Source localization of the Nogo-N2: A developmental study

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Abstract

Objective: The aim of the present study was to investigate whether similar neural sources are involved in generating Nogo-N2 scalp topography in children and adults.
Methods: Source analysis was performed on the Nogo-N2 data from two groups of children (sixteen 6/7 year-olds and seventeen 9/10 year-olds) and seventeen young adults (aged 19–23 years) that were obtained in a prior study by Jonkman LM. The development of preparation, conflict monitoring and inhibition from early childhood to young adulthood; a go/nogo ERP study. Brain Res 2006;1097:181–93.
Results: In both children and adults a bilateral source pair in the medial frontal cortex (near ACC) was involved in the generation of Nogo-N2 activity. However, children needed an additional, posteriorly located source pair to adequately explain the Nogo-N2 distribution. In 6/7 year-olds this posterior source was localized in occipito-temporal areas, whereas in 9/10 year-olds the posterior sources shifted to parietal locations.
Conclusions: Although children recruit similar frontal regions as adults in the Nogo-N2 time window, the additional activation of posterior sources might indicate that early executive control performance is less automatic or requires more effortful control in children. This in turn might cause them to rely on more basic stimulus processing or to activate additional attention-related areas.
Significance: Results from the present study show that in children, a more diffuse brain network is involved in executive control processing (conflict monitoring) in the Nogo-N2 time window than in adults.
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Keywords: Child development; Conflict monitoring; Dipole modeling; Nogo-N2; Anterior cingulate cortex

1. Introduction

The present study is aimed at elucidating which brain sources underlie the development of the Nogo-N2 event-related brain potential (ERP) component, by applying source analyses methods to the data from an earlier paper by Jonkman (2006). In the latter paper we compared the performance and ERPs of 6–7 and 9–10 year-old children and young adults during performance of a Go–Nogo (cued CPT-AX) task. In this task the subjects are presented with a series of letters and have to respond to the letter X (target), but only when it is preceded by the letter A (cue), this

is the Go condition. In situations in which the cue letter A is not followed by the target stimulus (Nogo condition), the response that has been prepared during the cue-probe interval has to be inhibited. In the Nogo-condition (compared to Go) an ERP response consisting of a negativity (Nogo-N2) followed by a positivity (Nogo-P3) above fronto-central cortex is evoked. In adults the Nogo-N2 has been linked to the process of response inhibition in some studies (Falkenstein et al., 1999; Fallgatter and Strik, 1999; Jodo and Kayama, 1992), whereas in later studies (Donkers and Van Boxtel, 2004; Nieuwenhuis et al., 2003; Van Veen and Carter, 2002a) the negativity was linked to the process of conflict monitoring. In the prior developmental study by Jonkman (2006) it was concluded on the basis of performance measures that attention processing in the CPT-AX task improved most strongly

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between the age of 6 and 10, whereas inhibitory behavior started to improve later, after the age of 10. Nogo-N2 effects were, however, found to be largest in the youngest (6- to 7-year-old) children and decreased linearly with age. On the basis of these and other ERP responses in reaction to the cue, it was concluded that the Nogo-N2 was linked to the process of conflict monitoring rather than to inhibition. The topographic Nogo-N2 analyses across 30 electrodes showed that the Nogo distributions of both children and adults were dominated by the commonly reported negative field above medial prefrontal cortex (Bekker et al., 2005; Kiefer et al., 1998; Nieuwenhuis et al., 2003). However, the distributions of children showed extra posterior positivity at bilateral temporal–parietal locations in 6- to 7-year-olds and above medial parietal cortex in 9- to 10-year-olds. Such enhanced posterior activity in the Nogo-N2 interval in children (compared to adults) was reported earlier by Ciesielski et al. (2004) in a similar task. These ERP findings are also supported by developmental functional imaging studies that report activation of larger and more diffuse networks in children or adolescents during performance of tasks requiring cognitive control (for reviews, see Durston and Casey, 2006; Luna and Sweeney, 2004). In Jonkman (2006) the extra posterior activation in children in the Nogo-N2 interval was hypothesized to be associated with increased attentional processing or enhanced attention allocation during conflict monitoring in childhood. The present study had the aim to verify these hypotheses by performing further source analyses on the data.

In prior source localization studies in which Go/Nogo tasks were presented to adult subjects the source of the Nogo-N2 has been repeatedly localized in Anterior Cingulate Cortex (ACC; Bekker et al., 2005; Kiefer et al., 1998; Nieuwenhuis et al., 2003; Van Veen and Carter, 2002a), a brain structure that has been frequently linked to conflict monitoring and response competition in fMRI studies (Botvinick et al., 1999, 2001, 2004; Barch et al., 2001; Braver et al., 2001). To our knowledge, as yet no developmental source localization studies on Nogo-activity have been performed. However, there have been several developmental fMRI studies investigating brain activation differences between children (ranging from 6 to 12 years-old) and adults during performance of a Go/Nogo task (Booth et al., 2003; Bunge et al., 2002a; Casey et al., 1997; Durston et al., 2002; Tamm et al., 2002). These studies have yielded different patterns of Nogo-activation in prefrontal cortex in children and adults, some studies reporting enhanced and others reporting reduced activation in children (compared to adults) in different regions of PFC. Furthermore, congruent with topographical results from Jonkman (2006), in two studies Nogo performance was reported to be more strongly associated with activation of posterior areas in children than adults (Bunge et al., 2002a; Durston et al., 2002). The fact that such Nogo-posterior cortex activations in children were only reported in two out of six developmental fMRI studies might be explained by different factors, an important one being differences in task design. In most of the above-mentioned fMRI studies blocked, instead of event-related, designs (that are more comparable to those used in ERP research) were applied. In fact, the studies that did use an event-related design did report prefrontal as well as posterior activation in children and adults in the Nogo condition. In Durston et al. (2002) adults showed significantly higher activation in the Nogo condition in bilateral ventral PFC, left ACC and left caudate nucleus. Children were reported to have higher Nogo-activation than adults in right DLPFC as well as in right parietal cortex. In Bunge et al. (2002a) the Nogo condition activated multiple prefrontal, temporal and parietal association areas in adults, whereas overall, only small Nogo-activation was seen in children. However, inhibition success was more strongly associated with activation of posterior (parietal, occipital and temporal), instead of prefrontal, areas in children, whereas no activation-inhibition behavior associations were seen in adults. Another important difference between fMRI and ERP studies is that, albeit with considerably lower spatial resolution, it is possible to localize sources on a millisecond time-scale whereas in fMRI studies it is impossible to conclude to what extent the Nogo-activation explains Nogo-N2 or Nogo-P3 activity. This is especially important since Nogo-N2 and Nogo-P3 have been interpreted as reflecting different stages of Nogo processing, respectively, monitoring of response conflict and response inhibition.

In most previous studies, source analysis has been performed on Nogo–Go difference waves (Bokura et al., 2001; Kiefer et al., 1998; Nieuwenhuis et al., 2003; Van Veen and Carter, 2002a). Although the use of difference waves enables one to get rid of activity that is similar in Go and Nogo conditions, the task assignment in the go condition to press a button leads to specific motor and attention related effects on only the go-ERP signal that will also contribute to the Nogo–Go difference wave. Accordingly, in several studies, besides a source in prefrontal cortex additional sources were required to adequately explain the Nogo-N2 distribution. Bokura et al. (2001) for instance reported an additional source in the left thalamus, whereas Nieuwenhuis et al. (2003) reported medial posterior involvement in a task condition with 80% Nogo trials. To prevent the contribution of such motor or attention processes from the Go condition, in the present study, dipole models were computed directly on the Nogo ERP. However, a complicating factor in localizing sources on the Nogo-wave only is the presence of the fronto-central Nogo-P3 positivity that has been demonstrated by Bekker et al. (2005) to dominate the Nogo-N2 scalp topography and source models in adults. Bekker et al. circumvented this problem by subtracting peak Nogo-P3 activity from the average. It was shown that such corrected Nogo-N2 data yielded better source estimates, i.e. in the vicinity of the ACC, than Nogo-N2 data that were not corrected for P3 activity. Following Bekker et al. (2005) this baseline correction method was also applied in the present study. It was