differences were found where impulsivity assessment was based on executive-response inhibition tasks, such as Go/Nogo, stop-signal, or CPT (Cross et al., 2011). Measures of behavioral impulsivity have been very inconsistent, with some suggesting greater male impulsivity, some suggesting greater female impulsivity, and some showing no effect of sex differences.

Although the evidence for a role of sex in determining impulsive action is still mixed, if we take into account the relationships between trait impulsivity and ERP components revealed by previous studies, we would conclude that sex should be another critical factor that affects ERP components related to impulse control. In particular, it has been reported that N2 is larger in males, suggesting sex differences in the allocation of attention to novel, task-relevant stimuli (Golgeli et al., 1999). Nagy, Potts, and Loveland (2003) found that N2 was more negative in males, and concluded that this increased negativity might indicate a top-down process of attention bias toward novelty. They used a passive auditory oddball design, in which N2 was examined for evidence of attention-allocation differences related to sex. The Eriksen Flanker task (Eriksen & Eriksen, 1974) is frequently used to elicit a conflict-N2 due to the activation of competing response options (Clayson, Clawson, & Larson, 2011). In this paradigm, N2 amplitude may reflect neural activity associated with increased attentional control in response to conflict. Males exhibited larger N2 amplitudes compared to females in response to irrelevant flanker information (Clayson et al., 2011). In contrast, on a two-choice oddball task (Yuan et al., 2008) that required subjects to respond as quickly as possible to both the standard and the deviant stimuli by pressing different keys, females showed larger amplitudes than males at deviant-elicited N2 and P3 components. This paradigm is similar

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