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How do Females and Males Differ in Neurophysiological Correlates of Impulse Control?

Kazufumi Omura* **and Kenji Kusumoto**

Faculty of Education, Art and Science, Yamagata University, 1-4-12 Kojirakawa-machi, Yamagata-shi, Yamagata 990-8560, Japan

***Corresponding author:** Omura K, Faculty of Education, Art and Science, Yamagata University , 1-4-12 Kojirakawa-machi, Yamagata-shi, Yamagata 990-8560, Japan, **Fax:** +81-23-628-4439; **Tel:** +81-23-628-4439; **E-mail:** omura@e.yamagata-u.ac.jp

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Abstract

Recently, we reported sex differences in neurophysiological correlates of impulse control during the early stages of stimulus evaluation using electroencephalographic recording. In the study, males showed significantly larger N2 amplitudes in the frontal area in the Nogo condition (Nogo-N2) than females; Nogo-N2 is assumed to be an index of response inhibition. Furthermore, Nogo-N2 amplitudes in the frontal area were positively correlated with attentional trait impulsivity subscale scores, but negatively correlated with executive attention subscale scores; interestingly, both correlations were observed only in males. These results suggest that attentional aspects of impulse control modulate the Nogo-N2 amplitude only in males. These sex-specific modulatory effects in inhibitory control mechanisms during early stimulus evaluation may explain why and how females and males behaviorally differ in impulse control at the neurocognitive level. The effects may provide a useful measure of impulse control deficits, which are more prevalent in males than in females. This commentary summarizes the study, placing emphasis on the outcomes of previous conventional neurophysiological studies of sex differences.

Keywords: Event-related potentials; Continuous performance task; Trait impulsivity; Executive attention

Commentary

Sex differences in human cognition have long been a popular research topic. Indeed, differences between females and males are seen in many domains of our everyday life. For example, males drive more recklessly, show more physical and verbal aggression, and use drugs (alcohol, tobacco, and cocaine) more frequently than females [1]. Behavioral problems based on poor impulse control have consistently been reported in a variety of psychiatric and developmental disorders, such as drug and alcohol use disorders, anti-social disorders, obsessive compulsive disorders, borderline personality disorders, schizophrenia, and attention-deficit/hyperactivity disorder (ADHD). Epidemiologically, some of these are more prevalent in males than females. It is of interest to elucidate how these sex-related differences are represented at the neurocognitive level. A better understanding of underlying neurocognitive differences between females and males and their possible causes could lead to better interventions for such psychiatric disorders. We have recently discussed sex differences in terms of interactions between behavior and neurocognition [2].

These sex differences in behavior may be characterized by personality traits such as impulsivity. In general, males seem to be more impulsive than females. Behavioral measures provide some evidence for sex differences in trait impulsivity: males experience greater difficulty in controlling their inappropriate behaviors than females [3,4]. Response inhibition, which is one the primary executive functions, is necessary for control of prepotent responses under changing situational demands. Individual differences in response inhibition are measured by trait impulsivity, which is a lack of response inhibition at the behavioral level. A behavioral task called the AX-type continuous performance task (AX-CPT) uses Go/Nogo tests to assess response inhibition [5]. In such tasks, 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. In neurophysiological research, two event-related potential (ERP) components have been associated with neurocognitive activity in the Go/Nogo task, namely N2 and P3. It has been suggested that N2 and P3 amplitude differences are associated with inhibition of the prepotent response on Nogo trials; these have been labeled Nogo-N2 and Nogo-P3 [6,7].

As well as behavioral tasks, self-report inventories that capture the ability to control impulses have been discussed in relation to these ERP components. One of these measures is the Barratt Impulsiveness Scale (version 11; BIS-11) [8], which comprise three related but dissociable facets (non-plan, motor, and attentional). Another measure is the Effortful Control (EC) scale, which measures executive attention, including three components: attentional, inhibitory, and activation control [9,10]. 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, which captures the opposite of the trait impulsivity measured by BIS-11. Previous research has shown that N2 and P3 components are related to impulse control ability, as measured by the BIS-11 or EC, and that each facet is differentially related to these components [11,12].

Taken together, it is plausible that there are behavioral/neurocognitive differences between females and males. Such differences would emerge in behavioral performance and neurophysiological responses during the AX-CPT. Furthermore, these differences might be modulated by the impulse control ability, as measured by BIS-11 or EC. However, concerning behavioral tasks, Weafer and de Wit concluded that human studies have provided inconsistent evidence for sex differences [13]. According to their review, in CPT and Go/Nogo tasks, males show greater impulsivity, while in stop-signal tasks, females require more time to inhibit a

prepotent response [13]. Another meta-analytic study found that sex differences in general measures of impulsivity, although statistically significant, were small in magnitude [1]. However, no sex differences have been found where impulsivity assessment was based on executive-response inhibition tasks, such as Go/Nogo, stop-signal, or CPT [1]. Sex differences may vary depending on the task or inventory. Thus, the evidence suggesting sex determines impulsive action is still mixed.

When we consider the relationships between trait impulsivity and ERP components revealed by previous studies, we speculate that sex differences in impulse control are complex, with behavioral and neurocognitive interactions. It would be of great value to elucidate which neurocognitive processes are fundamentally influenced by sex and at what processing stages any differences emerge. Neurophysiological methods using electroencephalography (EEG) can segregate processes occurring at different neurocognitive stages due to its fine temporal resolution, of the order of hundreds of milliseconds. In summary, it is of value to assess sex differences in neurophysiological correlates of impulse control, and their relation to impulse control abilities.

The aim of this study was to evaluate sex differences in the amplitudes of the N2 and P3 ERP components during response inhibition, and their relationship to impulse control. We addressed how females and males differ in neural correlates of impulse control during the AX-CPT using EEG. Specifically, we hypothesized that the amplitudes of Nogo-N2 and Nogo-P3 differ between sexes, and the amplitudes of these components may be modulated by individual differences in attentional aspects of impulse control, which occurs in an inhibitory controlling mechanism during early stages of stimulus evaluation.

Twenty-four healthy Japanese subjects, 11 females (mean age = 20.36 ± 0.67 years) and 13 males (mean age = 20.85 ± 0.69 years), were finally enrolled in this study. The study was performed using carefully screened subjects, and ages of males and females were closely matched, in order to control for age effects. Participants were asked to perform the AX-CPT during EEG recording. They were instructed to press a button with their right index finger as quickly and accurately as possible whenever the letter "X" followed the letter "O" (Go condition). For all other letters ("A," "B," "C," "D," "E," "F," "G," "H," "J," or "L") following the letter "O," the prepared motor response had to be suppressed (Nogo condition). The BIS-11 and EC scale were used to assess personality traits related to trait impulsivity and executive attention.

Males and females performed similarly in behavioral tasks, and had comparable self-reported personality traits. However, we found that males had larger (more negative) Nogo-N2 amplitudes, suggesting the presence in males of larger attentional aspects of impulse control than in females. It is worth noting that only in males was smaller Nogo-N2 amplitudes correlated with increased impulsiveness and decreased attentiveness. In males, BIS-attentional subscale scores correlated positively with the amplitudes of Nogo-N2 responses at the frontal sites, whereas EC-attentional subscale scores correlated negatively with the amplitudes of Nogo-N2 responses at these sites. In contrast, there were no differences between males and females in Nogo-P3 amplitudes, a component which has been associated with motor inhibition at a processing stage prior to motor execution [14]. There were also no correlations between Nogo-P3 and BIS-11 or EC scores. In structural terms, source localization estimation showed that greater Nogo-N2 activity in males was localized to the anterior cingulate cortex (ACC), which is associated with response inhibition and cognitive control. The results of this study suggest that females control their behavioral inhibition more effectively with less neural activation than males to achieve similar behavioral performance. Or possibly females control differentially their impulse behavior at the early stages of selective attention and conflict monitoring.

This study has some remarkable advantages as compared with the previous conventional ERP studies of sex differences. First, a power analysis was conducted (a priori and post hoc) to overcome disadvantages of small sample size. Generally, larger sample sizes provide better statistical power. However, when examining effects using large samples, significance testing can be misleading because small or trivial effects are likely to produce statistically significant results. Determining the optimal sample size has not been emphasized in previous studies of sex differences. The sample size used in a study will often be determined by the expense of data collection. To recruit sufficiently many subjects, especially in a small laboratory, it is important to conduct a power analysis in order to achieve cost-efficient sampling. For a priori analysis, as a precaution, the required effect size (Cohen's f or r) was calculated by fixing the sample size, α (0.05), and power (0.80). The required effect size was judged a useful benchmark for confirming that the effects detected by a post hoc power analysis would be sufficient given the small sample size. Subsequently, for post hoc analysis, the value of the effect size, partial eta squared (η^2_p), and power (1 - β) were reported. The η^2_p statistic was included throughout as an indicator of effect size; it is the effect expressed as a proportion of the sum of the effect and the error variance and can exceed 1.00. The power of a statistical test (1 - β) is the probability of falsely retaining an incorrect null hypothesis (H0) [15]. Thus, power can be defined as the probability of finding a real difference if it exists. Usually, 0.8 (or at least greater than 0.7) is considered an acceptable value for power. In this paper, effect size and power values were provided for each ANOVA or correlation analysis and the values were almost acceptable to justify the statistical significance. Nevertheless, the sample size was not large in the study; results should be replicated with larger sample sizes.

Second, this study performed topographical comparisons between sexes, using permutation tests [16], and the source of Nogo-N2 differences was estimated with source analysis using the standardized low-resolution electromagnetic tomography (sLORETA) algorithm [17]. Traditional ERP studies of response inhibition have investigated only a few frontocentral electrode sites on the midline. Although it is plausible that the Nogo-N2 source generators are close to these sites, it is difficult to verify this using the information from few electrodes. Using all electrodes, these methods revealed that sex differences in neurophysiological responses during inhibitory control at the frontal electrode sites were definitely localized in the ACC. Although ERP is a very useful tool to understand neural function in almost real time, the spatial resolution of conventional ERP methods is clearly inferior to functional magnetic resonance imaging (fMRI). These spatial analyses of ERPs employed in this study compensate for this weakness and allowed us to successfully recognize the source of the sex differences during impulse control with good spatial resolution. The ACC has been repeatedly reported as the source of Nogo-N2 [18,19]. The source localization methods confirmed this finding and further successfully replicated that the Nogo-N2 ACC activity is greater in males than females, as show in previous fMRI studies [3,20].

The disadvantages of this study should be recognized. A possible explanation for the sex modulatory effects could lie in the choice of paradigm; sex differences depend upon the task that is used. Task-specific features might affect the correlations between Nogo-N2

amplitude and the attentional subscale scores of the BIS and EC. In addition, the task demanded little impulse control and we found near-perfect behavioral performance. Further studies will be needed in which task difficulty is manipulated to induce impulse control more appropriately. Although the modulatory effect of attention on impulse control may be sensitive to the use of AX-CPT, it will be necessary to evaluate whether this modulatory effect is task-specific by using other behavioral paradigms. Furthermore, it may be necessary to take into account the effects of circulating sex hormones as an individual factor, because evidence suggests that hormones are influential in sex differences in impulsive action [21].

In conclusion, this study suggests that Nogo-N2 amplitude is modulated by attentional aspects of impulse control only in males. Nogo-P3, which has been linked to response-related cognitive processes, did not differ between sexes and was not modulated by attentional aspects of impulse control. These findings suggest that Nogo-N2 amplitude, which is modulated by trait impulsivity and executive attention, is more sensitive to sex than Nogo-P3, and may be linked to sex-specific inhibitory control mechanisms during the early stages of stimulus evaluation. Thus, Nogo-N2 amplitude related to response inhibition might be a suitable biological marker for evaluating impulsiveness and attentiveness in individuals, particularly males. It may also be useful for explaining the epidemiological sex differences in deficits of impulse control in a variety of psychiatric and developmental disorders, such as drug and alcohol use disorders, anti-social disorders, schizophrenia, and ADHD, which are more prevalent in males than in females. Going forward, it will be important to recognize the interactions between individual differences in neurophysiological responses and behavioral performance, and to determine the biological markers of the aforementioned disorders, controlling for the effects of task differences and circulating sex hormones, with larger sample sizes.

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