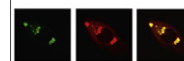


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Research Report

Exogenous orienting of visual-spatial attention in ADHD children

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ABSTRACT

Visual spatial orienting of attention towards exogenous cues has been one of the attentional functions considered to be spared in ADHD. Here we present a design in which 60 (30 ADHD) children, age: 10.9 ± 1.4 , were asked to covertly orient their attention to one or two (out of four) cued locations, and search for a target stimulus in one of these locations, while recording behavioral responses and EEG/ERP. In all conditions, ADHD children showed delayed reaction times and poorer behavioral performance. They also exhibited larger cue-elicited P2 but reduced CNV in the preparation stage. Larger amplitude of CNV predicted better performance in the task. Target-elicited N1 and selection negativity were also reduced in the ADHD group compared to non-ADHD. Groups also differed in the early and late P3 time-windows. The present results suggest that exogenous orienting of attention could be dysfunctional in ADHD under certain conditions. This limitation is not necessarily caused by an impairment of the orienting process itself, but instead by a difficulty in maintaining the relevant information acquired during the early preparation stage through the target processing stage, when it is really needed.

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1. Introduction

Attention deficit-hyperactivity disorder (ADHD) is a highly prevalent neurodevelopmental disorder in childhood, characterized by inattention, hyperactivity, and impulsivity that often persist into adulthood (Kessler et al., 2006; McLoughlin et al., 2010). Several competing, though not necessarily

mutually exclusive, explanatory models for ADHD have dominated the literature in the last decade: the dysfunctional behavioral inhibition hypothesis (Barkley, 1997), the cognitive-energetic model (CEM) (Sergeant, 2000, 2005), the dual pathway model of delay aversion and dysfunctional reward (Sonuga-Barke, 2003), the dynamic developmental behavioral theory (Sagvolden et al., 2005), and the abnormal function of the

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frontostriatal and frontocerebellar neural loops (Sonuga-Barke and Halperin, 2010). A more recent interpretation of this condition specifies that the resting state or “default mode” activity network in the brain interferes with the consolidation of task-positive networks that are required for cognitive performance (Aboitiz and Castellanos, 2011; Sonuga-Barke and Castellanos, 2007). All these models have acquired some empirical support throughout the years (Bush, 2010; Sonuga-Barke, 2005) and a common view of ADHD as neuropathologically heterogeneous disorder caused by multiple neurodevelopmental pathways has come to prevail (Nigg et al., 2005; Sonuga-Barke, 2005).

Although the search for a comprehensive understanding of the physiopathology of ADHD may point in a different direction, the process of attention remains central in explaining the disorder. The name of the disorder suggests a deficit, but it is currently accepted that attention reflects a variety of brain processes that are unevenly affected by ADHD (Lopez et al., 2006; Manly et al., 2001). The incapacity to maintain focalized attention on a task for a relatively long period of time (sustained attention) is a frequent description of ADHD behavior in everyday activities. This is congruent with their overall performance in continuous performing tasks (CPT) in experimental settings (Conners et al., 2003). Nevertheless, a smaller effect size has been reported for more specific measures of sustained attention like “performance over time” (Huang-Pollock et al., 2012). Dysfunction of other cognitively defined attention processes has been a controversial matter for years (Barkley, 1997; Huang-Pollock and Nigg, 2003; Huang-Pollock et al., 2005).

One such controversy is the case of visual spatial orienting (Nigg, 2005). Several reports claim that spatial orienting is dysfunctional in ADHD children, who present lateralized or global orienting deficits (Carter et al., 1995; Nigg and Casey, 2005; Perchet and García-Larrea, 2000; Perchet et al., 2001; Swanson et al., 1991). Using meta-analytic techniques, others have challenged this conclusion stating that no consistent deficit can be found (Huang-Pollock and Nigg, 2003). A similar situation pertains to the capacity to divide attention. There are reports of ADHD children having preserved divided attention, committing fewer errors in these tasks than their non-ADHD counterparts (Koschack et al., 2003). Meanwhile, other studies point exactly in the opposite direction, reporting the increased number of errors in a divided attention task as the second best factor in differentiating children with and without ADHD, surpassed only by response-time variability in a Go/No-Go task (Kaufmann et al., 2010).

These contradictory findings may expose, precisely, the existence of a more general deficit that may or may not be assisted in visual spatial orienting and divided attention tasks depending on factors such as task complexity, timing, perceptual, and working memory load, etc. While some authors point to behavioral inhibition dysfunction as the explanatory factor (Barkley, 1997), others propose that, at least the ADHD combined type, suffers from suboptimal energetic state regulation that affects attentional orienting among other functions (Banaschewski et al., 2003; Sergeant, 2005), in this context, empirical results usually interpreted as supportive of dysfunctional behavioral inhibition in ADHD (e.g., performance in Go/No-Go tasks) have been recently re-interpreted as resulting also from energetic state factors

(Benikos and Johnstone, 2009). This is partly consistent with the hypothesis of default-mode network interference over task-related neural networks in ADHD (Aboitiz and Castellanos, 2011; Sonuga-Barke and Castellanos, 2007). The regulation of physiological arousal in accordance with task demands also seems to influence the results of ADHD patients in divided attention tasks (Karatekin et al., 2008). All this emphasizes the need to consider the state in which the subject faces the target stimuli, resolves the task at hand, and responds. Unfortunately, behavioral measures (reaction times, hits, errors) by themselves provide useful but rather general information about the specific cognitive processes that underlie a response.

Electrophysiological measures, such as event-related brain potentials (ERPs), have greater time resolution and are better suited to assess the period previous to target processing and response. Nevertheless, most ERP studies regarding orienting visual spatial attention and divided attention in ADHD subjects focus on the target processing and response periods (Barry et al., 2003; Lopez et al., 2006, 2008). The amplitude of early visual P1/N1 and the derived selection negativity (SN) is larger when the target is selectively attended (Anllo-Vento et al., 1998; Hillyard and Anllo-Vento, 1998). Later components like P3 and late positivity are also modulated by attention (Herrmann and Knight, 2001). These electrophysiological indicators are frequently used to study the distribution of visual spatial attention in children with ADHD (Barry et al., 2003).

ERP components elicited by endogenous and exogenous attentional orienting cues have been also well studied and characterized (Harter et al., 1989; Jongen et al., 2007). Cues are usually considered as “endogenous” when an informative sign (e.g., an arrow), is presented in the center of the visual field and the orienting process results from the conceptual information conveyed by the cue. On the contrary, “exogenous” cues are presented lateralized and the orienting is supposed to occur by the reflexive capture of attention (Carrasco, 2011). Orienting attention towards an exogenous cue is supposed to differ little between children and adults, at least when the spatial location is unambiguous. This process is present since early childhood and its maturation with age depends more on other aspects like the speed of executing responses and use of explicit knowledge (Rueda et al., 2004). In studying cue-evoked ERPs in ADHD endogenous orienting cues are often utilized, as exogenous orienting is supposed to be reflexive and automatic (Mayer et al., 2004) and, thus, less susceptible to be affected by the executive control or behavioral inhibition impairments that characterize ADHD (Carter et al., 1995; Huang-Pollock and Nigg, 2003). Nevertheless, from the state regulation hypothesis, the exogenous orienting of attention should also be affected.

The cue-evoked components P2 and CNV have been reported to differ between ADHD and non-ADHD children (ages: 8–14 years) especially in CPT and Go/No-Go tasks (Banaschewski et al., 2003, 2008; Broyd et al., 2005). The P2 component has been associated with automatic processing and inhibition of non-relevant information (Barry et al., 2003). There are several reports of larger amplitude and different scalp topography for this component in ADHD (Banaschewski et al., 2003; Barry et al., 2009; Broyd et al., 2005). On the other hand, the CNV has been associated with expectancy (Gaillard,

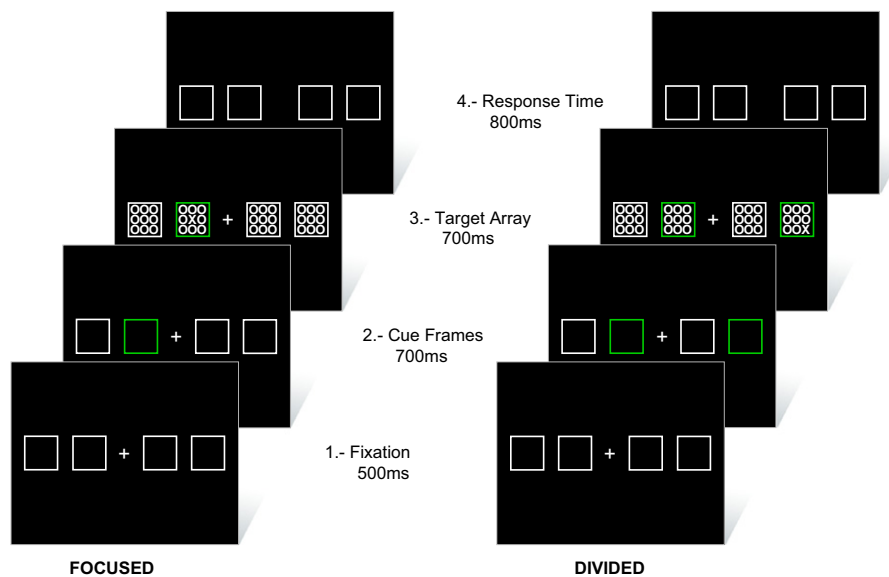


Fig. 1 – Trial sequence: left column represents a trial from the focused attention condition. The divided attention condition is depicted in the right column. Time in milliseconds (ms).

1977) and its amplitude has also been related to working memory load (McEvoy et al., 1998). CNV and the readiness potential that precedes the appearance of a target stimulus have been considered indices of cortical arousal related to anticipatory attention (Tecce, 1972). Reduced CNV amplitude has been reported in ADHD subjects in several experimental designs (Banaschewski et al., 2003, 2008; Barry et al., 2009; Broyd et al., 2005). These findings are frequently interpreted as consistent with impaired resource allocation toward attentional orienting cues in subjects with ADHD and often persist into adulthood (McLoughlin et al., 2010).

In the present study we considered the CNV amplitude as an index of arousal and resource allocation, and therefore, suitable to study the period that precedes target processing and the allocation of attentional resources on exogenous orienting cues, depending on the cognitive load. Task demands were manipulated by cueing attentional focus to a single spatial location versus dividing attention resources between two possible loci. We then measured the impact of this additional effort on the capacity of covertly orienting attention and searching for the target within an array.

Our main hypothesis was that ADHD children would perform poorer than non-ADHD in an exogenous cuing visuospatial orienting task if state regulation is impaired during the preparatory stage. That would be reflected by larger P2 and reduced CNV amplitudes. In addition, the target-related ERP components would also reflect a dysfunctional allocation of attentional resources in the ADHD group.

2. Results

2.1. Behavioral results

A mixed ANOVA design to compare reaction times (RTs) (Group \times Cue validity \times Type of attention, with repeated measures in the last two factors) showed a significant main effect for Group

($F(1,58)=48.81, p<0.001$). The ADHD group showed slower RTs than the non-ADHD group in all conditions (see Fig. 2A). Cue validity was also significant ($F(1,58)=119.13, p<0.001$). Uncued targets resulted in delayed RTs compared to responses to correctly cued targets (see Fig. 2B). Regarding the type of attention, the RTs analysis was also clear, showing significant main effect ($F(1,58)=74.00, p<0.001$) due to longer RTs when the two cues forced the division of attention in anticipation of the target (see Fig. 2C). A significant interaction was also found between Cue validity and Type of attention ($F(1,58)=88.69, p<0.001$). Follow up univariate planned comparisons showed that RTs differed between focused and divided attention conditions only when the target was correctly predicted by the cue ($F(1,58)=154.66, p<0.001$) but they were equally slowed regardless of the type of attention in all invalidly cued conditions ($F(1,58)=3.29, p=0.07$). No significant interaction with Group was observed.

The analysis of behavioral accuracy (i.e., hit and error rates) showed significant differences for main factor Group (Fig. 2D). In general ADHD had fewer hits ($F(1,58)=12.68, p<0.001$), more commission errors ($F(1,58)=7.48, p<0.01$) and omission errors ($F(1,58)=9.73, p<0.01$) than non-ADHD in all conditions (Fig. 2E). A significant interaction was observed between Group and Cue validity for hits ($F(1,58)=6.85, p<0.01$) and omission errors ($F(1,58)=9.40, p<0.01$) due to fewer hits and more omissions in the ADHD group following invalid cues. The interaction between Group and Type of attention did not reach the statistical significant level for hits ($F(1,58)=1.31, p=0.25$) neither for commission ($F(1,58)=0.03, p=0.95$) nor for omission errors ($F(1,58)=1.42, p=0.23$). A significant interaction Group \times Cue validity \times Type of attention was observed for hits ($F(1,58)=6.84, p<0.01$) and omission errors ($F(1,58)=9.40, p<0.01$). Univariate planned comparisons showed that when targets were invalidly cued by a single cue, ADHD had significantly fewer hits ($F(1,58)=21.37, p<0.001$) and more omission errors ($F(1,58)=13.78, p<0.001$) than their non-ADHD counterpart. In the divided attention condition, despite the large difference between groups

Table 1 – ERP components amplitudes.

Amplitude values (μV)			ADHD		Non-ADHD	
Component	Time range (ms)	Region	FOCUSED	DIVIDED	FOCUSED	DIVIDED
P2	230–280	Central	3.54 \pm 1.89	4.93*** \pm 2.16	2.28 \pm 2.20	3.29*** \pm 2.19
CNV	430–700	Central	1.19 \pm 1.70	1.80 \pm 1.79	-0.96*** \pm 2.07	-1.23*** \pm 2.22
			CUED	UNCUED	CUED	UNCUED
N1	150–200	Occipital	-3.84** \pm 4.13	-1.63 \pm 3.90	-5.67** \pm 3.59	-3.44 \pm 3.41
Early P3	350–450	Occipital	7.37 \pm 3.78*	7.50 \pm 3.65*	6.26 \pm 4.57	5.03 \pm 4.57
Late P3	600–700	Occipital	2.30 \pm 4.49*	4.53 \pm 3.86*	1.62 \pm 4.01	2.09 \pm 3.89
SN	240–290	Occipital		-0.28 \pm 5.52		-1.36 \pm 3.74*

Mean and standard deviation (mean \pm SD) values for each ERP component in each condition and group. ANOVA factors: Group (ADHD, non-ADHD), Type of attention (focused, divided), Cue validity (cued, uncued). For P2 and CNV: Group \times Type of attention. For N1 and P3: Group \times Cue validity. SN: between groups one-way ANOVA. $n=60$.

* = $p < 0.05$.
 ** = $p < 0.01$.
 *** = $p < 0.001$ (μV : microvolts; ms: milliseconds).

in all accuracy measures, there were no significant differences regarding cue validity in neither group.

2.2. Electrophysiological results

ERPs to cues were time-locked to cue onset, thus capturing the process of re-orienting attention and the effect of either focusing attention onto a single frame, or dividing it between two possible locations.

Two components from these cue-evoked ERPs showed significant differences between groups and conditions. The first was an anterior P2, which clearly varied in amplitude depending on the Type of attention. P2 amplitude was larger in the divided attention condition than in the focused one ($F(1,58)=37.97$, $p < 0.001$). There was also a significant main effect of Group ($F(1,58)=8.07$, $p < 0.01$), as a result of ADHD children having larger P2 amplitudes than non-ADHD children in both types of attention. P2 was also topographically more widely distributed in the ADHD than in the non-ADHD group ($F(1,58)=8.28$, $p < 0.01$), when comparing relevant electrodes sites.

The second significant component was a CNV that onset after P2 resolution and was larger in non-ADHD than in ADHD children. Main effect Group was statistically significant ($F(1,58)=30.66$, $p < 0.001$) (see Fig. 3). The main effect Type of attention did not reached statistical significance ($F(1,58)=0.79$, $p=0.37$).

Analysis of ERPs evoked by targets yielded interesting differences between groups and conditions. A mixed ANOVA design Group \times Cue validity \times Type of attention showed a significant main effect for Group ($F(1,58)=6.36$, $p < 0.05$). The amplitude of the early N1 component was larger for non-ADHD than for ADHD children. The main effect Cue validity was also a significant ($F(1,58)=11.82$, $p < 0.001$). N1 amplitude was consistently larger in both groups when targets were preceded by valid cues. However, there were no significant differences as a function of the type of attention ($F(1,58)=0.00$, $p=0.98$), so that N1 amplitude was comparable whether targets were preceded by one or two cues (see Fig. 4). Analysis of the latencies of these ERP components did not yield any statistically significant difference between groups or conditions. Neither did, the

search for laterality effects comparing latency and amplitude of N1 in left and right electrodes sites.

A selection negativity (SN) was obtained subtracting, in each group, the ERP elicited by the invalid cue from the one elicited by the valid cue (see Fig. 4). In the difference wave, a clear negative component was observed in the time-windows between 240 to 290 ms after target onset. This component was significantly larger in amplitude in the non-ADHD group than in the ADHD ($F(1,58)=4.30$, $p < 0.05$).

After these negative components, the ERPs evoked by target stimuli were characterized by a wide P3-like positivity with a peak around 340 ms but extended in time up to 700 ms. The earlier segment of this component, between 350 to 450 ms, exhibited larger amplitude in the ADHD group than in the non-ADHD. A mixed ANOVA design showed a significant main effect for the factor Group ($F(1,58)=8.03$, $p < 0.01$). The within-subject factors Type of attention and Cue validity did not reached the statistical significant level and there were no significant interactions. The latter part of this positivity (600–700 ms) is characterized by a trend towards the baseline that resolves faster in the non-ADHD than in the ADHD group, especially in the invalid cue conditions. A similar mixed ANOVA resulted in significant main effects for Group ($F(1,58)=5.24$, $p < 0.05$), Cue validity ($F(1,58)=4.13$, $p < 0.05$), and Type of attention ($F(1,58)=5.48$, $p < 0.05$). There were no significant interactions (Table 1).

2.3. Correlation analyses

Considering all participants as a single sample ($n=60$), the total score from the Conner's Abbreviated Parent-Teacher Questionnaire exhibited significant correlations with several behavioral and electrophysiological measures. As expected, this index of ADHD symptoms correlated significantly and positively with the percent of errors ($r=0.47$, $p < 0.001$), the percent of misses ($r=0.37$, $p < 0.01$) and negatively with the percent of hits ($r=-0.48$, $p < 0.001$). The correlation with RTs was not statistically significant. It also exhibited significant correlation with the Cue-related ERP components P2 ($r=0.30$, $p < 0.05$) and CNV ($r=0.60$, $p < 0.001$). There were no significant

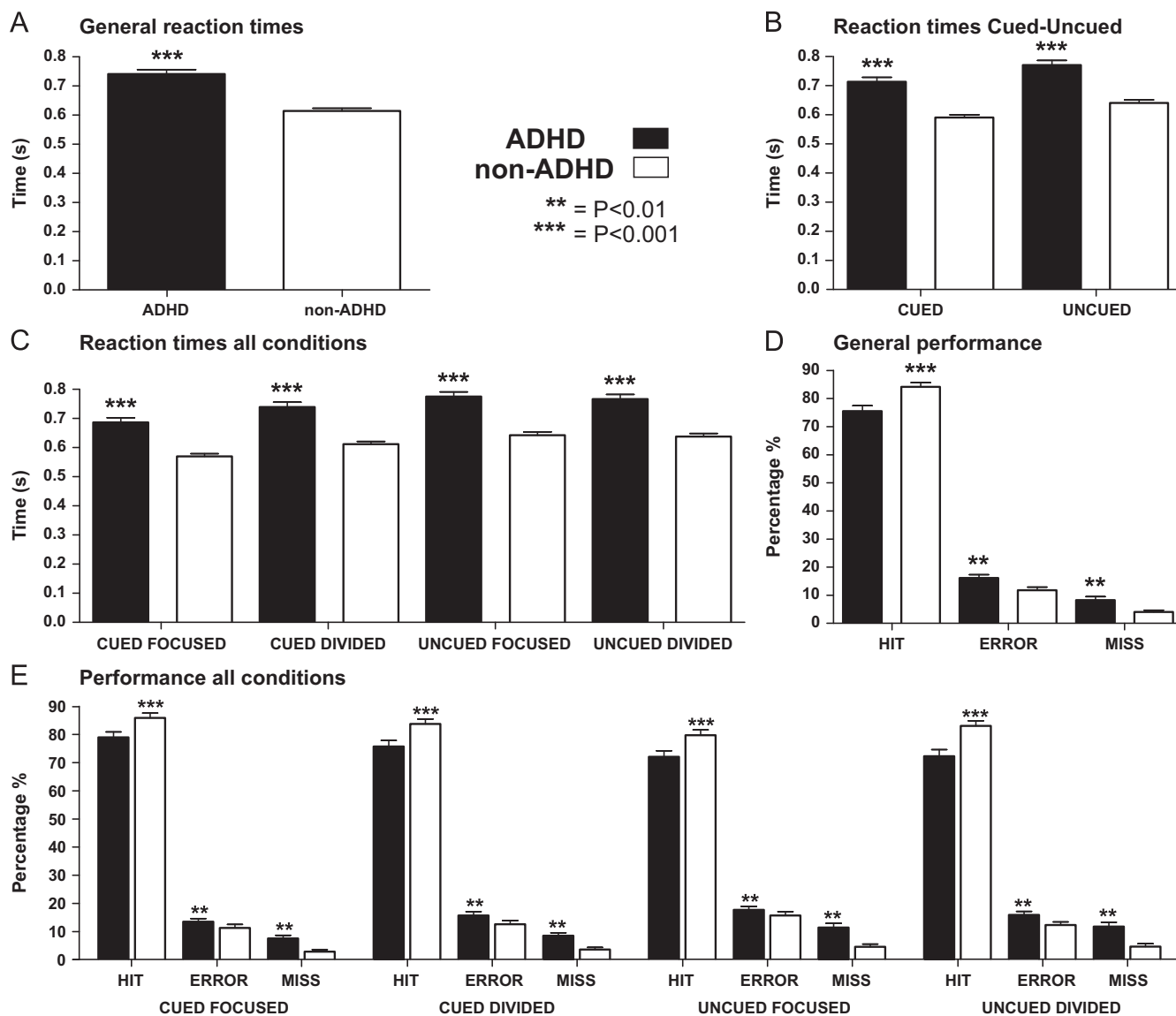


Fig. 2 – Behavioral results: reaction times and accuracy results. Black columns represent ADHD children; white columns represent non-ADHD subjects. Reaction times in seconds. Accuracy in percentages. ERROR=commission errors, MISS=omission errors. Bars depict standard error of the mean.

correlation between this index and target-related ERP components.

Correlations between electrophysiological and behavioral measures were also explored. There were no significant correlations with RTs. Nevertheless, the amplitude of the CNV component predicted a better performance regardless of the type of attention, that is, a larger CNV was significantly correlated with more hits and fewer commission and omission errors. The correlation values were: (i) Focused attention: hits ($r = -0.41$, $p < 0.001$), commission errors ($r = 0.30$, $p < 0.05$), omission errors ($r = 0.39$, $p < 0.05$); (ii) divided attention: Hits ($r = -0.47$, $p < 0.001$), commission errors ($r = 0.38$, $p < 0.01$), omission errors ($r = 0.45$, $p < 0.05$).

Target N1 amplitudes were also significantly correlated with behavioral performance when the target was correctly predicted by the cue and only in the focused attention

condition: Focused attention hits ($r = -0.28$, $p < 0.01$), commission errors ($r = 0.28$, $p < 0.01$).

3. Discussion

In the present study, ADHD children exhibited poorer performance than their non-ADHD counterparts in an exogenous cued visual spatial attention task. Exogenous orienting is commonly assumed to be intact in ADHD due to its reflexive and automatic nature. Nevertheless, as predicted by state regulation hypothesis, both behavioral and electrophysiological measures indicated the opposite.

Increased number of errors and longer RTs are, perhaps, the most frequent findings in almost every cognitive task applied to ADHD (Nigg, 2005). It has also been consistently

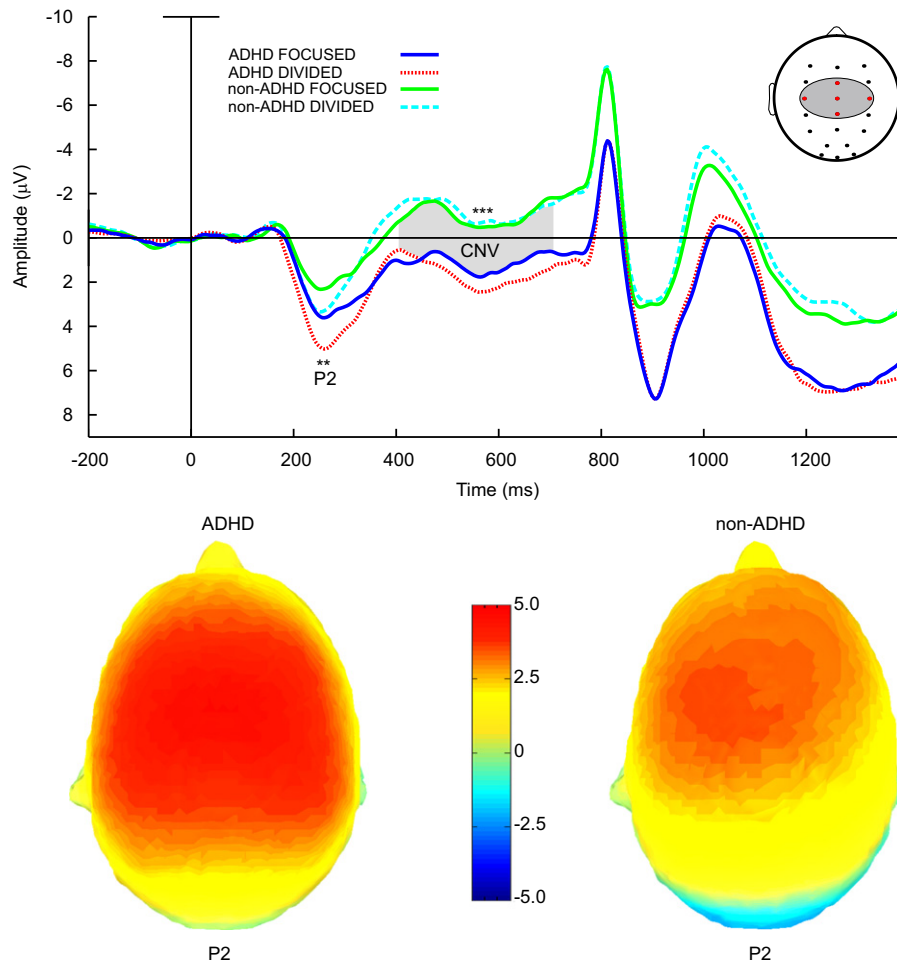


Fig. 3 – ERPs to cues, Upper panel: Grand average ERPs from the central ROI (FCz, C3, Cz, C4, CPz). Amplitude in microvolts (μV). Time in milliseconds (ms). Lower panel: Scalp maps of the P2 component evoked under all conditions. Color scale values in microvolts (μV)* = $p < 0.01$, * = $p < 0.001$.**

described that the more complex and demanding the task is or the longer it takes, the larger these effects become (Benikos and Johnstone, 2009; Mullane and Klein, 2008). In this regard, the present findings add to a large list of previous reports on the poor performance of ADHD subjects in covert orienting (Huang-Pollock and Nigg, 2003; McDonald et al., 1999; Swanson et al., 1991) and visual search (Mullane and Klein, 2008) tasks. RTs were slower in the ADHD group. They were also affected, in both groups, after invalid cues and when the attention was divided. There was a significant interaction between cue validity and type of attention, but no significant interaction with Group and type of attention. Regarding accuracy, ADHD children had more commission and omission errors. As expected, cue validity yielded a significant effect in both groups, revealing better performance in children when they responded to validly cued targets. But more importantly, invalid cuing in the focalized attention condition resulted in significantly fewer hits and more omission errors in the ADHD group. The triple interaction Group \times Cue validity \times Type of attention shows a significant worsening of ADHD performance when a single exogenous cue misdirect attention. This apparent failure to reorient attention could also be explained by a more general factor, especially considering a

cue validity rate of 50% and targets presence in all trials. ADHD seems to be less aware of the possible occurrence of uncued targets following a single cue. In other words, ADHD children fail integrating contextual information about incorrectly predicted locations for targets. But again, this might point more to a preparation state dysfunction than to a failure in orienting itself.

In an apparent contradiction with accuracy results, the interaction Group \times Cue validity \times Type of attention was not statistically significant for the RT measures. The interpretation of RT and accuracy variations due to endogenous and exogenous visual cuing in attention orienting tasks has been a matter of discussion (Prinzmetal et al., 2005). The traditional cost-benefit analyses of RTs described in endogenous orienting are only partially applicable to exogenous cuing tasks. The evidence suggests that exogenous orienting is essentially automatic and unaffected by cue validity (Giordano et al., 2009). Subjects cannot use the information of cue validity to reorient their attention efficiently in terms of speed. Exogenous cues could trigger shifts in visuospatial attention even if they never predict target locations (Remington et al., 1992). In the present study invalid cuing was the main factor in slowing RTs in both groups. Although

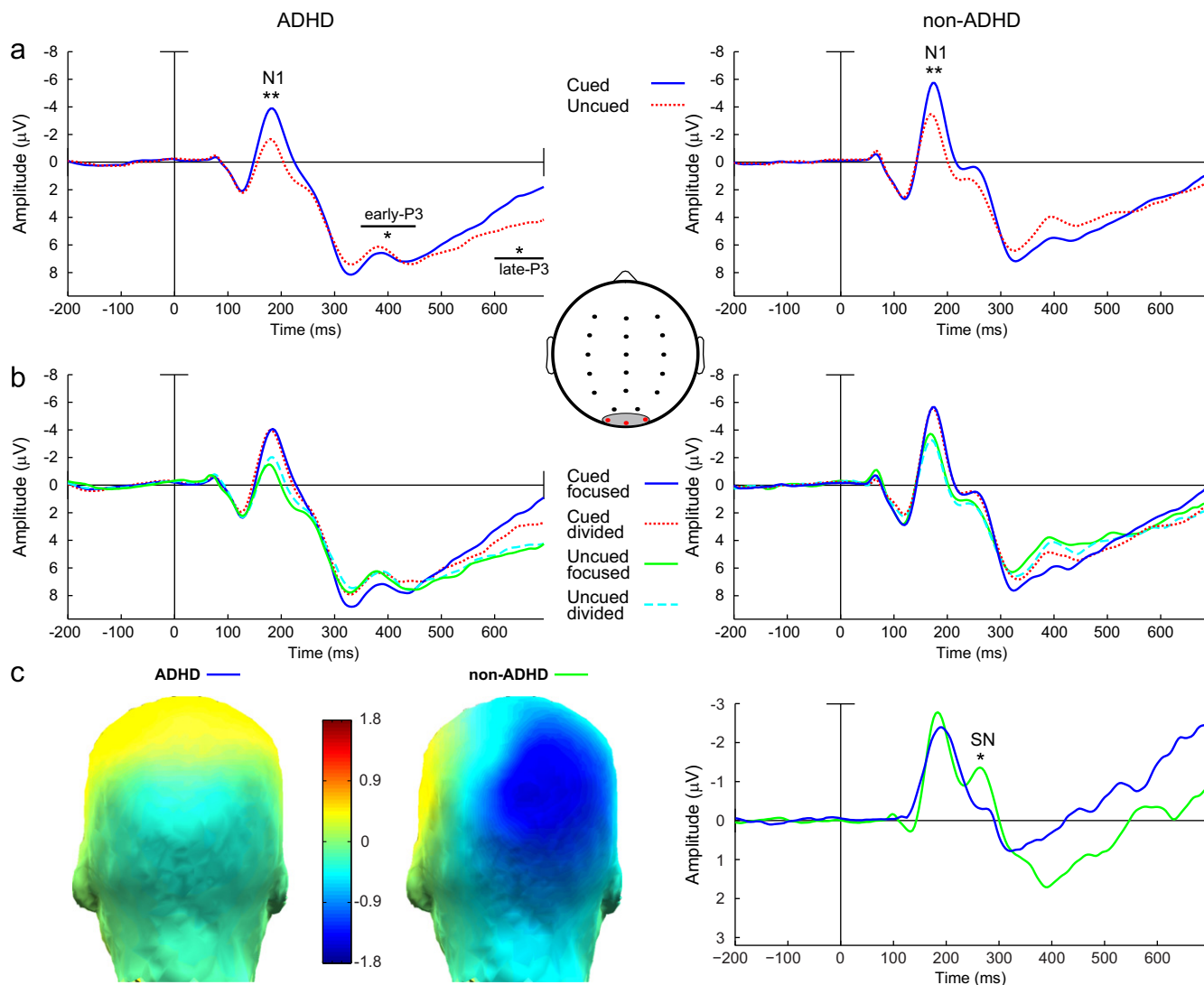


Fig. 4 – ERPs to targets: (a) grand-average ERPs elicited by CUED and UNCUED targets for ADHD (left) and non-ADHD (right) children. (b) Grand-average ERPs to targets in each of the four experimental conditions. Occipital ROI (O1, Oz, O2). (c) Scalp maps at 260 ms in each group (left), showing the topography of the selection negativity (SN) and difference waveforms (CUED-UNCUED) in each group (right). Color scale values and amplitude in microvolts (μV). Time in milliseconds (ms). * = $p < 0.05$, ** = $p < 0.01$.

divided attention also resulted in slower RTs when the target was correctly predicted by the cue, in the opposite situation, when the cue was invalid there were no significant differences between divided and focused attention. This could be interpreted as a ceiling effect, the second invalid cue did not add up significantly in the already slowed RTs. In line with this, the difference in accuracy due to cue validity was only evident in the focused attention condition and larger in the ADHD group.

3.1. The use of exogenous cues by ADHD subjects

The effect of spatial cuing of attention has been largely studied and described (Hillyard and Anllo-Vento, 1998). There is also a large corpus of literature regarding the orienting of attention and the preparation for target processing (Flores et al., 2009; Harter et al., 1989; Harter and Anllo-Vento, 1991;

Jongen et al., 2007). Nevertheless, most of the studies on the matter, especially in ADHD subjects, and even more those that combine behavioral and electrophysiological data, have used endogenous cues exclusively (Banaschewski et al., 2003; Huang-Pollock and Nigg, 2003). That is, perhaps, due to the fact that endogenous attention orienting is better suited to assess the anterior attention system (AAS) which is presumably impaired in ADHD (Barkley, 1997; McDonald et al., 1999; Swanson et al., 1991). On the contrary, exogenous cuing is considered to measure the posterior attention system (PAS), especially at a validity rate of 50%, which precludes strategy benefits, and stimulus onset asynchronies between 350 and 800 ms (Huang-Pollock and Nigg, 2003). The present study pertains to the second category. The PAS is supposed to be spared in ADHD (Carter et al., 1995; Swanson et al., 1991). However, this schema has been frequently challenged, especially regarding the involvement of other systems, like

alerting or vigilance (Huang-Pollock et al., 2006; Johnson et al., 2008), and other state factors (Banaschewski et al., 2003, 2008) that operate in conjunction with executive function impairments.

3.2. Cue-elicited P2 component

The P2 component elicited by the cues was larger in the divided attention condition than in the focused attention one. It also had larger amplitudes and more widespread scalp topography in the ADHD compared to the non-ADHD group. This last finding has been previously reported (Barry et al., 2009; Broyd et al., 2005). If the amplitude of this component reflects inhibitory effort, a larger P2 might imply more effort to orient attention while inhibiting irrelevant areas of the visual field. This pattern might represent atypical inhibition or a deficient process of resource allocation in ADHD children (Barry et al., 2003). In fact, a previous study has suggested that the P2 effect might predict some kind of compensatory processing in ADHD, being larger in those ADHD subjects with better cognitive performance (Robaey et al., 1995). In that study, among others (Barry et al., 2003), a larger P2 component was interpreted as indicating higher activation of automatic processes as part of a more effortful task performance strategy in ADHD.

3.3. Cue-elicited CNV component

The most evident ERP difference between the groups was the amplitude of the CNV elicited while preparing for the target stimulus. This electrophysiological index predicted the behavioral performance of the child, whether ADHD or non-ADHD. The reduced amplitude of CNV in the ADHD group seems consistent with ADHD deficits in executive function as predicted by the dysfunctional behavioral inhibition hypothesis (Barkley, 1997). This component shows reliable differences between children and young adults (Flores et al., 2009). Thus, the reduction in CNV amplitude observed in ADHD children could result from the documented delay in regional cortical maturation that affects most prominently the prefrontal regions in this developmental disorder (Shaw et al., 2007). Similarly, the fronto-parietal networks, related to attention and working memory, have also been described as main contributors to the CNV component (Gomez et al., 2007). Nevertheless, there is an alternative explanation to a delay in maturation of frontal structures. Reduced CNV amplitudes could also be interpreted as evidence of a deficiency in energy pools that points specifically to reduced effort to meet task demands (Benikos and Johnstone, 2009). Again, a deficit in inhibition of the default mode network during the expectancy period might also underlie a reduced CNV and a poorer performance (Aboitiz and Castellanos, 2011; Sonuga-Barke and Castellanos, 2007). In either case, smaller CNV amplitudes have been consistently reported in ADHD children and adults (Banaschewski et al., 2008; Doehner et al., 2010; McLoughlin et al., 2010; Valko et al., 2009).

Perchet et al. (2001) used the Posner paradigm to study attention shifts and anticipatory mechanisms and found a CNV component only in the “no cue” condition. This

component was absent in ADHD subjects. They interpreted this as “a lack of strategic planning/anticipatory mechanisms in the absence of a warning stimulus”. In the present study there was always a cue or warning stimulus and there was still a considerable reduction of the CNV in the ADHD group. More than lack of planning, we interpret this finding as reflecting the child’s difficulty in effortfully maintaining anticipatory mechanisms in place until the target processing stage. This explanation is in line with previous studies (Banaschewski et al., 2003; Benikos and Johnstone, 2009; Tecce, 1972) suggesting that an abnormal energetic state regulation may also explain attentional modulation mechanisms in ADHD.

Finally, there are other negative components, with overlapping scalp topography, in the time frame of the CNV described here that cannot be ruled out in the present data. That is the case of the contralateral delay activity (CDA) (Fukuda et al., 2010), a large negativity observed over posterior sites, contralateral to the stimulus location, when the subject has to maintain a number of items or their spatial location in working memory. The amplitude of CDA increases with the number of items to be remembered (Fukuda et al., 2010). Given that an impairment of spatial working memory is one of the most consistent findings in ADHD (Nigg, 2005), a reduction in CDA may also contribute to the reduced amplitude of the negativity described here in ADHD subjects.

3.4. Target-elicited ERPs

The early ERP components in the target processing stage are also in line with previous reports in the field. The increment in the amplitude of these components induced by attention has been interpreted as reflecting the amount of attentional resources allocated to the stimulus (Hillyard and Anllo-Vento, 1998). The amplitudes of the visual N1 and the selection negativity (SN) were significantly reduced in the ADHD group and were followed by a larger P3-like component with slower resolution at the end of the trial. As expected, N1 amplitude was also modulated according to cue validity; it was larger when targets were correctly predicted by the cue. In contrast, the type of attention (focused or divided) has no impact on N1. And yet, it was significantly correlated with behavioral performance, with larger N1 amplitudes predicting better performance in the focused attention condition.

ADHD is usually characterized by a reduction in the amplitude of ERP components, especially in those attention-modulated components like the N1 and the SN (Brown et al., 2005; Satterfield et al., 1994; van Elk et al., 2010). This has also been correlated with behavioral performance (Mangun and Hillyard, 1991). SN is usually absent in response to stimulus presented at unattended locations (Hillyard and Anllo-Vento, 1998). Some previous studies about early attention selection deficits in ADHD have only found reduced amplitude of the frontal selection positivity (FSP) with non-significant effects over the posterior SN (Jonkman et al., 2004; van der Stelt et al., 2001). The differences in the experimental design could account for this apparently contradictory result. In any case, the presence of SN could be interpreted as a more effective attention allocation to the cued visual area and thus to the cued target in non-ADHD. This is congruent with the fact that

the P3-like positivity that follows the SN had a slower return to the baseline in the ADHD group, especially in the case of invalid cued targets, reflecting perhaps difficulties in cognitive closure (Polich and Kok, 1995).

3.5. Conclusion

Taken together, the present results suggest that even if the PAS is not affected in ADHD subjects, their exogenous orienting of attention could be dysfunctional under certain conditions. Perhaps that is not caused by the orienting process itself, but instead by a difficulty in maintaining the relevant information obtained in this stage until the target processing stage, when it is needed.

The long-lasting search for a consistent deficit pattern in ADHD has resulted in numerous descriptions of altered cognitive function in this population. There are still several discrepancies regarding which attention processes are compromised and which are spared in this disorder. This variability might be partially explained by more general factors than the cognitive processes evaluated in each task. In our perspective, the exploration of cognitive functions must take into account the preparatory states, which might be altered in ADHD.

4. Experimental procedure

4.1. Subjects

Sixty children participated in the study; 30 of them were diagnosed as ADHD (combined subtype) and 30 were age- and sex-matched controls (non-ADHD) subjects. ADHD children (seven females) had a mean age of 10.6 ($SD = \pm 1.7$) and non-ADHD subjects (nine females) had a mean age of 11.1 ($SD = \pm 1.1$). No significant differences were found between the groups in age, IQ, or educational level. IQ was assessed using the WISC-III test (Ramírez and Rosas, 2007). The ADHD group had a mean IQ of 107.6 ($SD = \pm 8.6$), while the non-ADHD group had a mean IQ of 111.2 ($SD = \pm 10.5$). All ADHD subjects were diagnosed as ADHD-Combined Subtype by a trained child neurologist according to DSM-IV criteria (American Psychiatric Association, A.P.A., 2000). All participants were also screened for psychiatric or neurologic comorbid conditions using a protocol that included parents' interview, M.I.N.I. Kid test (De la Peña et al., 2009), and general psychological and physical assessment of the children. All ADHD children were being treated with methylphenidate, but suspended medication 24 h prior to the study. The Conner's Abbreviated Parent-Teacher Questionnaire (Rowe and Rowe, 1997) is usually utilized to screen for symptoms of ADHD in the clinical setting. In the present study it was used as an additional symptoms count tool. Participants with ADHD and those from the non-ADHD group were evaluated using this instrument as a controlling variable. Parents granted informed consent for their children's participation, and children signed an informed assent form. No monetary or any other kind of reward was granted for their participation. The procedures in the study were approved by the Ethics Committee of the School of Medicine of the Pontificia

Universidad Católica de Chile and ratified by the Ethics Commission of the Fondecyt-Conicyt Program of the Chilean government.

4.2. Experimental design

The task was designed to assess children's ability to sustain attention, extract information from exogenous spatial cues and use it to covertly re-orient their attention towards (i) one of four possible locations of the target stimulus (focused attention condition) or (ii) two simultaneously cued locations (divided attention condition). The target stimulus appeared inside an array of distractors, so a covert visual search was necessary to respond successfully. Stimuli were presented using Presentation[®] software (Version 14.4, <http://www.neurobs.com>).

Each trial began with the appearance of a fixation cross at the center of the computer screen, located 80 cm away from the child's forehead. Participants were asked to maintain fixation throughout the trial. Simultaneously with the fixation cross, four white frames of 3×3 cm appeared (two to each side of the cross, see Fig. 1). The four frames were evenly distributed on a horizontal line in such a way that the two more central frames were placed at an eccentricity of 3.5° in each visual field, while the two outer frames subtended 10° of visual angle from the fixation cross. After a 500 ms interval, one or two of the frames lit up in green, signaling the frame where the target stimulus was likely to appear. Seven hundred milliseconds after this event, an array 3×3 of nine white "O"s, (0.7 cm each) appeared inside each frame but in one of the frames an "X" of same size and color replaced one of the "O"s. Children had to indicate which frame contained the target by pressing the one key out of the four that corresponded to the target frame in the screen. In 50% of the trials, the target "X" appeared in one of the previously cued frames; in the remaining 50%, it appeared in an uncued frame. Trials were classified in four categories or conditions: CUED FOCUSED: Only one frame is cued (in green), and the target stimulus appears inside the previously cued frame. CUED DIVIDED: Two frames are cued, and the target stimulus appears inside one of the two previously cued frames. UNCUED FOCUSED: Only one frame is cued, and the target stimulus appears inside a frame different from the previously cued one. UNCUED DIVIDED: two frames are cued, and the target stimulus appears inside one of the two uncued frames. A total of 432 trials (108 trials from each category) were presented in a semi-random sequence.

Behavioral indices (RTs, hits and errors) were obtained for each condition. The experiment was administered in four blocks of 5 min each, with resting periods of 3 or more minutes between them.

4.3. Electrophysiological recording

Electrophysiological signals were recorded using a NeuroScan 40-channel Digital Electroencephalograph with a high-resolution NuAmp amplifier. A 40-channel cap (Quick-Cap) from the same company was used for electrode placement. Impedances were kept below 5 k Ω throughout the recordings. A/D sampling frequency was set at 250 Hz. A band-pass

digital filter between 0.1 and 30 Hz was later applied to remove unwanted frequency components. Two additional bipolar derivations were used to monitor vertical and horizontal ocular movements (VEOG, HEOG). For the ERP evoked by the CUE, the EEG epoch started 200 ms before the cue and ended 1400 ms after it. For target-locked ERPs, the EEG signal was segmented from 200 ms before the target to 700 ms after it. Any EEG segment with amplitude fluctuations larger than 100 μ V or values exceeding ± 5 SD from the mean of the EEG signal; and those contaminated by ocular movements, electromyography, or any other technical or biological artifact, were removed from further analysis. Rejected trials were fewer than 15% for each condition and group. In order to minimize the number of rejected trials, children received a training session before the actual experimental session in which they were taught not to move their eyes while the stimuli (frames and targets) were on the screen. Correct fixation was monitored by direct visual inspection of the subject with a video camera. The subjects could ask for a rest whenever needed. Artifact-free segments were averaged separately for each of the four experimental conditions. The EEGLAB Matlab toolbox (Delorme and Makeig, 2004) was used for off-line EEG processing and analysis. ERPs to cues and targets were obtained for each condition. Latencies and amplitudes of various ERP components (P2, CNV, N1, and P3) were measured and statistical analyses were conducted on these values.

4.4. Statistical analysis

A mixed ANOVA design with repeated-measures was conducted on behavioral and electrophysiological dependent variables. The main factors were: Group (ADHD vs. non-ADHD) \times Cue validity (CUED vs. UNCUE) \times Type of attention (FOCUSED vs. DIVIDED). This way the indices of behavioral speed and accuracy (RTs, hits, commission and omission error rates) were compared between groups and experimental conditions. All statistical calculations on ERPs were performed using individual waveforms. A repeated-measures ANOVA design with two factors (Group \times Type of attention) was conducted to assess the P2 and CNV components evoked by the Cues, and a repeated-measures ANOVA design with three factors (Group \times Cue validity \times Type of attention) was conducted to assess the N1 and P3 components evoked by the targets. P2 scalp distributions for ADHD and non-ADHD children were compared by means of a repeated-measures ANOVA with two factors (Group \times Topography). Two groups of electrodes were collapsed into regions of interest (ROI) in order to avoid loss of statistical power (Oken and Chiappa, 1986): a Central ROI (FCz, C3, Cz, C4, CPz), which better represented the scalp maximum amplitude of P2 and CNV, and a posterior occipital ROI (O1, Oz, O2) to measure the N1, SN, and early and late P3 components. Latency windows for statistical analysis of ERP effects were: P2 [230–280 ms], CNV [430–700 ms], N1 [150–200 ms], SN [240–290 ms], early P3 [350–450 ms], late P3 [600–700 ms]. Results were corrected with Greenhouse-Geisser and Huynh-Feldt methods to adjust the univariate output of repeated measures ANOVA for violations of the compound symmetry assumption.

Correlations between the symptoms count resulting from the Conner's Abbreviated Parent-Teacher Questionnaire, behavioral measures (RTs and performance accuracy) and electrophysiological measures (ERP components: P2, CNV, N1 and SN) were explored using Pearson's correlation coefficient (r). In these analyses both groups were considered as a single sample ($n=60$) controlling for ADHD symptoms. This sample yielded significant correlations with a minimum statistical power of 0.59 (refined Fisher Z for $H_0: \rho=0$) in two-tailed analyses and 0.70 (refined Fisher Z) in one-tailed analyses.

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