Weak proactive cognitive/motor brain control accounts for poor children's behavioral performance in speeded discrimination tasks

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Abstract

Background. Motor and inhibitory control rely on frontal cortex activity, which is known to reach full maturation only in late adolescence. The development of inhibitory control has been studied using event-related potentials (ERP), focusing on reactive processing (i.e. the N2 and the P3 components). Scarce information exists concerning pre-stimulus activity as that represented by the Bereinshafstpotential (BP) and by the prefrontal negativity (pN). Further, no literature exists concerning the post-stimulus components originating within the anterior insula (pN1, pP1, pP2). This study aims at associating children performance with these motor-cognitive processing in frontal brain areas.

Methods. High-resolution EEG recordings were employed to measure ERPs from 18 children (12 years old) and 18 adults (28 years old) during a visuo-motor discriminative response task. Response time (RT), commission (CE) and omission errors, and RT variability were compared between groups. At brain level, two pre-stimulus (BP and pN) and seven post-stimulus (P1; pN1; N1; pP1; N2; pP2; P3) ERP components were compared between groups.

Results. Children showed slower and more variable RTs and poorer inhibition (higher CEs) than adults. At electrophysiological level, children presented smaller BP and pN. After stimulus onset, children showed lower amplitude of N1, pP1, P3, and pP2 components. The P1, pP1, N2 and P3 were delayed compared to adults.

Conclusions. Our results demonstrate that children are characterized by less intense task-related proactive activities in frontal cortex, which may account for subsequent poor and delayed reactive processing and, thus, for inaccurate and slow performance.

Introduction

The human cognitive control includes many brain functions, such as attention, working memory, flexibility and inhibition necessary for individuals to interact with the surrounding environment. Inhibitory control has been defined as the ability to prevent undesired responses (Aron, Robbins, & Poldrack, 2004). At a behavioral level, this ability is displayed when successfully stopping an ongoing response or withholding a dominant one to accomplish the required task (Davidson, Amso, Cruess Anderson, & Diamond, 2006).

Several brain regions have been associated to an efficient inhibitory control, but the most accredited one is the right inferior frontal gyrus within the prefrontal cortex (PFC) (Aron, Robbins, & Poldrack, 2004; Friedman, Nessler, Cycowicz, & Horton, 2009; Perri, Berchicci, Spinelli, & Di Russo, 2014; Vidal, Mills, Pang, & Taylor, 2012). Compared to other brain regions, the development of the PFC appears to occur later in the growth process (Diamond, 1988; Sowell, 2004). Measures of myelination (Giedd et al., 1999), grey matter reduction (Sowell, Delis, Stiles, & Jernigan, 2001), resting metabolism (Diamond, 2002) and brain activation (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Casey et al., 1997; Vidal, Mills, Pang, & Taylor, 2012; VijayaKumar et al., 2014) indicate that the PFC reaches its full maturation only in adult age. In fact, neuroimaging studies observed that children failed to activate the right ventrolateral PFC during visual discriminative response tasks (DRTs) (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002), or adopted a different strategy to inhibit the motor response, consisting in the activation of the left middle frontal and pre-central gyri (Vidal, Mills, Pang, & Taylor, 2012; but see Casey et al., 1997 and Luna et al., 2001 for different results). The different functional neuroimaging profile observed in children likely accounts for their poorer behavioral performance observed in children when compared to adults (Casey et al., 1997; Ciesielski, Harris, & Cofer, 2004; Jonkman, 2006).

The development of brain functions has been widely studied also using electrophysiological methods, such as event-related potentials (ERPs), which allow measures of the magnitude (amplitude), speed (latency) and the time-course of cognitive processing. Compared to adults, children demonstrate a general tendency towards larger and slower ERPs, with the former likely accounted by lower skull thickness and density (Holcomb, Coffey, & Neville, 1992; Knott, Hazony, Karafa, & Koltai, 2004) and higher synaptic density (Huttenlocher, 1979) of children, and the latter explained by the incomplete myelination process (Barry & Blasio, 2015; Barry, De Blasio, & Borchard, 2014; Ciesielski, Harris, & Cofer, 2004; Giedd et al., 1999; Johnstone et al., 2007; Lamm, Zelazo, & Lewis, 2006).

Most of the existing ERP studies in children cognition focused on two post-stimulus ERP components: the N2 and the P3, either during auditory (Barry & Blasio, 2015; Barry, De Blasio, & Borchard, 2014; Ciesielski, Harris, & Cofer, 2004) or visual tasks (Ciesielski, Harris, & Cofer, 2004; Davis, Bruce, Snyder, & Nelson, 2003; Jonkman, 2006; Jonkman, Lansbergen, & Stauder, 2003; Lamm, Zelazo, & Lewis, 2006; Okazaki et al., 2004); for a review see Segalowitz, Santesso, & Jetha, 2010). In children, the amplitude of the N2 was related to individual differences in inhibitory control (Barry & Blasio, 2015), with a more frontal distribution compared to adults (Barry & Blasio, 2015; Ciesielski, Harris, & Cofer, 2004; Jonkman, Lansbergen, & Stauder, 2003). Cross-sectional studies showed that N2 amplitude decreases with age (Davis, Bruce, Snyder, & Nelson, 2003; Jonkman, Lansbergen, & Stauder, 2003), reflecting developmental changes in cognitive control (Lamm, Zelazo, & Lewis, 2006). The later P3 component was associated with decision/inhibition processes (Johnstone et al., 2007; Jonkman, Lansbergen, & Stauder, 2003; Polich, 2007); however, due to its late timing, concomitant or following the response, this association seems rather unlikely, whereas an association with the "reset" or task closure processes seems more plausible (see Falkenstein, Hoormann, & Hohnsbein, 1999).

Notwithstanding the large body of research on the developmental modifications in cognitive control, existing ERPs evidence focused primarily on some of the post-stimulus components, providing a

somehow limited view of the entire decision-making processes. Indeed, several ERP studies from our research group (Berchicci, Lucci, Perri, Spinelli, & Di Russo, 2014; Berchicci, Lucci, Pesce, Spinelli, & Di Russo, 2012; Berchicci, Spinelli, & Di Russo, 2016; Bianco, Berchicci, Perri, Quinzi, & Di Russo, 2017; Bianco, Di Russo, Perri, & Berchicci, 2017; Di Russo et al., 2016; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015a, 2016; Perri, Berchicci, Spinelli, & Di Russo, 2014; Sulpizio et al., 2017) revealed that the entire decision-making processes is characterized not only by the well-studied post-stimulus components, but also by two pre-stimulus components and three recently discovered post-stimulus components. Despite the importance of brain preparatory activity in the decision processing, only few studies in children focused on the pre-stimulus brain activity. Some of these studies used the contingent negative variation (CNV) paradigm (Jonkman, 2006; Jonkman, Lansbergen, & Stauder, 2003), showing reduced response preparation (Jonkman, 2006) in young children compared to older children and adults, and comparable preparatory brain activities between these latter age groups (Jonkman, Lansbergen, & Stauder, 2003). Berchicci et al. (2015) investigated the effect of physical fitness on motor and cognitive preparation in children represented respectively by the Bereitschaftspotential (BP) and by the prefrontal negativity (pN) during a flanker task showing lager cognitive preparation in high-fit children. The BP, is a slow-rising negativity originating in the supplementary and cingulate motor cortex (Di Russo et al., 2017; Shibasaki & Hallett, 2006) and reflecting motor preparation whereas the pN, is another slow rising negativity detected on prefrontal sites concomitantly to the BP (Berchicci, Lucci, Perri, Spinelli, & Di Russo, 2014; Berchicci, Lucci, Pesce, Spinelli, & Di Russo, 2012; Berchicci, Spinelli, & Di Russo, 2016; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015a, 2016; Perri, Berchicci, Spinelli, & Di Russo, 2014). It has been related to proactive cognitive preparation (Di Russo et al., 2016), in particular to the inhibitory control (Bianco, Berchicci, Perri, Quinzi, & Di Russo, 2017; Bianco, Di Russo, Perri, & Berchicci, 2017), and its origin has been localized in the inferior frontal gyrus (Di Russo et al., 2016; Sulpizio et al., 2017).

In visuo-motor tasks after stimulus onset, in addition to the well documented sensorial (P1 and N1) and endogenous (N2 and the P3) components, three more components have been identified: the prefrontal N1, P1 and P2 (pN1, pP1 and pP2 respectively) peaking between 110 and 300 ms after the stimulus onset and localized in the rostral part of anterior insula (Di Russo et al., 2016; Sulpizio et al., 2017). While the pN1 and pP1 are related to top-down perceptual processing associated with stimulus physical salience and awareness and sensory-motor integration respectively (Perri et al., 2018; Perri, Berchicci, Bianco, Spinelli, & Di Russo, 2018; Perri & Di Russo, 2017; Sanchez-Lopez et al., 2017), the pP2 has been associated with evidence accumulation process, that is the efficacy of the stimulus-response mapping (Berchicci, Spinelli, & Di Russo, 2016; Darriba & Waszak, 2018; Di Rollo et al., 2016; Di Russo et al., 2016; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015b, 2015a, 2016; Perri & Di Russo, 2017). These anterior insular ERP components were recently characterized by the present research group; however, in the past, several research groups found that anterior ERP components were generically localized in frontal areas (Foxe & Simpson, 2002; Potts, Liotti, Tucker, & Posner, 1996).

To the best of our knowledge, these latter prefrontal components (pN1, pP1 and pP2) have never been investigated in children so far.

In the present study, ERP and behavioral measures were recorded during the whole preparation, perception and action phases of a visual DRT, allowing to accurately identify the time-course of the underlying cognitive processes. Specifically, we investigated the neural correlates of proactive inhibitory control and decision-making in a group of preadolescent children, and compared them with a group of young adults, providing a comprehensive picture of the differences of the entire decision-making processes between the two age groups.

Consistent with previous literature on this topic (e.g. Casey et al., 1997; Ciesielski, Harris, & Cofer, 2004; Jonkman, Lansbergen, & Stauder, 2003), we expect that, at the behavioral level, children will present slower response times and higher commission error rate. At the neurophysiological level, this

pattern might be associated with later and reduced ERPs when compared to adults. We hypothesize that this scenario could be subtended by an immature contribution of premotor and prefrontal regions, such as reduced cognitive preparation in the younger participants.

Methods

Participants

Thirty-six healthy individuals volunteered to participate in this study. Participants were divided in two groups depending on their age; a group of 18 children (Age: 9-14 years Mean: 11.6 ±1.4 years; 12 females), and a group of 18 adults (Age: 21-35 years Mean: 28.2±9.6 years; 10 females). Participants had a normal or corrected to normal vision, were free from neurological disorders and were right handed. Santa Lucia Foundation ethical committee approval was obtained for this study. Adult participants and children' legal guardians signed a written informed consent after a thorough explanation of the study.

Procedure

The experiment was carried out in a sound attenuated, dimly lit room. Participants were seated in front of a computer screen at 114 cm distance; their right arm was comfortably positioned on the armrest to allow them to push with the index finger of their right hand on a computer keyboard. In a randomized, equally probable order, four stimuli were presented on the computer screen for 250 ms (Contrast 80%). Two of them were defined as Go stimuli and the other two were defined as No-go stimuli (please see Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2016 for further details). The inter stimulus interval randomly varied from 1 to 2 s to avoid the possibility for the participants to easily predict the stimulus onset and to avoid overlapping of ERP activity. Participants were asked to press the keyboard button as quickly as possible when Go stimuli were presented and to withhold their response when No-go stimuli were shown. For the entire duration of the test, accuracy and speed were equally encouraged. Stimuli

were presented in runs lasting 2 minutes each. Adults performed ten runs (400 Go and 400 No-go trials) whereas children endured the task for six to eight runs (240-320 Go and 240-320 No-go trials). After each run, volunteers were granted 1-2 min rest.

Data Recording and Processing

EEG signals were recorded using two BrainAmp[TM] amplifiers and the Recorder 1.2 software and were analyzed using the Analyzer 2.1 software (Brain-Products GmbH, Munich, Germany). A total of 64 nonpolarizable sintered Ag/AgCl electrode electrodes were placed on the participants scalp according to the international 10-10 system and referenced to the left mastoid. An electrode placed below the right eye and referenced to Fp1 recorded vertical electrooculogram (EOG), whereas horizontal EOG was recorded from an electrode on the left external canthi and referenced to that on below the right eye. EEG and EOG were digitized at 250 Hz, amplified and band pass filtered (0.01-80Hz). Additionally, a 50Hz notch filter was applied to the recorded signals. For all participants, impedance was kept below 5kΩ. EEG and EOG were stored for further analysis.

EEG continuous recordings were visually inspected to detect the presence of gross artifacts. Independent component analysis (ICA) "Infomax" algorithm was applied to correct EOG artifacts. 12.8 (6-8) components were discarded in the children group whereas 10 (6.2) in the adult group; no significant difference (p=0.09) between the two groups was observed in the number of discarded components. The EOG-corrected EEG signals were separately (Go and No-go stimuli) segmented in stimulus locked epochs of 2000 ms, starting from -1100 to 900 ms with time-zero considered as the stimulus onset (for some similar studies investigating pre-stimulus ERP, please see Berchicci, Lucci, Perri, Spinelli, & Di Russo, 2014; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015a, 2016; Perri, Berchicci, Spinelli, & Di Russo, 2014). Prior to signal averaging, the artifact rejection was performed to discard epochs contaminated by muscular activity or movement related artifacts. For all participants, epochs containing

amplitudes larger than ±50 µV were systematically discarded. The percentage of removed signal was 0.7% ±0.8 for children and 0.4% ±0.5 for adults. This percentage was not significantly different between the two groups (p=0.19). Afterwards, for each participant Go and No-go epochs were separately averaged. Moreover, to further reduce high-frequency noise, an IIR low-pass filter (25 Hz; 24db/oct) was applied to the individual grand averages.

To investigate pre-stimulus ERP, Go and No-go trials were averaged and baseline-corrected during the initial 200 ms of the epoch (from 1100 to 900 ms before stimulus onset). For the analysis of post-stimulus ERPs, the baseline was computed in the interval ranging from -200 ms to stimulus onset.

According to literature, the BP was quantified as the average activity over medial central (Cz and CPz) sites in three intervals of time preceding the stimulus presentation. In particular, the interval ranging from -900 to -600 ms was defined as early BP; while from -600 to -300 ms it was defined as mid BP; the interval ranging from -300 ms to the stimulus presentation was defined as late BP. Similarly, the pN was computed bilaterally in the same intervals over prefrontal sites (Fp1, Fp2 and AFz).

Peak amplitudes and latencies of post-stimulus ERP components were computed for Go and No-go conditions separately over the following electrodes and time-windows based on previous literature (e.g. Berchicci, Spinelli, & Di Russo, 2016). Peak latency and amplitude of the P1 and the N1 components were computed over PO7 and PO8 electrodes in the 80-150ms and 150-250ms intervals, respectively. Peak latency and amplitude of the N2 component were computed over medial central-frontal electrodes (Cz, FCz and Fz) from 150-350ms after stimulus onset. Peak latency and amplitude of the P3 component were computed over medial central-parietal electrodes (Cz, CPz, and Pz) from 300-800 ms. Peak latency and amplitude of the pN1 and pP1 components were computed over prefrontal sites (Fp1, Fp2 and AFz) in the 80-180 ms and 150-250 ms interval, respectively. In addition, to highlight the amplitude modulation of the pP2 component between Go and No-go conditions, for each participant, differential waves over prefrontal derivations were computed by subtracting No-go from the Go ERP, as previously

described in Perri and colleagues (2014). The individual differential waves were band pass filtered (IIR filter, 0.5-15Hz, 24db/oct) and the differential prefrontal positivity (dpP2) was identified as the positive peak in the interval from 200 to 400 ms post-stimulus over AFz electrodes.

ERPs Normalization

To account for the well-documented, anatomy-related, amplitude differences between children and adults, a normalization process was carried out on ERPs amplitude (hereinafter referred to as "corrected"). In detail, for each participant and for each condition (Go and No-go stimuli), the peak amplitude of a given component (e.g. BP, pN, P1, N1, pN1, pP1, dpP2, N2, P3) was divided by the maximal amplitude of the P1 recorded over parieto-occipital electrodes (PO7, PO8, PO3, PO4, O1, and O2). This normalization method allowed us to maintain the original component polarity**.** The choice to adopt such a normalization process and to use the P1 amplitude as a reference for the other ERP components can be justified on the basis of the consideration that the cortical generators of the P1, that is the occipital extrastriate visual cortex (Di Russo et al., 2016; Sulpizio et al., 2017), is thought to reach a mature condition within 10 years of age, prior to other cortical areas as frontal cortex (Deoni, Dean, Remer, Dirks, & O'Muircheartaigh, 2015). Breaking down the uniform bias across present age groups explained by differences in the skull anatomy and synaptic density, this normalization should allow to detect any other group difference in cognitive processing.

Behavioral Data

For each participant, response accuracy was measured computing the percentage of Omission errors (%OE; response withheld when a Go stimulus was presented) and Commission errors (%CE; response to No-go stimuli). For each stimulus, the response time (RT) was computed as the time elapsed from stimulus onset and correct response (i.e. button press for Go stimuli). Individual RT was computed as the median of all single trial across correct responses. The group RT was calculated as mean value. The

consistency of the RT was computed by means of the intra-individual coefficient of variation (ICV), calculated as the ratio between SD and mean RT.

Statistical Analysis

All the statistical procedures have been performed using the SPSS statistical package (SPSS version 20). For all statistical tests, the null hypothesis was rejected with $\alpha < 0.05$. A one-way analysis of variance (ANOVA) was employed to test the effect of group [Children; Adults] on behavioral data (RT; ICV; %OE; %CE). For all of the ERP components, statistical analysis was carried out both on original and corrected ERPs amplitudes. The effects of group [Children; Adults], condition [Go; No-go], and electrode [Cz; CPz] on the BP were analyzed by means of a 2 x 2 x 2 ANOVA for early, mid and late BP. Similarly, the effects of group [Children; Adults], condition [Go; No-go], and electrode [Fp1; Fp2; AFz] on the pN component were analyzed by means of a 2 x 2 x 3 ANOVA for the three intervals defined for the BP. The effects of group [Children; Adults], condition [Go; No-go], and electrode [PO7; PO8] on peak latency and amplitude of P1 and N1 components were analyzed by means of a 2 x 2 x 2 ANOVA. A 2 x 2 x 3 ANOVA was employed to test the effect of group, condition and electrode [Fp1; Fp2; AFz] on the pN1 and the pP1 peak latency and amplitude. Group, condition and electrode [Cz; FCz; Fz] effects in peak latency and amplitude of the N2 component were analyzed by means of a 2 x 2 x 3 ANOVA. Whereas, group, condition and electrode [Cz; CPz; Pz] effects in peak latency and amplitude of the P3 were analyzed by means of a 2 x 2 x 3 ANOVA. One-way ANOVA was employed to test the effect of group on the amplitude and latency of the dpP2 component. Tukey post-hoc test was performed when appropriate. To control for the possible effect of the different number of the trials per condition between groups (about 300 in children and 400 in adults), we recomputed the adults' grand average using the first 300 trials per condition, as for the children group. The results of the statistical analysis between groups did not change, confirming the results stability.

To verify for the presence of a relationship between ERP components and behavioral data, for each group, Pearson's product moment correlations were performed between RT, %OE, %CE and corrected ERP components amplitude.

Results

Behavioral Data

Behavioral data of the two groups and statistics are presented in Table 1. Compared to adults, children exhibited slower RTs, higher %CE and higher ICV. Conversely, no difference emerged between the two groups in %OE. In addition, we calculated the post-error slowing (RT in correct trials both after correct and incorrect trials). Statistical analysis showed lack of effect in children (6 ms slowing, from 563±89 ms to 569±90 ms; p=0.74), whereas it was present in adults, showing a significant 29 ms slowing (from 429±49 ms to 456±68 ms, p = 0.001), However, the average number of correct go-trials after incorrect trials was relatively low in both groups (12 in children and 10 in adults).

Table 1. Behavioral data and statistics (**p<0.01, ns: not significant)

	Children mean(SD)	**Adults** mean(SD)	*F*
RT [ms]	563(86)	424(49)	34.8**
ICV	0.187 (0.035)	0.153 (0.020)	12.2**
CE [%]	13.21(9.43)	4.52(3.88)	13.1**
Om [%]	2.29(4.24)	0.63(1.15)	2.5; ns

ERP data

Figure 1a shows the average of Go and No-go trials to focus on the pre-stimulus ERP components pN and BP. In both groups, the BP and the pN are clearly visible. When uncorrected data are considered, Children (red lines) showed larger and earlier activity than adults (black lines), but after the correction (green lines) it became clearly smaller than adults. The pN and the BP initiated at approximately 900 ms in children and at 750 ms in adults. Figure 1b, shows the topographical distribution of the BP and the pN components (uncorrected ERP amplitudes). A similar scalp distribution of the two components can be observed, even though the pN was more anterior and the BP more posterior in children than in adults. In addition, a clear presence of these preparatory components in the earlier interval (-900/-600 ms) is visible in children.
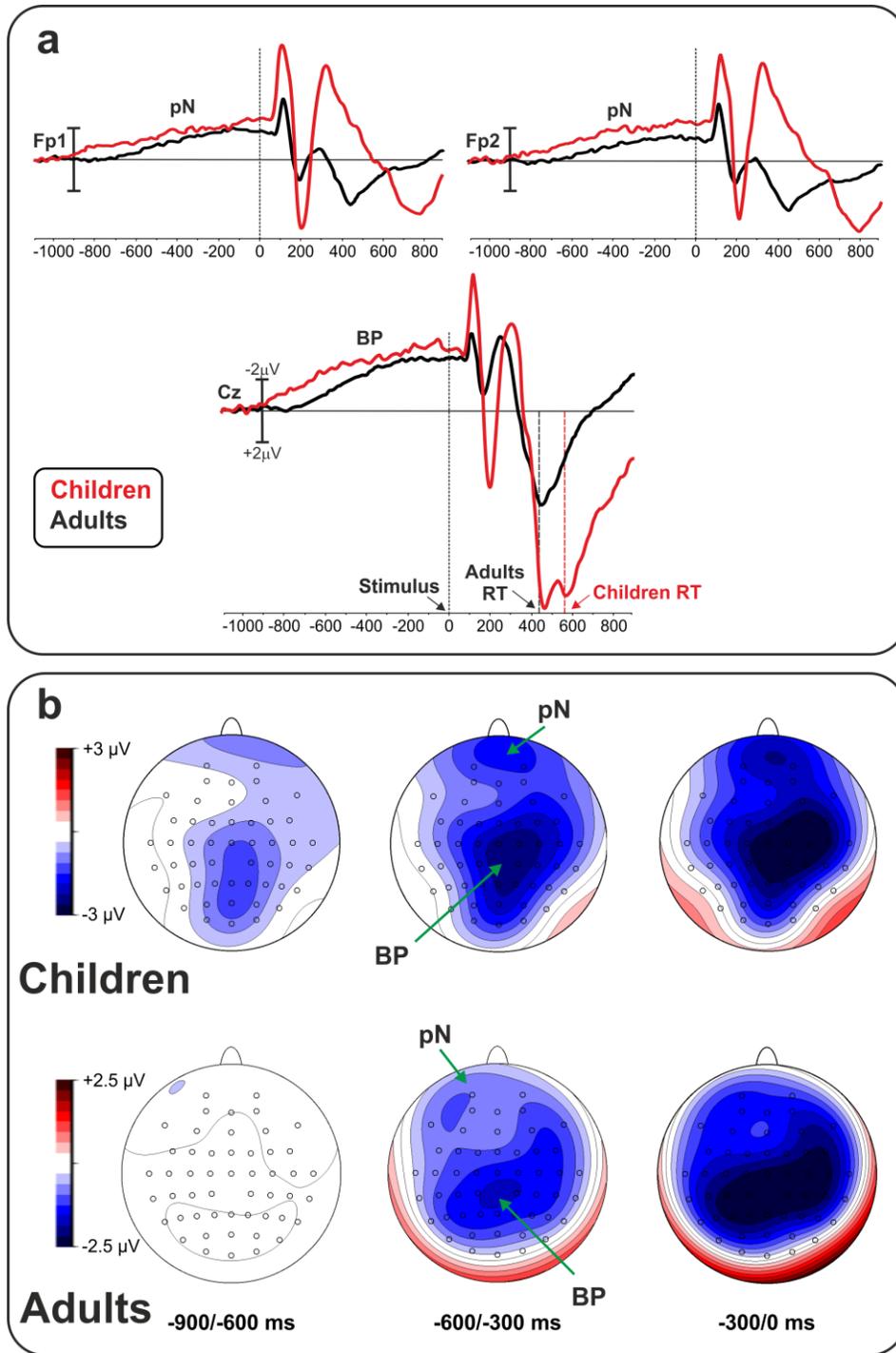
Figure 1

Figure 2 shows the post-stimulus ERP components for Go (continuous lines) and No-go (dashed lines) trials of both groups plus the corrected ERP of children (the color code is the same of Figure 1). Figure

3 shows the topographical distribution of the relative components (original ERP amplitude). After stimulus onset, the P1 peaking at 100-130 ms and the N1 at about 200 ms can be observed in both groups, regardless the condition (Go and No-go). The P1 and the N1 components typically peak at bilateral parietal-occipital electrodes (PO7 and PO8) in adults; although the bilateral topographical distribution of the N1 is observed in children too, the P1 showed a more medial distribution over occipital areas. At medial prefrontal electrodes, the pN1 peaking from 100 to 135 ms and the pP1 at 180-210 ms can be observed in both groups and conditions, even though the pP1 focused more posteriorly in children. The N2 peaked at medial central-frontal sites between 250 and 350 ms in both groups. The P2 that is usually not visible in DRTs because of the concomitant central negativities (e.g. Berchicci, Spinelli, & Di Russo, 2016), was instead clearly present in children with its typical medial parietal-occipital distribution. In adults, the P3 peaked at medial central and central-parietal (Cz and CPz) sites between 400 and 450ms and showed its typical No-go anteriorization, which was less marked in children. The prefrontal pP2 was clearly visible in adults between 200 and 400 ms, especially for the Go condition. In children, this positivity was not present, and it was replaced by a strong negativity. However, being this activity consistently less negative in the Go than No-go condition, differential waveforms were computed (Go minus No-Go) to unmask it (Figure 4a). In adults, a positive peak can be clearly identified in the differential wave peaking over medial prefrontal areas at approximately 320 ms, the dpP2; a component that previous authors named differential prefrontal positivity (dpP; Perri, Berchicci, Spinelli, & Di Russo, 2014). Compared to adults, children showed a similar scalp distribution of the dpP2. In children, this component seems to be delayed in time with respect to adults (although the statistical significance was not reached). Differential ERP also shows the P3 effect over medial parietal areas.
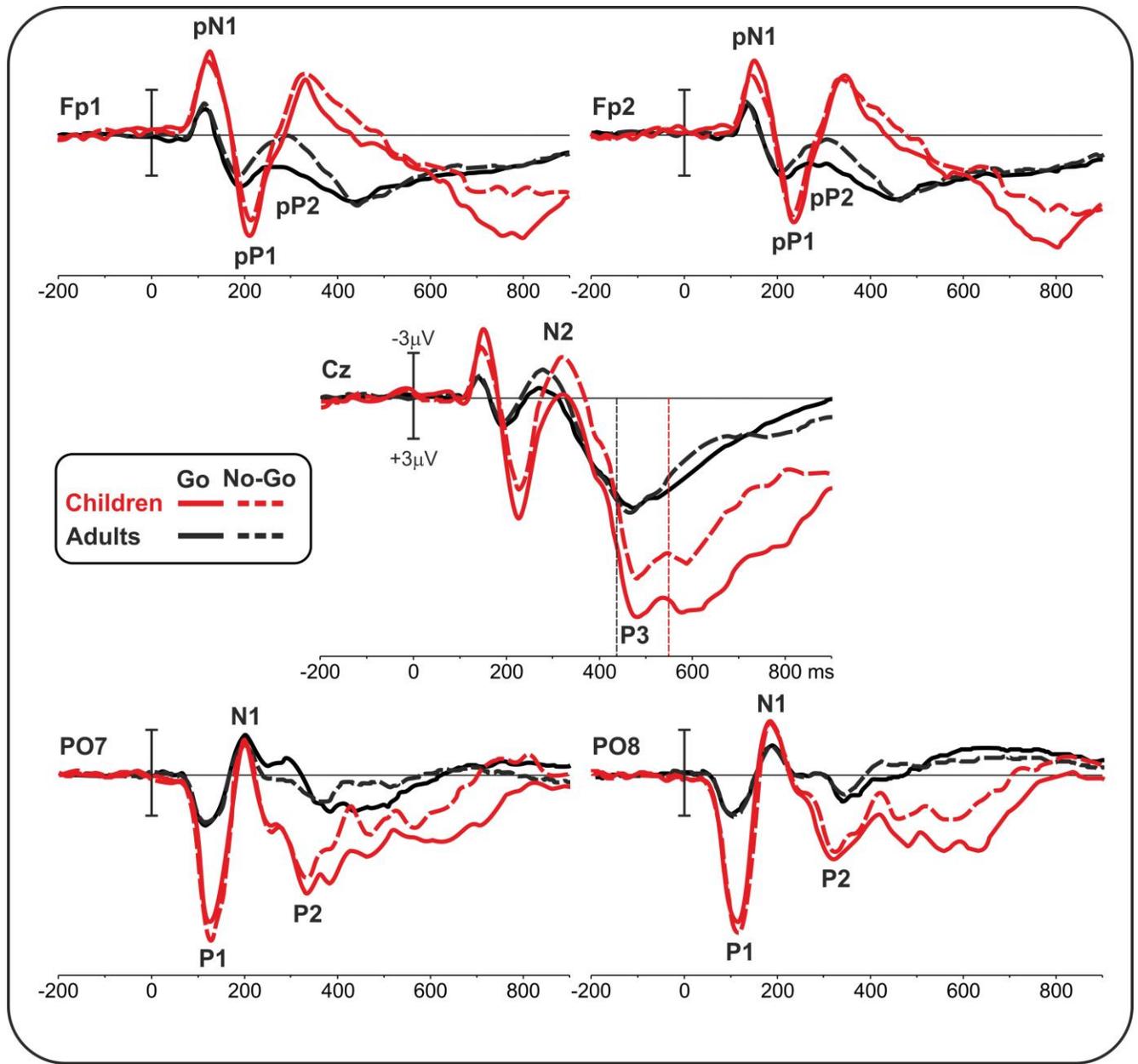
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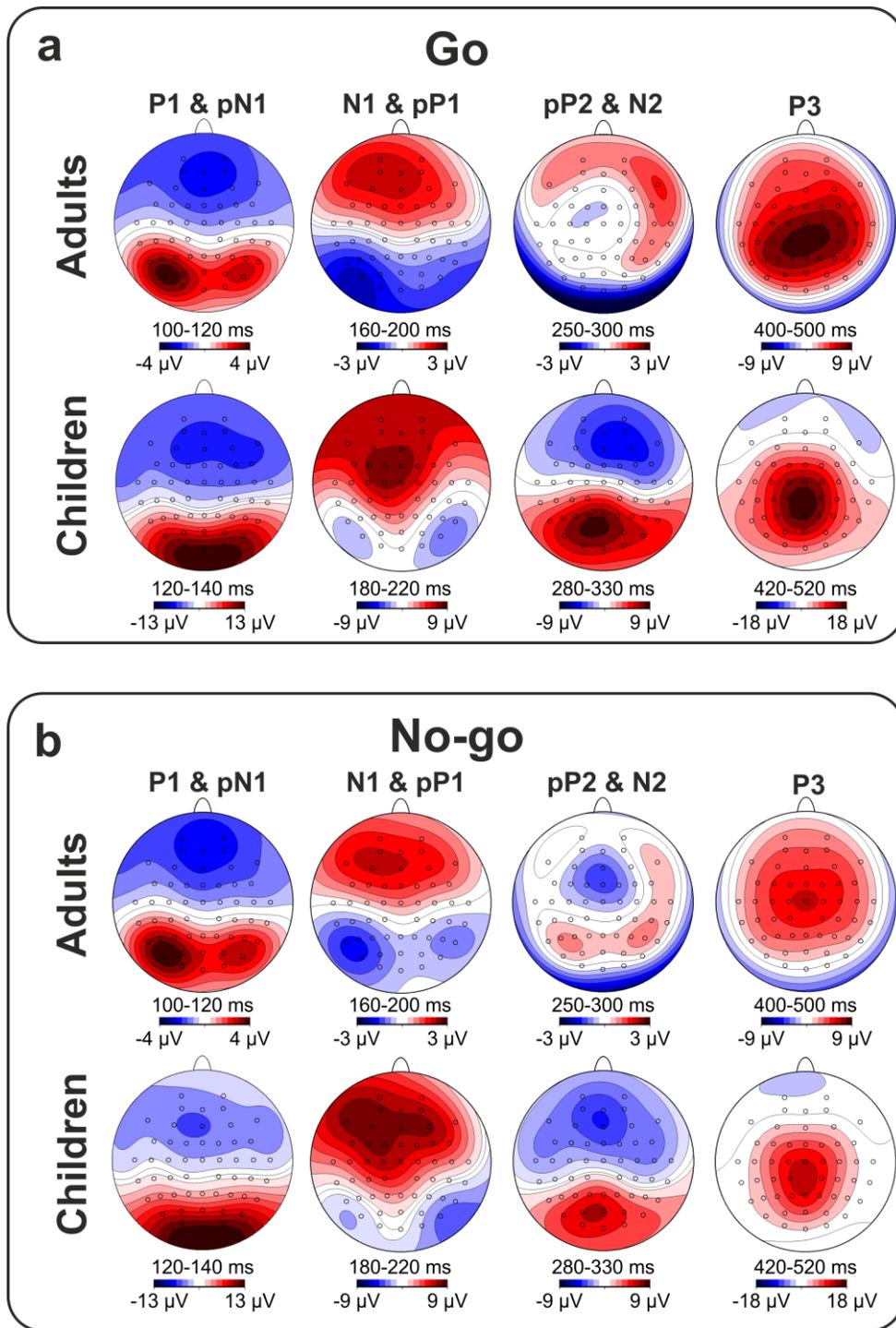
Figure 3
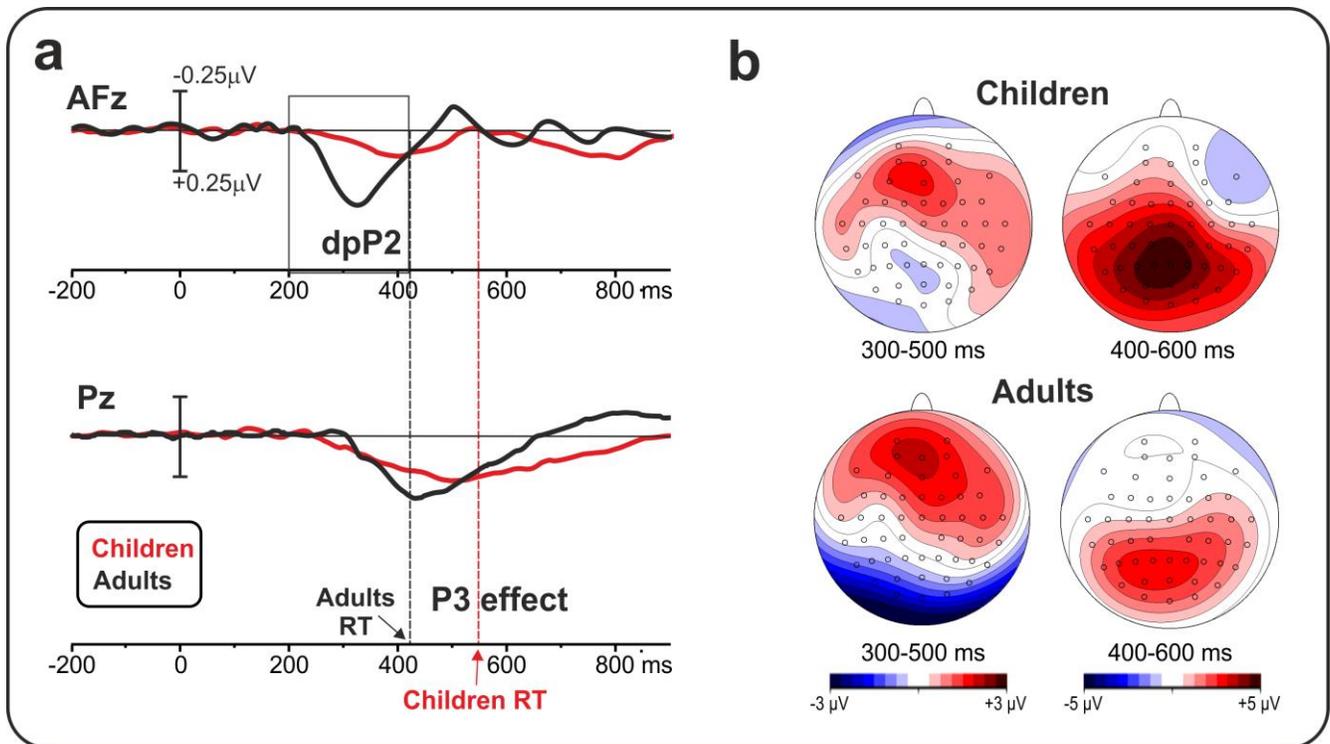
Figure 4

Statistical results

Pre-stimulus components

Statistics on corrected and un-corrected pre-stimulus components is reported in Table 2. Children exhibited larger uncorrected early BP (from -900 to -600 ms) compared to adults. No significant differences were observed between the two groups for uncorrected mid (from -600 to 300 ms) and late BP (from -300 to 0 ms). No significant effect of condition and electrode, and no significant group x condition and group x electrode interactions were observed in any interval. Children exhibited larger uncorrected pN with respect to adults in the early and mid-intervals (-900/300 ms). No significant effect of condition and electrode were observed for this component, as well as no significant interactions emerged in the considered intervals.

When the BP amplitude was corrected, groups exhibited no difference in the early BP (-900/-600 ms), whereas in children BP amplitude was lower than adults in the mid and late intervals (-600/0 ms). In addition, children showed lower corrected pN amplitude only in the late interval (300 ms preceding the stimulus), whereas no difference between groups was observed in the early and mid-intervals.

Table 2. Pre-stimulus ERP component amplitude (mean and SD) and statistics (*$p<0.05$, **$p<0.01$, ns: not significant) for original and corrected data (mean and SD).

	Interval (ms)	-900/-600		-600/-300		-300/0	
BP	Child	-1.30 (1.40)	$F= 17.6**$	-2.41 (2.85)	$F= 1.6$; ns	-2.91 (3.86)	$F<1$; ns
	Adult	-0.23 (0.57)		-1.74 (1.26)		-2.75 (1.81)	
	Child (Corrected)	-0.07 (0.08)	$F= 1.1$; ns	-0.13 (0.18)	$F= 8.7**$	-0.15 (0.22)	$F= 17.8**$
	Adult (Corrected)	-0.04 (0.13)		-0.31 (0.30)		-0.49 (0.41)	
pN	Child	-0.86 (1.32)	$F= 15.3**$	-1.74 (2.49)	$F= 3.2*$	-2.24 (3.14)	$F= 1.1$; ns
	Adult	-0.10 (0.46)		-1.01 (1.59)		-1.65 (2.61)	
	Child (Corrected)	-0.06 (0.11)	$F= 2.9$; ns	-0.11 (0.21)	$F= 2.9$; ns	-0.14 (0.22)	$F= 4.8*$
	Adult (Corrected)	-0.03 (0.08)		-0.24 (0.50)		-0.41 (0.86)	

Post-stimulus components

All the original post-stimulus components in children presented larger amplitudes (see Table 4, supplementary material). In the following paragraphs, only the corrected ERP amplitudes will be presented and discussed.

Statistics on post-stimulus components latency and corrected amplitude are reported in Table 3. As it can be seen, with the notable exception of pN1, N1 and dpP2, in children all the post-stimulus components presented a delayed peak compared to adults. In addition, a significant interaction was observed for pN1 latency ($F_{1,34}=7.5$, $p=0.007$), with children showing delayed peaks in the Go conditions with respect to adults.

Children exhibited smaller corrected N1 when compared to adults, while no effect of condition was observed for the corrected N1 amplitude.

When the pN1 and pP1 amplitudes were corrected (Table3), a tendency ($p=0.065$) toward smaller pN1 amplitude in children was observed. Conversely, a clear main effect of group was observed for the corrected pP1, with children showing smaller amplitudes. For both components, no significant effect of condition was observed, as well as no significant interaction for the corrected amplitudes.

The statistical analysis performed on the corrected N2 amplitude showed no significant effect of group, while in both groups the No-go condition presented larger amplitudes than Go.

When corrected, the P3 amplitude was larger in adults than children, while no effect of condition was observed for this component. Finally, once corrected, a significant effect of group was also observed, with adults presenting enhanced dpP2.

Table 3. Corrected post-stimulus ERP component amplitude (Amp), latency (Lat) and statistics (*p<0.05, **p<0.01, ns: not significant). Data are mean and SD.

			Group			Condition	
P1	Amp	Child	0.63 (0.23)	$F<1$; ns	Go	0.63 (0.26)	$F<1$; ns
		Adult	0.68 (0.28)		No-go	0.67 (0.25)	
	Lat	Child	124 (17)	$F=4.9*$	Go	118 (19)	$F<1$; ns
		Adult	116 (21)		No-go	121 (20)	
pN1	Amp	Child	-0.36 (0.19)	$F=3.4$; $p= .06*$	Go	-0.38 (0.26)	$F<1$; ns
		Adult	-0.44 (0.40)		No-go	-0.42 (0.36)	
	Lat	Child	127 (25)	$F=1.7$; ns	Go	124 (21)	$F<1$; ns
		Adult	122 (24)		No-go	125 (28)	
N1	Amp	Child	-0.33 (0.38)	$F=8.2**$	Go	-0.51 (0.68)	$F<1$; ns
		Adult	-0.66 (0.87)		No-go	-0.48 (0.69)	
	Lat	Child	204 (26)	$F=3.0$; ns	Go	201 (26)	$F<1$; ns
		Adult	196 (29)		No-go	200 (30)	
pP1	Amp	Child	0.36 (0.24)	$F=14.3**$	Go	0.60 (1.01)	$F<1$; ns
		Adult	0.83 (1.24)		No-go	0.59 (0.83)	
	Lat	Child	207 (25)	$F=5.2**$	Go	196 (27)	$F<1$; ns
		Adult	188 (47)		No-go	199 (48)	
N2	Amp	Child	-0.34 (0.39)	$F< 1$; ns	Go	-0.26 (0.50)	$F= 5.2*$
		Adult	-0.34 (0.63)		No-go	-0.42 (0.54)	
	Lat	Child	304 (40)	$F=49.2**$	Go	284 (44)	$F<1$; ns
		Adult	268 (36)		No-go	288 (42)	
P3	Amp	Child	1.02 (0.68)	$F=25.1**$	Go	1.39 (0.86)	$F= 2.9$ ns
		Adult	1.57 (0.88)		No-go	1.20 (0.80)	
	Lat	Child	517 (83)	$F=20.1**$	Go	488 (82)	$F<1$; ns
		Adult	465 (84)		No-go	494 (93)	
dpP2	Amp	Child	0.24 (0.22)	$F=3.9*$			
		Adult	0.42 (0.30)				
	Lat	Child	324 (59)	$F<1$; ns			
		Adult	313 (50)				

Pearson's product moment correlations

Table 4 shows the results of the Pearson's product moment correlations between behavioral data and corrected ERP components performed separately for children and adults. This statistical analysis yielded no significant results.

Table 4. Pearson's product moment correlations (*r*) and statistical significance (*p*) between pre- and post-stimulus ERP components and behavioral data. The correlational analyses were performed separately for children and adults.

		pN1 Go	pP1 Go	pN1 No-go	pP1 No-go	BP	pN
Adults (*n* = 18)							
RT	*r*	-0.06	0.13	-0.04	0.13	-0.28	0.16
	p	0.83	0.61	0.88	0.62	0.25	0.53
ICV	*r*	0.04	-0.07	0.03	-0.11	0.16	0.11
	p	0.61	0.79	0.71	0.65	0.54	0.65
%CE	*r*	-0.10	0.19	-0.17	0.16	-0.14	-0.46
	p	0.25	0.45	0.17	0.51	0.57	0.85
%OE	*r*	0.20	-0.18	0.25	-0.25	0.09	0.20
	p	0.30	0.47	0.32	0.33	0.69	0.43

		pN1 Go	pP1 Go	pN1 No-go	pP1 No-go	BP	pN
Children (*n* = 18)							
RT	*r*	0.04	0.10	-0.20	0.23	0.28	-0.34
	p	0.73	0.57	0.45	0.37	0.26	0.16
ICV	*r*	-0.01	0.33	0.07	0.06	0.32	0.29
	p	0.70	0.13	0.58	0.56	0.19	0.25
%CE	*r*	0.01	0.22	0.02	-0.06	-0.03	0.17
	p	0.64	0.48	0.35	0.68	0.89	0.49
%OE	*r*	-0.14	0.39	-0.21	0.16	-0.17	-0.12
	p	0.58	0.09	0.41	0.56	0.49	0.64

Discussion

The present study confirmed that children performance in a visuo-motor DRT was slower and less accurate than adults. This finding can be explained as the correlate of the less intense proactive cognitive

and motor preparation, as indexed by the pN and BP components, respectively. Moreover, children exhibited reduced attentional processing, as revealed by the smaller N1, pP1 and P3 components with respect to adults. More importantly, children showed a less intense evidence accumulation process in the anterior insular cortex, as showed by the reduced dpP2 component.

Behavioral Performance

Consistently with previous literature (Casey et al., 1997; Ciesielski, Harris, & Cofer, 2004; Jonkman, Lansbergen, & Stauder, 2003), in the present study children were less efficient in suppressing unwanted responses compared to adults (higher %CE). Considering that inhibitory control largely relies on the engagement of the prefrontal cortex (Aron, Robbins, & Poldrack, 2004; Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Casey et al., 1997), and that this brain region reaches full maturation only in adult age (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002), the poor behavioral performance of children is not surprising. In line with previous studies (Bellgrove, Hester, & Garavan, 2004), the poor inhibitory control was also associated with low response consistency (high ICV). Since the activity of the prefrontal cortex allows also a more consistent response speed (Bellgrove, Hester, & Garavan, 2004; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015a), the higher variability observed in children further supports the hypothesis of an immature contribution of the prefrontal cortex. Similarly, the post-error slowing found in adult only confirms the presence of proactive control in adults, but not in children. However, due to the low trials number, the reliability of these measure should be carefully considered.

Pre-stimulus ERP

The BP emerged earlier in children than adults (Figure 1), suggesting prolonged and less efficient motor preparation within the cingulate and supplementary motor areas, a pattern similar to that of adult non-athletes when compared to élite athletes (Di Russo, Pitzalis, Aprile, & Spinelli, 2005). Following the BP

trend, also the pN emerged earlier and was smaller in children than in adults. Since the pN originates from the pars opercularis of the inferior frontal gyrus (BA 44) (Di Russo et al., 2016; Sulpizio et al., 2017), it was proposed to be an index of cognitive preparation (Berchicci, Lucci, Pesce, Spinelli, & Di Russo, 2012; Di Russo et al., 2016), as also suggested by earlier studies using CNV paradigms (e.g. Cui et al., 2000). However, the pN, particularly in the right hemisphere, seems especially associated with proactive inhibitory control (Bianco, Berchicci, Perri, Quinzi, & Di Russo, 2017; Bianco, Berchicci, Perri, Spinelli, & Di Russo, 2017). The earlier pN onset might be explained in the framework of a less efficient cognitive preparation, as already observed by other researches on aging showing larger frontal CNV (Wild-Wall, Hohnsbein, & Falkenstein, 2007) and pN (Berchicci, Lucci, Pesce, Spinelli, & Di Russo, 2012) in older people. On the other hand, in the present study lower BP and pN could be associated with the uncompleted development of the proactive control.
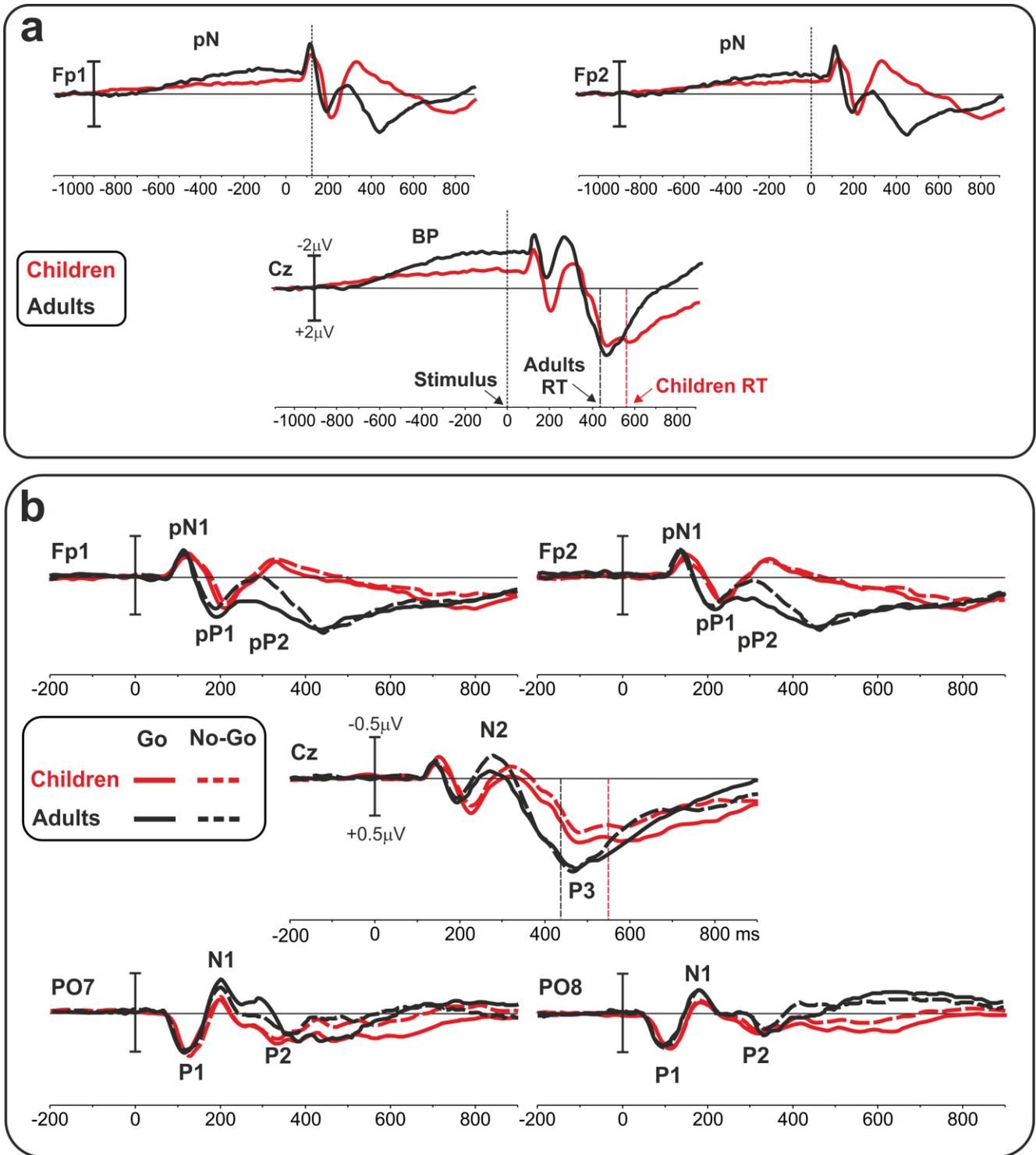
Figure 5

Post-stimulus ERP

The post-stimulus components observed over prefrontal sites, i.e. the pN1 and the pP1, are consistent with those presented in a previous study of our research group, where we investigated the effect of aerobic fitness on brain health in children (Berchicci et al., 2015). In the present study, children exhibited smaller pN1 and pP1 compared to adults. Moreover, they presented a delayed pP1 with respect to adults. It has been proposed that this component, associated with the activity of the anterior insula, reflects top-down visual processing (Berchicci, Spinelli, & Di Russo, 2016; Perri, Berchicci, Bianco, Spinelli, & Di Russo, 2018), including awareness of the sensory-motor integration (Perri et al., 2018). It seems that the top-down visual processing of children requires longer time to be accomplished, explaining, to some extent, the slower RTs observed in this group. The delayed latency of this and other components could be interpreted considering the neuro-anatomical development of the brain, presenting an ongoing myelination process (Barry & Blasio, 2015; Barry, De Blasio, & Borchard, 2014; Ciesielski, Harris, & Cofer, 2004; Giedd et al., 1999; Johnstone et al., 2007; Lamm, Zelazo, & Lewis, 2006). Compared to adults, children showed reduced attentional processing during both stimulus- and response-evaluation stages, as indexed by the smaller N1 and P3 components.

The subtractive waves allowed isolating the pP2 Go/No-go effect, showing in children a topographical distribution similar to the adults, although their amplitude was lower. This lower activity may likely represent a reduced efficacy of the evidence accumulation process, which may account, along with a reduced attentional processing (N1) and sensory awareness (pP1), for the slower and the more error-prone performance observed in children. Indeed, the pP2 activity was related to stimulus-response mapping process and efficacy of the decision process (Berchicci, Lucci, Perri, Spinelli, & Di Russo, 2014; Perri, Berchicci, Lucci, Spinelli, & Di Russo, 2015a, 2016; Perri, Berchicci, Spinelli, & Di Russo, 2014; Perri & Di Russo, 2017). Without the subtraction procedure, the pP2 was not visible in children, possibly because of the overlapping negative activity observed over fronto-central sites. Indeed, in the

same interval, children exhibited a large negativity over frontal-central sites, the frontal N2, which is consistent to previous findings during auditory (Barry & Blasio, 2015) or visual (Jonkman, Lansbergen, & Stauder, 2003) Go/No-go tasks. Considering the delayed children RT (ms) and the premotor interpretation of the N2 origin (Di Russo et al., 2016, 2017; Perri, Berchicci, Bianco, Spinelli, & Di Russo, 2018), the large frontal N2 may represent delayed motor preparation, which reach its peak when the adult response in already emitted.

Some considerations should be taken into account when interpreting present results. First, the absence of information concerning the anatomical and neural maturational status of children, prompts us to interpret cautiously the electrophysiological differences observed between our experimental groups. Second, it may be questioned whether the referencing system adopted in the present (left mastoid) study may have altered the topographical distribution of pre- and post-stimulus ERP components. To unravel any possible bias of the selected reference (left mastoid) we performed additional analysis adopting the average reference. These analyses showed no effect of the reference on the ERP topography (see supplementary Figures 1-3) confirming previous studies indicating that the used reference channel may add or subtract a constant value at all channel locations resulting in a substantially unmodified topography (Yao, 2001; Yao et al 2005, 2007; Tian and Yao, 2013). Third, it could be questioned why the present study failed to show significant correlations between ERPs and behavioral data. A possible explanation of this aspect may be the limited sample size to perform correlation analyses separately for the two groups. Indeed previous studies (Bianco, Berchicci, Perri, Quinzi, & Di Russo, 2017; Bianco, Di Russo, Perri, & Berchicci, 2017; Perri, Berchicci, Spinelli, & Di Russo, 2014) in a larger sample size (n>39), showed significant correlations between the BP and RTs. On the other hand, a correlation analysis with Children and Adults pooled together may result in significant correlations due to the heterogeneity of the two groups rather than to a functional modulation of a given ERP component. Last the experimental design

adopted in the present study assumes that the two groups differ only in the maturational status and no other factors influenced their electrophysiological and behavioral performance.

Conclusions

This is the first ERP study investigating developmental changes during both pre- and post-stimulus stages of cognitive processing during a complex visuo-motor discrimination task. We propose that the larger ERP components commonly observed in children compared to adults should not be interpreted as the sign of enhanced cognitive processes, as demonstrated also by the poor behavioral performance; rather, as revealed by the analysis on the "corrected" data, they appear to represent an EEG epiphenomenon related to the anatomical and neural modifications occurring in developing children. Summarizing, based on the available electrophysiological and behavioral data, we propose that children are characterized by less intense task preparation processes compared to adults, which may account, together with a reduced attentional processing and with a poor sensory awareness, for their inaccurate and slow behavioral performance. Educational and motor programs for preadolescents should consider that their brain is not only immature in proactive prefrontal inhibitory functions but also in motor preparation and in the reactive focus of attention and in the decision-making processes.

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Figure Captions

Figure 1. (a) Pre-stimulus ERPs components (BP and pN) for children (red lines) and adults (black lines). (b) Topographical distribution of the original ERPs for children (upper part) and adults (lower part) in the three intervals considered for statistical analysis.

Figure 2. Post-stimulus ERPs components for children (red lines) and adults (black lines) for Go (solid lines) and No-go (dashed lines) trials.

Figure 3. Topographical maps of post-stimulus ERP components for Go (a) and No-go (b) trials for adults and children.

Figure 4. (a) Go minus No-go corrected differential waveforms of children and adults are presented in red and black lines respectively. (b) Differential-waves topographical maps in two intervals of interest.

Figure 5. Post-stimulus corrected ERPs components for children (red lines) and adults (black lines) for Go (solid lines) and No-go (dashed lines) trials.

Supplementary Figure 1. Comparison of average reference and left mastoid reference on the topography of the early prefrontal (pN1 and pP1) and occipital (P1 and N1) ERP components in children and adults (upper and lower maps, respectively). As it can be noticed in both groups, the topographical distribution of these potentials is not affected by the reference.

Supplementary Figure 2. Comparison of average and left mastoid reference on the ERP waveforms at prefrontal electrodes (Fp1, in blue and Fp2 in red) for children and adults. Compared to the left mastoid reference, the average reference results in an overall reduction of the amplitudes of the waveforms. Notwithstanding this aspect, no effect of lateralization can be observed between the two references as depicted by the subtractive wave (black line – Fp2-Fp1).

Supplementary Figure 3. Comparison of average and left mastoid reference on the topography of pre-stimulus ERP components (BP and pN) in children and adults (upper and lower maps, respectively). As it can be noticed in both groups, the topographical distribution of these potentials is not affected by the reference. However, the adoption of the average reference seems to reduce the amplitude of the preparatory activities (BP and pN) enhancing their positive counterparts (the positive pole of the dipole generating the pN and the BP).
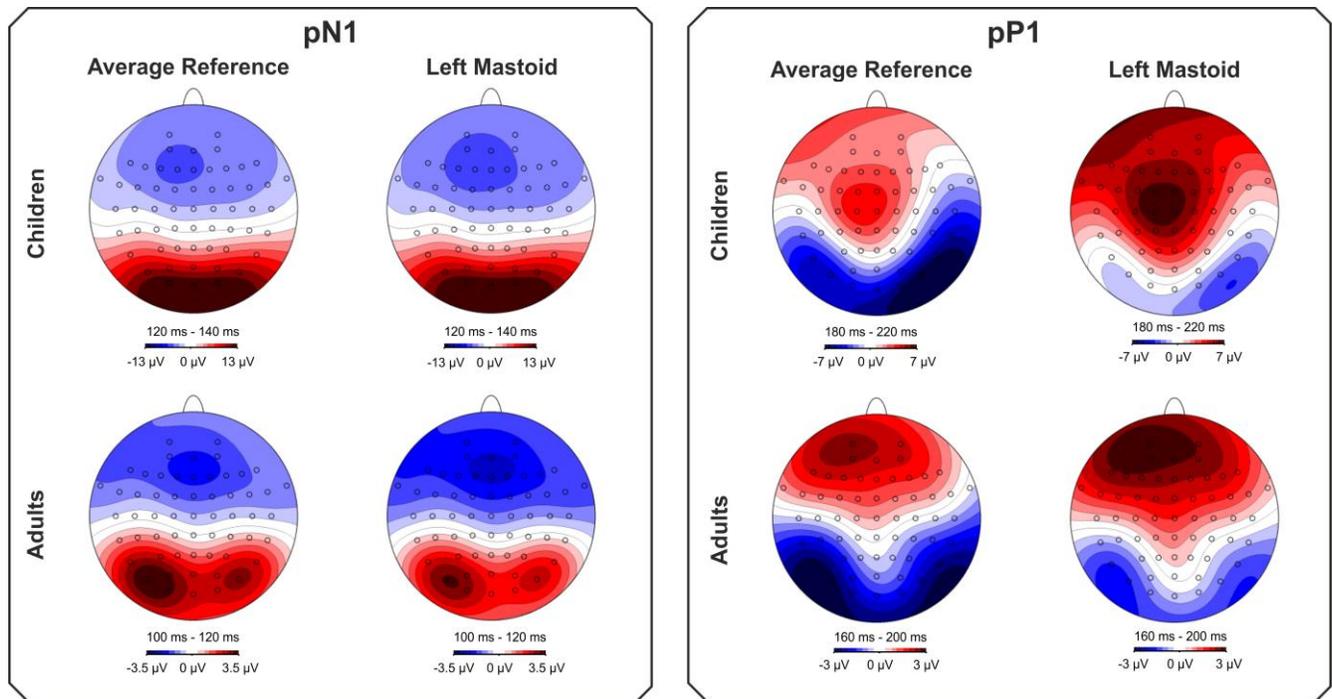
Supplementary Figure 1
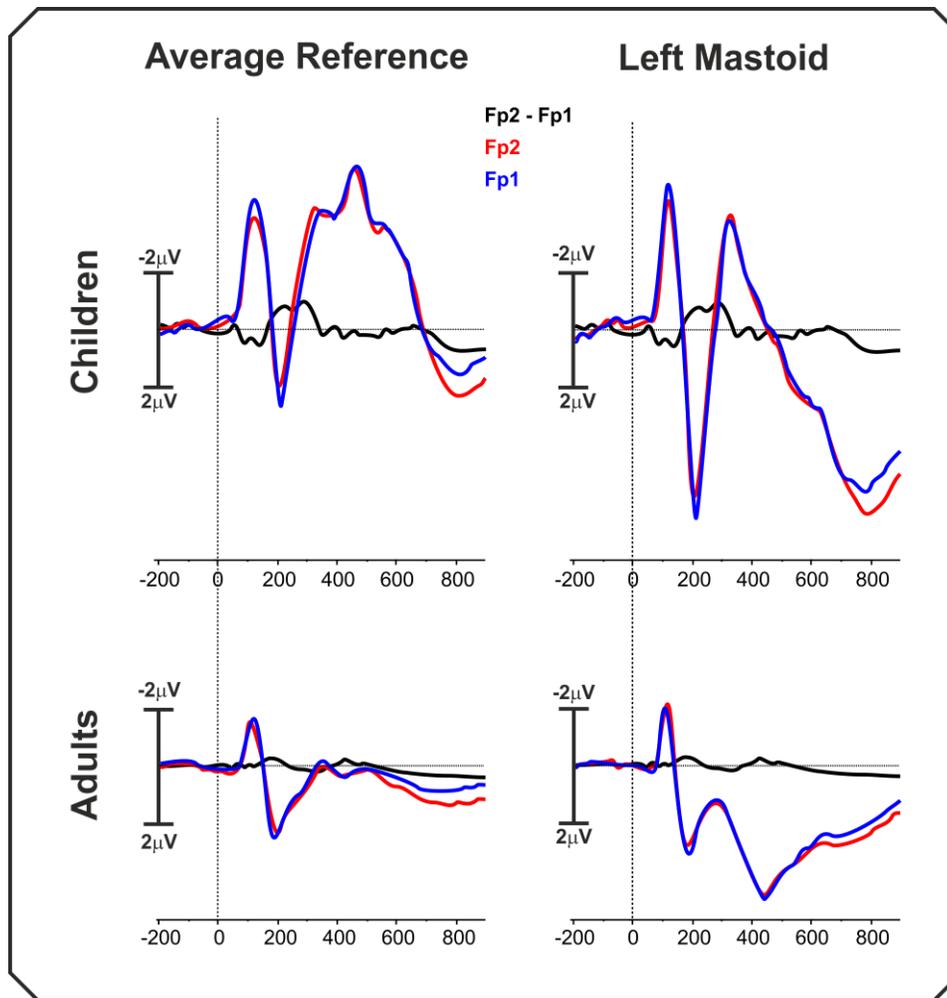
Supplementary Figure 2

Supplementary Figure 3