

# P300 Component Modulation During a Go/Nogo Task in Healthy Children

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## ABSTRACT

**Introduction:** Several differences in the P300 component are observed when responses must be executed or inhibited in the Go/Nogo task. However, few studies were established by using well-controlled task with respect to the preparatory processing and stimulus probability. In the present study, we examined the peak amplitude and latency of Go-P300 (P300 evoked by visual Go stimuli) and Nogo-P300 (P300 evoked by visual Nogo stimuli) component in healthy children.

**Methods:** High resolution EEG data were recorded from 13 children (7-11 years old) during a cued equiprobable Go/Nogo task. The P300 component was measured at frontal (F3, Fz, F4) and parietal (P3, Pz, P4) regions in response to both Go and Nogo stimuli. Data were analyzed using a three-way repeated measures ANOVA.

**Results:** These children displayed higher P300 amplitude in the Go relative to Nogo condition at parietal region. In addition, decrease in P300 latency was observed at the frontal in comparison to parietal region.

**Discussion:** The results might suggest that the P300 is related to different processes or arise from different generators in execution and inhibition conditions.

## 1. Introduction

Inhibitory control is an essential aspect of human behavior. Without such processes efficient goal-directed behavior would be difficult to achieve. Inhibitory processes can be evaluated by both neuropsychological tests (i.e. Go/Nogo task or Stroop test) and neurophysiological tools (i.e. event-related potentials (ERPs)). Moreover, functional neuroimaging experiments have started to examine the brain regions engaged by tasks in which response inhibition is a characteristic, such as the Go/Nogo and Stroop.

Quantitative electrophysiological assessments, using ERPs, provide the temporal and spatial information of neural networks. Some components of ERPs, together with well-controlled experimental manipulations, can be very useful in evaluating cognitive processes in man (Barry, Johnstone, & Clarke, 2003). Moreover, ERP measurements can reveal both specific neurophysiological correlates of poor performance and specific differences in covert neural processing in the absence of performance differences (van Leeuwen, Steinhausen, Overtoom, Pascual-Marqui, van't Klooster, et al., 1998). The waves evidenced by a task reveal two types of cognitive components: exogenous and endogenous

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components (Donchin, Ritter, & McCallum, 1978). The exogenous components (i.e. P100) occur between 0 and 150 ms after stimulus onset, they are sensitive to physical stimulus features (loudness, brightness, color, size, etc.) and they reflect primarily sensory and early attention processes. In contrast, the later ERP components (i.e. P300) represent the higher cognitive processing.

P300 (P3) component of ERPs obtained by time-locked averaging electroencephalography has been used to investigate the neural processes of response execution/ inhibition during a Go/Nogo paradigm. The difference between Go and Nogo waveforms is frequently described as the 'Go/No-go effect', which has been mainly evoked using visual and auditory stimulation. Several studies employing a visual Go/Nogo task have demonstrated some differences in the ERPs between Go (subject has to respond) and Nogo (subject has to refrain from responding). One of the main differences concerns the topographic differences across response types: on Nogo trials the P300 has a more central maximum than on Go trials, on which it has a parietal maximum (Bruin, Wijers, & van Staveren, 2001). Both effects have been interpreted as reflections (or an outcome) of inhibitory processes (Falkenstein, Hoormann, & Hohn, 1999).

However, some difficulties appear in interpretation of ERP components. In fact, ERP components are sensitive to several experimental factors (Kemner, Verbaten, Koelega, Buitelaar, van der Gaag, 1996). In these experiments, the target processing may be confounded with effects on preparatory processing such as orienting and preparation (van Leeuwen et al., 1998). In this context, during a Go/Nogo paradigm, the features of the P300 appear more likely to be due to the relative rarity of the Go or Nogo stimulus (Smith, Johnstone, & Barry, 2004). Hence, the factors such as probability and task relevance mediate components elicitation (Brown, Clarke, Barry, McCarthy, Selikowitz, et al., 2005). In most of studies, these manipulations were inseparable in the target stimuli. Thus, it appears indispensable to choose equal relative probabilities conditions using a cued equiprobable target/non-target trials.

To our knowledge, only few studies investigated the P300 component in healthy children using abovementioned paradigm. In a neurodevelopmental study, by using an auditory Go/Nogo task, behavioral and electrophysiological indices of developing response activation and inhibition processes in child, young-adult, and adult groups were investigated (Johnstone, Pleffer, Barry, Clarke, and Smith, 2005). Consistent with the literature, they reported that the NoGo-P300 had a more anterior

distribution than the Go, caused mainly by greater activation in the central region for NoGo stimuli. Furthermore, a P300 Nogo>Go effect was found in adults, and opposite (but insignificant) pattern in children, representing developmental effect on P300 modulation in inhibition tasks. It might reflect that the mechanism of inhibitory processing is not the same in children and adults, and, thus, further research is required in the area. Hence, this study provides much-needed data on the response activation and inhibition, as operationalized by the visual Go/Nogo task, in children. Furthermore, investigation of the brain bases of inhibitory mechanisms in healthy children is also important for understanding neuro-developmental disorders that may result from altered or deficient inhibitory processing. This is particularly the case for those disorders that arise in childhood. For example, in Attention-Deficit Hyperactivity Disorder (ADHD) (inability to maintain attention and inhibitory influences on behavior), patients have demonstrated deficits in inhibitory processing (i.e. Nazari, Berquin, Missonnier, Aarabi, Debatisse, et al., 2010).

In view of the paucity of data in the literature, we decided to evaluate the late ERP component during a cued equiprobable Go/Nogo trials, requiring cued response execution/ inhibition in healthy children. More specifically, it was hypothesized a more posterior distribution of Go-P300 relative to Nogo-P300.

## 2. Methods

### 2.1. Subjects

At the first stage of sampling, nineteen children were addressed to the Pediatric neurology department of the Amiens University Hospital. These subjects attended regular classes and presented normal academic achievement. All subjects were tested in a single session that lasted approximately 2.5 hours including full version of the Wechsler Intelligence Scale for Children – Third Edition (WISC-III) (Wechsler, 1991) and the second version of Continuous Performance Task (CPT-II) (Conners, 2003). A cued equiprobable Go/Nogo task was administered during high resolution electroencephalogram (EEG-HR) recording for ERP analysis. In the period of EEG, parents completed the Swanson, Nolan and Pelham (SNAP-IV) questionnaire (Swanson, Wigal, Udre, Lerner, Agler, et al., 1998) and the Child Behavior Checklist (CBCL) (Achenbach and Edelbrock, 1983) to ensure the absence of behavioral problems.

All subjects had a full-scale WISC-III IQ score of 100 or above, with no significant discrepancy between

verbal and performance sub-tests. They had normal or corrected-to-normal vision. Exclusion criteria for all children included a history of problematic prenatal or neonatal period, a disorder of consciousness, head injury with cerebral symptoms, history of central nervous system diseases, convulsions or a history of convulsive disorders or EEG spike wave activity, sensory-motor deficits, attentional difficulties and/or other behavioral problems. Six children were excluded for further analysis because of abovementioned criteria. Hence, the data of thirteen right-handed healthy children (4 girls and 9 boys; age range: 7-11; mean age:  $8.5 \pm 1.3$  SD) were analyzed.

This protocol was approved by the local ethics committee. Parents received detailed information about the study protocol before giving informed consent. After being shown the study apparatus, children verbally assented to participation. No monetary compensation was given. They and their parents agreed to participate in the study and signed written consent forms.

## 2.2. Stimuli and Procedure

The subjects, comfortably seated, watched a computer-controlled display screen at a distance of 70 cm to perform the cued equiprobable Go/Nogo task. This task was defined according to the Go/Nogo paradigm that requires the preparation and execution of responses to pre-defined target-stimuli (Go) and, also, the inhibition of a prepared motor response following other stimuli (Nogo).

Letters stimuli ( $2.5 \times 2.5$  cm), subtending  $3.5^\circ$  of visual angle, were sequentially presented at the center in a pseudo-randomized order. The letters were black and the screen on a grey background. All stimuli were created and presented using the *eevoke*<sup>TM</sup> version 2.0.0.3 (ANT Software®). The whole stimulus set consisted of 320 letters as follow: 80 (25%) primer conditions 'O' with 40 (12.5%) Go (O followed by W) and 40 (12.5%) Nogo (O followed by any other letter), and 160 (50%) distracters (other letters, or letter W without a preceding O). Thus, probability ratios of the Go vs. Nogo conditions were kept equal. The letters were presented for 200 ms, separated by an interval of 1650 ms. And it lasted about 10 min.

The participants were instructed to press a button with their right index fingers as fast as possible whenever the letter "O" was followed directly by the letter "W" (Go-condition), but if the letter was a "non-W" the button has not be pressed (Nogo-condition). These conditions

of the test represent the execution and inhibition of an anticipated motor response. The participants performed 30 practice trials in order to ensure that they understood and could perform correctly the task. They received feedback and guidance after each practice but they performed the tasks without any feedback, while the ongoing high resolution EEG was recorded.

## 2.3. Recording Methods

Continuous electroencephalographic was recorded using 64 surface electrodes (Easy cap®) placed over the scalp. The recording system involved a multi-channel DC amplifier by ANT® and the *eemagine* software®. EEG was recorded with a right-mastoid reference at a sampling rate of 512 Hz. The impedance of electrodes was kept below 10 k $\Omega$ . The spatial positions of the 64 electrodes were digitalized using a 3 dimensional magnetic digitizer (Polhemus 3Space Fastrak ®), and the ANT software *EETrack*®.

## 2.4. Waveform Analysis

After artefact removal and off-line correction of ocular artefacts (amplitude threshold detection algorithm, *eemagine*® software), the EEG signals were analyzed using a common hardware average reference. Data from trials with correct answers were averaged according to the task conditions (Go- and Nogo). ERPs were averaged over a window of 900 ms with 200 ms pre-stimulus and band-pass filtered between 0.3Hz and 30 Hz, 3dB/octave for low-pass filter. On average, the percentage of artefact-free trials was  $76\% \pm 15$  and  $70\% \pm 13$  for Go- and Nogo trials, respectively.

## 2.5. Statistical Analysis

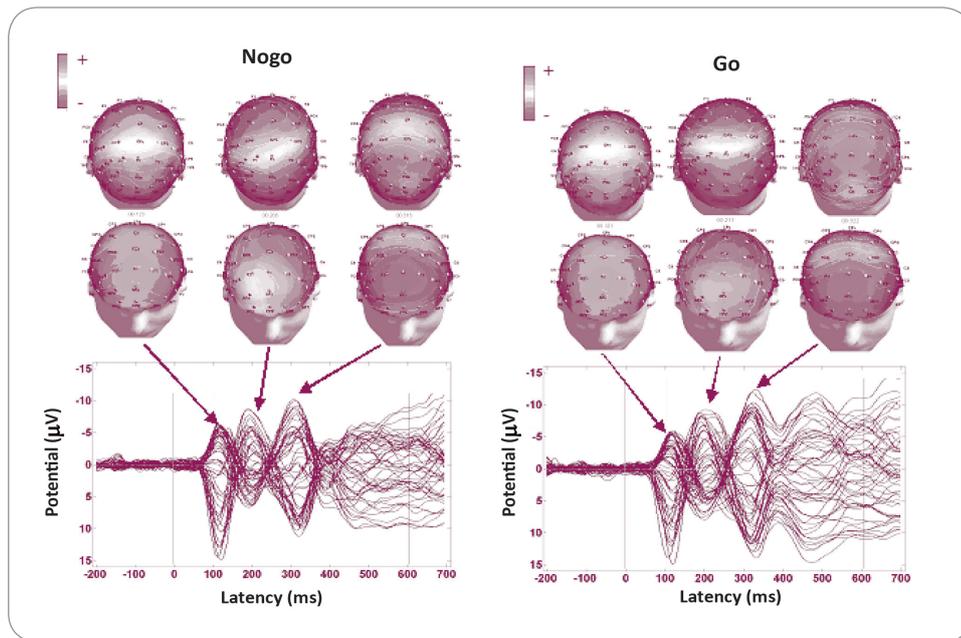
The normality of data distribution was verified with Kolmogorov-Smirnov test (KS-test). Statistical analysis was performed on P300 amplitude and latency separately using a three-way repeated measures ANOVA, with within-subjects factor of condition (Go vs. Nogo), electrode (right, midline, left), and region (frontal vs. parietal). Analyses were repeated using across electrodes (right + midline + left<sup>3</sup>). As this did not change the results, for data reduction purpose, results will be presented for the across electrodes. Statistical analysis was processed using SPSS® (version 16).

## 3. Results

In Fig. 1, electrode overlaid grand averaged ERP topographies are separately shown for each condition

to illustrate the occurrence of the peaks. As shown in the Fig., three major components were identified on the time dimension as follows: 79–175, 167–278, and 261–423 ms post-stimulus. These components were labeled P100, N200, and P300, respectively. The P300 was best distinguished at parietal and frontal sites. P3,

Pz, P4, F3, Fz and F4 electrodes were thus selected for the P300 component. The quantitative values for peak amplitude and latency of the P300 components across electrodes are summarized in Table 1. In Fig. 2, averaged waveform ERPs were plotted for both Go and Nogo conditions.



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Fig. 1: Scalp distributions of P100, N200, P300 components. Left: Nogo- and right: Go- conditions.

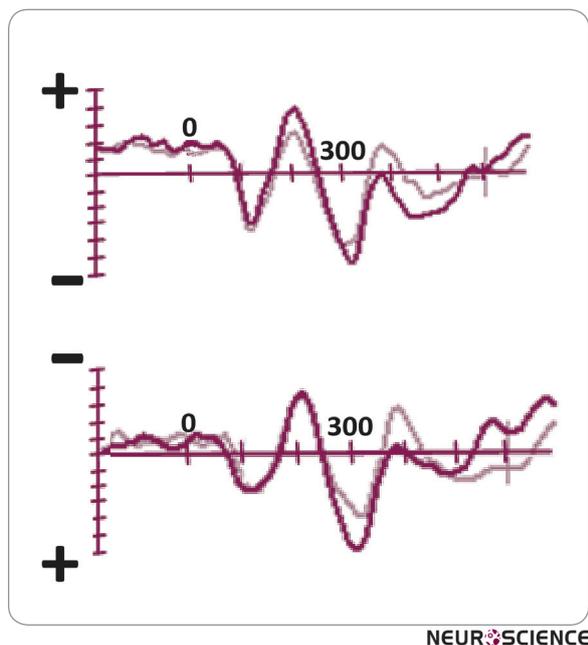
Table 1. Mean and Standard Deviation of P300 Amplitude (µV) and Latency (ms) per Region, as a Function of Condition

	Parietal	Frontal	Total
Amplitude- GO	14.9 ± 5.3	11.6 ± 4.5	11.6 ± 4.5
Amplitude- NOGO	11.1 ± 5.6	11.1 ± 5.7	11.1 ± 5.7
Amplitude- TOTAL	13.0 ± 5.1	11.3 ± 4.4	11.3 ± 4.4
Latency- GO	328.5 ± 11.2	316.8 ± 12.4	322.7 ± 13.0
Latency- NOGO	324.0 ± 15.1	312.7 ± 13.4	318.4 ± 14.2
Latency- TOTAL	326.3 ± 13.2	314.8 ± 12.8	320.5 ± 14.1

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Amplitude: there was no main effect region or condition on the P300 amplitude. However, interaction effect of region × condition reached significant ( $F_{1,12} = 8.72, p = 0.012$ ). As shown in the Fig. 2, the P300 amplitude was higher in the Go as compared to Nogo condition at parietal site.

Latency: there was significant main effect region ( $F_{1,12} = 7.79, p = 0.016$ ), indicating that P300 latency at frontal region was shorter than latency at parietal region. There was no significant main effect or interaction.



**Fig. 2.** Grand average ERPs as a function of conditions; Go (black line) and NoGo (Grey line) for frontal (top) and parietal (bottom) regions, separately. Note: The polarity in frontal region is shown inversely in order to simplify the anterior-to-posterior comparisons.

#### 4. Discussion

One important goal of electrophysiological studies of human perception and cognition must be to define the specific information-processing transactions indexed by the various ERP components found to be sensitive to psychological manipulations (Mangun and Hillyard, 1991). The aim of the present study was to investigate the P300 modulation in response to execution/ inhibition condition in healthy children by using an equiprobable Go/Nogo task. The stimuli consisted of some letters similar in; size, shape, color, speed, Inter-Stimulus-Interval (ISI), probability and location. In this case, physical property, spatial attention, feature detection, temporal attention, expectancy or prepotent Go/Nogo response were not manipulated; which implies differences between conditions.

In the present study, the P300 showed topographic differences between Go and Nogo trials: amplitude for Go trials was larger at parietal region, and smaller at frontal region, than for Nogo trials. This Go/Nogo P300 effect at parietal region is consistent with previous topographic studies (i.e. Bokura, Yamaguchi, & Kobayashi, 2001; Fallgatter, Ehlis, Seifert, Strik, Scheuerpflug, et al., 2004; Oddy, Barry, Johnstone, and Clarke, 2005) indicating P300 component in the Go condition to be maxi-

mal at centro-parietal site (typically at Pz), whereas in the Nogo condition it is more anterior (fronto-central). Some researchers have concluded that the P300 in a Go/ Nogo paradigm is confounded by motor response effects, such as the contingent negative variation (CNV), producing false amplitude and latency variations (Oddy, et al., 2005). The CNV was identified in the early research of Walter, Cooper, Aldridge, McCallum, and Winter (1964), who concluded that it is a motor anticipation and preparation process continuing until activation of a motor response such as a button press. Hence the parieto-occipital enhancement of the P300 on Go versus Nogo trials can be explained by the contribution of movement-related potentials, which is larger on Go than on Nogo trials.

Previously, a P300 NoGo>Go effect has been reported in young-adult and elderly subjects, with no auditory/ visual modality differences evident (Falkenstein et al., 2002; Johnstone et al., 2005). However, in the present study children did not show a significant NoGo /Go effect for P300. This result suggests different utilization of the inhibition processing sequence in children and adults (with differential activity related to the degree inhibition required). It may confirm that the mechanism of execution/inhibition processing is not the same in children and adults, and, thus, further research (with visual and auditory modalities) is required in this area.

An additional aim of this research was to investigate the time course of the cortical response to Go and Nogo stimuli; an issue that can not be fully addressed in behavioral studies because overt responses could not de represented the discrete stages of information processing (including response inhibition). In terms of the P300 latency, our results indicated that latency was shorter at frontal than latency at parietal region. P300 peak latency is proportional to stimulus evaluation timing, sensitive to task processing, and it varies with individual differences in cognitive capability (see Polich, 2007). On the other hands, some researchers have argued that the Go/ Nogo task is a special conflict-inducing task requiring a choice between two decisions/responses (e.g., Gomez, Ratcliff, Perea, 2007). As P300 latency reflects stimulus evaluation time, shorter P300 latencies at frontal region could be interpreted as a fast reactivity of frontal cortex with respect to information processing in decisions/responses conditions.

One limitation of the present research was the participants' being limited to right-handed children as is the case in most ERP studies. As a result, our present findings can only apply to right-handed individuals and

how the brains of left-handed people work still requires further investigation.

## 5. Conclusion

The scalp topography of the P300 component is different for Go and Nogo stimuli. Our results might suggest that the P300 is related to different processes or arise from different generators in execution/inhibition conditions. Different P300 Go/Nogo effect in children compared to adults might represent that the mechanism of execution/inhibition processing is age-related

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