Hemodynamic and behavioral peculiarities in response to emotional stimuli in children with attention deficit hyperactivity disorder: An fNIRS study

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ABSTRACT

Background: Children with attention deficit hyperactivity disorder (ADHD) exhibit behavioral inhibition deficits, which often lead to emotional dysregulation (ED) affecting individual ability to control emotions and behavioral responses. In ADHD, ED is associated with poor outcomes and comorbidities, with both externalizing and internalizing disorders. This work aims to evaluate sensitivity to emotional stimuli in children with ADHD using functional Near Infrared Spectroscopy (fNIRS).

Methods: During frontal fNIRS recording, 20 children with ADHD and 25 typically developing (TD) peers performed a visual continuous performance task with stimuli of different emotional content (i.e., positive, negative, neutral, and control stimuli without emotional content). This is a cognitive task designed to evaluate the ability to recognize emotional stimuli and to deal with emotional interference.

Results: The ADHD sample showed more variability in response time to stimuli and more false alarms compared to TD group. fNIRS data showed between-group differences in right prefrontal and frontal cortices, with wider hemoglobin concentration changes in the TD group, during positive, negative, and neutral conditions.

Limitations: Owing to the limited possibility of near infrared light to penetrate tissue, fNIRS can only measure cortical activations, while it would be of interest to identify the subcortical areas linked to emotional processing, too.

Conclusions: Findings suggest the presence of emotional processing deficits in children with ADHD, as suggested by poor performances on the e-CPT task, and of peculiar sensitivity to emotional stimuli, linked to atypical hemodynamics of right prefrontal and frontal areas.

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by dysregulated cognition and behaviors, resulting in difficulties in paying attention, excessive motor activity and high impulsivity (American Psychiatric Association, 2013). Barkley (1997) stated that the core ADHD deficit is the difficulty in response inhibition.Response (or behavioral) inhibition deficit refers to three interrelated processes: i) a difficulty to inhibit an initial prepotent response (i.e., a response associated to immediate reinforcement); ii) an inability to stop an ongoing response, a skill which usually enables a delay in decision process; iii) an incapacity to remain focused and to operate interference control. In addition to the behavioral domain, impairment in response inhibition also affects the ability to control emotions, arousal, and self-regulation (Barkley, 1997).

In daily living, emotional self-regulation includes the individual ability to identify and properly interpret environmental emotional stimuli, to recognize individual self-emotions, and to deal with them, generating appropriate social responses (Doumond et al., 2019).

Emotional dysregulation (ED) is a transdiagnostic psychopathological trait which is frequently found in ADHD and associated with poor outcomes and comorbidities with both externalizing (e.g., oppositional...
defiant disorder) and internalizing (e.g., depression, dysthymia) disorders (Shaw et al., 2014; Wang et al., 2018).

ED refers to deficits in physiological arousal regulation and in inhibition of disruptive behavioral response to emotions, an inability to refocus attention after a strong emotional feeling and to have a goal-directed behavior after emotional activation (Biederman et al., 2012). Therefore, ED reflects both failure of cognitive control and high intensity of arousal (Soloff et al., 2015). These deficits cause higher sensitivity to emotional arousal, slower return to baseline activation, and deficits in coping strategies. Especially in children and adolescents, ED is responsible for low tolerance to frustration, impatience, easy anger and excessive emotional excitement (Biederman et al., 2012).

Previous studies on general populations found that ED is present in 38% of children with ADHD, ten times more frequently than in the general population (Stringaris and Goodman, 2009). A longitudinal 4-year follow-up study showed that ADHD is associated with ED in children with a higher number of psychiatric comorbidities, greater social impairment, and persistence of ADHD, if compared with ADHD without ED or healthy controls (Biederman et al., 2012).

Near Infrared Spectroscopy (NIRS) might be a viable approach in the study of the neural bases of emotional processing in samples of children and adolescents with ADHD. NIRS is an optical technique that uses light at specific wavelengths to probe changes in oxygenated and deoxygenated hemoglobin (HbO and HbR, respectively) concentration over time.

Previous functional magnetic resonance imaging (fMRI) studies highlighted a relation between subcortical areas activity and emotional processing (Soloff et al., 2015). For its intrinsic characteristics, NIRS technology does not offer evidences of subcortical activations; still, it presents several advantages in the study of clinical populations. As NIRS is an optical technique that non-invasively monitors the cerebral cortex metabolism with less body fixities than other neuroimaging techniques (Mauri et al., 2014), it gives the opportunity to include patients with behavioral regulation difficulties.

Previous functional Near Infrared Spectroscopy (fNIRS) studies on children with ADHD investigated patients’ peculiarities in cortical activations related to impairment in cognition and inattention. These studies successfully used NIRS during different neuropsychological tasks (e.g., Grazioi & Crippa et al., 2019; Mauri et al., 2018). Conversely, a wealth of studies used NIRS to investigate neural correlates of emotional regulation, a field of research frequently overlooked in ADHD.

To our knowledge, only two fNIRS studies previously evaluated the cortical bases of emotional processing with emotional tasks in samples of children with ADHD (Ichikawa et al., 2014; Köchel et al., 2015). Ichikawa et al. (2014) recorded NIRS signals in bilateral occipital cortices in 13 children with ADHD and 13 typically developing (TD) peers (aged 8 to 12 years), while they were passively watching happy and angry facial expressions, in order to evaluate group differences in emotional processing. They found higher HbO concentration changes in the TD vs. ADHD group, in the right hemisphere during the “angry face” condition. In fact, the ADHD group showed increased HbO levels only in response to happy faces, while the TD group showed increased HbO levels in response to both happy and angry faces. In the second study, 14 children with ADHD and 14 TD children were presented emotionally intoned or neutral sentences in order to investigate neural correlates of affective prosody processing. The authors found peculiarities in temporal cortices in the ADHD group compared with the control group. In particular, fNIRS results showed a minor activation of cortical areas linked to emotional identification, despite task execution during angry prosody condition requires higher attention allocation.

Given these premises, the present study aimed to evaluate sensitivity to emotional stimuli in children with ADHD compared with TD children. We measured cortical activation with fNIRS while children were performing a visual emotional continuous performance task (e-CPT) presenting stimuli with different emotional valences, in blocks with specific emotional targets (Soloff et al., 2015).

The task has been previously validated in an fMRI study with adult patients with borderline personality disorder, a condition characterized by ED, especially in response to negative emotions. Former studies showed that this task activates cortical regions linked to cognition and subcortical areas linked to emotional arousal. Intriguingly, this study also found worse performances with negative emotional stimuli, demonstrating the possibility to evaluate neural correlates of emotional dysregulation (Soloff et al., 2015).

Based on the literature, we hypothesized that the worst behavioral performances would be found in the ADHD group, especially with negative emotional stimuli, as a result of the behavioral dysregulation. We also expected to identify hemodynamic cortical peculiarities in the clinical group, which might be a biomarker for behavioral and emotional dysregulation in ADHD patients, as revealed by a possible association between ADHD symptoms and NIRS signals. To our knowledge, the present study is the first fNIRS study aimed to assess emotional interference in cognitive processing in children with ADHD, through the measurement of cortical activations.

2. Methods

The present study is a cross-sectional observational study aimed to evaluate cortical sensitivity to emotional stimuli in children with and without a clinical diagnosis of ADHD. Participants underwent fNIRS while performing a visual performance-CPT in which faces with relevant positive, negative and neutral content were presented. In this study we recruited drug-naïve children with ADHD, admitted to our institute’s Child Psychopathology Unit. Our protocol was approved by our institute’s ethics committee in accordance with the Declaration of Helsinki (1989). Written informed consent and assent were obtained from all caregivers and participants.

2.1. Participants

Study participation was proposed to 26 drug-naïve children with ADHD, and 27 typically developing (TD) peers aged 6 to 16 years. Two children with ADHD were later excluded based on recruitment criteria.

For all patients, the ADHD diagnosis was made according to DSM-5 criteria (American Psychiatric Association., 2013) by a child neuropsychiatrist with experience in ADHD. A child psychologist (M.Ma.) independently confirmed the diagnosis through direct clinical observation and the administration of the Development and Well-Being Assessment (DAWBA) semi-structured interview to parents (Goodman et al., 2000). Thirty-one percent of patients exhibited ADHD with predominantly inattentive presentation, 11% with predominantly hyperactive/impulsive presentation, and 58% with combined presentation.

The control group was made of typically developing children. The presence of psychiatric disorders, if any, was excluded using the DAWBA parent diagnostic interview.

The exclusion criteria for the whole sample included the presence of intellectual disability, neurological diseases, epilepsy, genetic syndromes and previous treatment with psychoactive drugs. A diagnosis of other psychiatric disorders (e.g. ASD, anxiety, specific learning disorders) was not an exclusion criterion for the ADHD group.

All participants were Caucasian, spoke fluent Italian, and had normal or corrected-to-normal vision. Familial socio economic status (SES) was coded according to Hollingshead scale for parental employment (Hollingshead, 1975).

2.2. Measures

The intelligence quotient was estimated by the Wechsler Intelligence Scale for Children-III or -IV (WISC-III or -IV) (Wechsler, 2006; 2012) for all participants. Only participants with full scale intelligence quotient (FSIQ) scores higher than 80 were included in the study.
2.3. Clinical and behavioral profiles

Clinical and behavioral profiles were assessed through the Child Behaviour Checklist 6–18 (CBCL/6–18) (Achenbach and Rescorla, 2001) and Conners’ Parent Rating Scales (CPRS) (Conners, 1997) which were filled out by the participants’ parents.

The CBCL/6–18 is a parent report screening form for emotional, behavioral and social problems in children and adolescents aged from 6 to 18. It is an empirically based questionnaire with 8 syndromic scales and 6 DSM-oriented scales (Achenbach and Rescorla, 2001). T-scores of syndromic scales (i.e., Anxious/depressed, Withdrawn/depressed, Somatic complaints, Social problems, Thought problems, Attention problems, Rule-breaking behavior, and Aggressive behavior) were taken into account for analysis.

ED was evaluated by the CBCL-Dysregulation Profile (CBCL-DP) which is the sum of T-scores for the CBCL/6–18 Anxious/depressed, Attention problems, and Aggressive behavior scales (Althoff, 2010; Biederman et al., 2009).

The CPRS are one of the most widely used instruments to assess children with ADHD, measuring both inattention and hyperactivity domain; the “ADHD index” is the CPRS subscale that was considered in the study.

2.4. Stimulation protocol

The participants were seated at a desk, on a height-adjustable chair, approximately 50 cm away (about 34° of visual angle) from the screen such that their eyes focused on the center height of the monitor. During the fNIRS recording, each of them performed a visual emotional continuous performance task (e-CPT) in which stimuli with different emotional valence were presented (Soloff et al., 2015). The stimulation protocol was developed with the Presentation® software (Neurobehavioural Systems Inc.), and stimuli were displayed using a 17” computer screen. The protocol was organized in blocks and consists of a rest condition and task blocks. During the rest condition, participants passively looked at a 1 × 1 cm white cross on a black screen. During task blocks, children viewed 4 types of stimuli: i) positive: faces expressing positive emotions (e.g. joy); ii) negative: faces expressing negative emotions (e.g. anger, fear, sadness); iii) neutral: faces with neutral expressions; iv) distorted: distorted images with scrambled faces (Ekman and Friesen, 1976). For each type of stimuli, 16 different images were selected. All images were 11 cm wide and 16.33 cm high (about 13° of visual angle). The e-CPT requires continuous attention to the task with concurrent inhibition of a preponderant response. Target responses depend on the valence of emotion on which a target letter (i.e. “X”) or a distractor (i.e. “A”) is depicted. Target images were signaled at the beginning of each block. Children were asked to press a key whenever the target stimulus was on the valence of emotion on which a target letter (i.e. “X”) or a distracter (i.e., “A”) is depicted. Target images were signaled at the beginning of each block. Each block of task conditions comprised 36 trials presented in a pseudo-randomised order. Among these, 24 trials were defined as targets (e.g., faces expressing positive emotions combined with “X” letter). Of the remaining 12 trials, 4 images were target images presented with the distracter (i.e., faces expressing positive emotions combined with “A” letter), 8 were images evenly showing other stimuli (i.e., faces with negative emotions, neutral faces, or distorted images, presented either with “X” or “A” letter).

The whole task sequence was the following (Fig. 1):

Rest - Positive - Distorted - Negative - Neutral - Rest - Neutral - Negative - Distorted - Positive - Rest.

Stimuli were presented for 1000 ms with a jittered interstimulus interval (250–750 ms, 250-ms increments). Press responses with reaction times < 100 ms were excluded to avoid anticipation (response time window: 100 ms - 1000 ms). For each condition, two blocks (54 s each) were used, in addition to 3 rest blocks (30 s each). The whole task lasted 8 min:42 s.

2.5. fNIRS data acquisition, optode localization and data preprocessing

fNIRS data were acquired with a commercial continuous-wave fNIRS (DYNOT Compact 9–32, NIRx, Berlin, Germany). An elastic cap of proper size was placed on the participants head, with 6 light sources and 11 light detectors, placed on bilateral prefrontal and frontal areas with the probe center positioned on Fpz and the lowest probe line along the Fp1-Fp2 line (International 10–20 System) (Jasper, 1958). Optode positions, source-detector combinations and corresponding channel numbers are illustrated in Fig. 2. The source-detector distance was 3 cm. Recording wavelengths were set at 760 nm and 830 nm to measure HbO and HbR concentration changes, respectively. fNIRS data pre-processing was performed using the Homer2 v2.8 software (Huppert et al., 2009; Piazza et al., 2019). First, the raw data were converted into changes in optical density data. Then, a motion artefact correction technique was applied. The technique consisted in the wavelet-based motion artefact correction approach preceded by a moving average filter performed over 5 s data windows. In the present work, a threshold of 0.1 was used. Data were then filtered with a third order Butterworth 1 Hz low-pass filter, followed by a fifth order Butterworth 0.1 Hz high-pass filter, to further enhance the signal-to-noise ratio. Finally, the optical density data were converted into concentration changes (|HbO| and |HbR|) through the Modified Beer-Lambert Law. For the data conversion, the differential path length factor (DFP) was appropriately calculated according to the age of the tested subjects. Specifically, the DPF was set to 5.7 and 5.1 for the 760 nm and the 830 nm wavelength, respectively.

The preprocessed fNIRS time series were converted by applying the following formula at each data point (p0) of the 8 task blocks:

\[ p_1 = \frac{(p_0 - m_{3s})}{s_{3s}} \]

where \( m_{3s} \) and \( s_{3s} \) are the mean and standard deviation of the fNIRS time series in the 3 s before the first block beginning (Crippa et al., 2017; Graziosi et al., 2019; Ichikawa et al., 2014). Time point concentration data were averaged across different task conditions: i) “Positive”, ii) “Negative”, iii) “Neutral”, iv) “Distorted”. fNIRS data from bilateral temporal channels were excluded from further analysis because of a strong signal noise in more than 50% of participants.

HbO and HbR signals were averaged in four regions of interest (ROIs) that were identified as follows: i) left-prefrontal (channels 1–3), ii) right-prefrontal (channels 9–10), iii) left-frontal (channels 4–7), and iv) right-frontal (channels 11–14).

2.6. Statistical analyses

Statistical analyses were conducted using SPSS statistical software package (Version 21.0). Data were visually and statistically inspected to check normality, linearity, independence of observations, and homogeneity of variances.

Preliminary analyses were conducted to assess between-group differences for demographic characteristics. Between-group differences for clinical and cognitive measures were evaluated by Mann-Whitney or Independent-samples t-tests according to variable distributions.

In order to check for possible differences between the ADHD and TD groups in behavioral performances at e-CPT, a 2 × 4 non-parametric version of the repeated measures ANOVA -Wald-type statistic (WTS) was used, as provided in the nparLD package for R (version 2.15.1, The R Foundation for Statistical Computing; Noguchi et al., 2012), with condition (positive, negative, neutral, and distorted) as within-participant factor and group (ADHD, TD) as a between-participant factor. To explore differences in HbO and HbR signals averaged in each task condition in each ROI, a 2 × 5 × 4 Wald-type statistic (WTS) was calculated, with condition (positive, negative, neutral, distorted, and rest) and ROIs as within-participant factors and group as a between-participant factor. When significant main effects were found, pairwise comparisons were performed using either the Wilcoxon rank sum test between-group comparisons or the Wilcoxon signed rank test for
comparisons within groups. Pairwise comparisons included a Benjamini-Hochberg adjustment for multiple comparisons.

To check for a possible effect of co-diagnosis of autism spectrum disorder (ASD) in our sample of children with ADHD, the above mentioned analyses were carried out on a subsample of children with no ASD comorbidity as well. Indeed, children with ASD could present relevant difficulties in emotion identification via facial expressions (Griffiths et al., 2019).

Spearman correlation analyses were used to evaluate the presence of possible associations between ADHD symptoms and clinical impairment (evaluated with CPRS and CBCL/6–18 subscales), behavioral data from eCPT and hemodynamic characteristics in ROIs which were found to be significantly different between the two groups. The alpha level was set to 0.05 for all data analyses.

3. Results

Four participants in the ADHD group and 2 participants in the TD group were excluded from the study because of non-compliance with behavioral tasks. Twenty children with ADHD and 25 TD peers were evaluated. In the ADHD group, 2 patients were excluded because of technical problems during fNIRS acquisitions. The final sample consisted of 18 children with ADHD diagnosis and 25 typically developing children. In the ADHD group, 5 participants also had a diagnosis of specific learning disorders, 3 participants had an oppositional defiant disorder, 3 participants suffered of anxiety disorder, 2 participants of autistic spectrum disorder and 1 participant of mood disorder.

The two groups were matched for age, gender, FSIQ and familial socioeconomic status (Table 1).

3.1. Clinical and behavioral results

Regarding the clinical profile, children with ADHD showed higher impairments in several domains measured with CBCL/6–18 (with p values ranging from 0.017 to < 0.001), including the CBCL-DP. As expected, children with ADHD had higher clinical scores on the “ADHD index” of CPRS (p < 0.001).

The clinical characteristics of the two samples are summarized in Table 1.

Between-group differences were found in eCPT behavioral performances. A group by condition interaction effect emerged in mean reaction time of hit responses (WTS(3) = 12.27, p = 0.006), with children with ADHD having faster responses for positive (p = 0.020), negative (p = 0.038), and neutral stimuli (p = 0.003) when compared to TD children. Furthermore, the ADHD group showed more variability in response time to stimuli (WTS(1) = 4.86, p = 0.027) and more false alarms (WTS(1) = 5.71, p = 0.017) than did the group with typical development.

The same pattern of results was evident in the subsample of children with no ASD comorbidity.

3.2. fNIRS results

Between-group differences were found for HbO concentration changes. A significant group by condition by ROI emerged (WTS(12) = 45.78, p < 0.001), with wider changes in TD children than in children with ADHD in right prefrontal ROI during positive, negative, and neutral conditions, and in right frontal ROI in negative condition. No significant differences were found for HbR concentration changes. HbO results are reported in Table 3; HbO and HbR activations in each ROI and condition are depicted in Fig. 3.

As for behavioral task results, fNIRS results were unchanged after excluding participants with comorbid ASD.

Finally, Spearman correlations between HbO activation in right hemisphere, ADHD symptoms and clinical variables and behavioral performances at c-CPT revealed several associations (ranging from Spearman’s $\rho = -0.305$ between HbO activation in right-prefrontal ROI during neutral condition and CPRS “ADHD index” to Spearman’s $\rho = -0.394$ between HbO activation in right-prefrontal ROI during positive condition and CPRS “ADHD index”) particularly between cortical ROIs found activating significantly differently between the two groups (i.e., right frontal and prefrontal areas) and ADHD symptoms, both measured with the CPRS subscale and the CBCL/6–18 (see Table 4).
Fig. 2. NIRS optode localization: probe center was positioned on Fpz and the lowest probe line along the Fp1-Fp2 line. Red circles: sources; blue circles: detectors; regions of interest: left-prefrontal = source 1 (Fp1) and channels 1–3, right-prefrontal = source 3 (Fp2) and channels 8–10, left-frontal = source 2 (F3) and channels 4–7, and right-frontal = source 4 (F4) and channels 11–14.

Table 1
Participants’ demographic, cognitive and clinical characteristics.

<table>
<thead>
<tr>
<th></th>
<th>ADHD (N = 18)</th>
<th>TD (N = 25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female:Males</td>
<td>2:16</td>
<td>4:21</td>
<td>0.21*</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>11 ± 3.2</td>
<td>10.3 ± 2.9</td>
<td>0.73*</td>
</tr>
<tr>
<td>SES (mean ± SD)</td>
<td>53.5 ± 19.7</td>
<td>47.2 ± 12.3</td>
<td>1.18*</td>
</tr>
<tr>
<td>FS IQ (mean ± SD)</td>
<td>98.7 ± 14.2</td>
<td>106.4 ± 17.8</td>
<td>1.50*</td>
</tr>
<tr>
<td>CBCL/6-18 Syndromic Scales (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious/depressed</td>
<td>64.33 ± 8.07</td>
<td>56.57 ± 6.39</td>
<td>3.44*</td>
</tr>
<tr>
<td>Withdrawn/depressed</td>
<td>60.67 ± 9.97</td>
<td>57.26 ± 7.69</td>
<td>1.26*</td>
</tr>
<tr>
<td>Somatic complaints</td>
<td>56.56 ± 6.19</td>
<td>53.57 ± 5.34</td>
<td>1.66*</td>
</tr>
<tr>
<td>Social problems</td>
<td>63.67 ± 8.53</td>
<td>54.70 ± 4.34</td>
<td>4.07*</td>
</tr>
<tr>
<td>Thought problems</td>
<td>62.00 ± 9.79</td>
<td>55.22 ± 6.51</td>
<td>2.54*</td>
</tr>
<tr>
<td>Attention problems</td>
<td>71.78 ± 8.14</td>
<td>53.74 ± 4.31</td>
<td>8.52*</td>
</tr>
<tr>
<td>Rule-breaking behavior</td>
<td>63.67 ± 9.08</td>
<td>53.87 ± 5.62</td>
<td>4.02*</td>
</tr>
<tr>
<td>Aggressive behavior</td>
<td>69.06 ± 11.21</td>
<td>55.65 ± 7.42</td>
<td>4.38*</td>
</tr>
<tr>
<td>CBCL-DP</td>
<td>205.17 ± 23.48</td>
<td>165.96 ± 15.47</td>
<td>6.43*</td>
</tr>
<tr>
<td>CPRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD index</td>
<td>80.06 ± 10.46</td>
<td>46.17 ± 5.88</td>
<td>13.34*</td>
</tr>
</tbody>
</table>

Table 1: ADHD = attention deficit hyperactivity disorder patients group; TD = Typically developing peers group; SD = standard deviation; SES = Socioeconomic status; CBCL = Child behavior Checklist; SD = standard deviation; DP = Dysregulation Profile; CPRS = Conners’ parent rating scales;  
* = Fisher exact test.  
* = Independent Sample t-test.
The aim of the present study was to evaluate whether children with ADHD showed a peculiar sensitivity to emotional stimuli compared with TD peers by fNIRS measures of cortical activation during a visual e-CPT. Emotional regulation and processing abilities were evaluated both clinically and neurophysiologically in 18 children with ADHD and 25 typically developing peers.

As expected, the ADHD group showed higher impairments on several domains measured by the CBCL/6-18 and the CPRS. Children with ADHD did not only obtain higher clinical scores on scales strictly related to the core symptoms of the disorder (e.g., ADHD index) but also on clinical measures of internalizing issues. In fact, children with ADHD showed higher scores on the CBCL/6-18 “Anxious/depressed” and “Social problems” scales. Particular attention should be given to significantly higher “CBCL-DP” scores, in line with previous research (Peyre et al., 2015). Clinical CBCL-DP scores during childhood are indeed known as a transdiagnostic risk factor of worst prognosis for both internalizing and externalizing disorders in adolescence and adulthood (Althoff et al., 2010).

Regarding the e-CPT, this was the first time that e-CPT was used to evaluate individuals in developmental age, with and without neurodevelopmental disorders. Children in the ADHD group showed the worst behavioral performances, with a higher number of commission and omission errors and a greater reaction time variability for correct responses throughout the task. Those trends in between-group differences reach statistical significance for mean reaction time during “positive”, “negative” and “neutral” conditions with children with ADHD being faster than TD peers, as well as for reaction time variability and number of commission errors with children with ADHD showing significantly higher values. The e-CPT is a task that specifically requires subjects to pay attention to stimuli with affective content, allowing to measure possible different effects of emotional context on cognitive processing (Soloff et al., 2015). Hence, it explores the ability to recognize an emotional stimulus as well as the ability to deal with emotional interference –especially with negative valence. Therefore, with the e-CPT, it is possible to consider behavioral responses from both a neuropsychological point of view and an emotional point of view.

Regarding the former of the two perspectives, our results are in line with the literature on neuropsychological deficits in ADHD. Poor behavioral performances on continuous performance tasks are one of the most frequent neurocognitive deficits observed in patients with ADHD owing to their inability to inhibit responses (e.g. Pievsky and McGrath., 2018). Moreover, it is worth to underline that reaction time variability, measured in terms of standard deviation of reaction times, is one of the neuropsychological measures which better differentiate individuals with ADHD from control subjects (Di Martino et al., 2008; Pievsky and McGrath., 2018). From an emotional processing perspective, we found significant differences—regardless of the type of emotion block—in reaction time variability and a greater number of commission errors. As stated before, we expected worse performances on facial expression recognition in the ADHD group, particularly with negative blocks. Unexpectedly, our findings suggest that both positive and negative facial expressions may affect cognitive control in ADHD children during task performance. Therefore, there seems to be a greater burden of this interference effect in children with ADHD, likely linked to the general behavioral inhibition deficits. With respect to the whole sample, it seems nonetheless that negative emotional context causes a non-significant trend of greater difficulties in behavioral performances.

ED might result in deficits in identifying and properly interpreting environmental emotional stimuli (Doumond et al., 2019). Difficulties in recognition of emotional cues and in particular, facial emotional expressions have been previously identified in children with ADHD (Dickstein and Castellanos, 2011; Ichikawa et al., 2014). For humans, face expressions are the most important emotional stimulus. They are the most powerful means to communicate emotional state to others and, as a consequence, their recognition is essential to create relationships in any social context. A deficit in this area could therefore account for the difficulties in socializations frequently experienced by children with ADHD.

The neural network linked to emotional face recognition includes prefrontal areas, predominantly involved in top-down cortical regulation of attention, temporal areas linked to processing of facial expressions, and subcortical circuits that evaluate emotional valence and arousal of the stimulus (Dickstein and Castellanos, 2011; Ichikawa et al., 2014; Soloff et al., 2015). With optical techniques, such as NIRS, it is possible to measure hemodynamic changes only in cortical areas. We therefore focused on frontal and prefrontal bilateral cortices...
in order to evaluate possible peculiarities in areas linked to the attentive component of emotional processing.

We found different responses in HbO between ADHD and TD groups in right prefrontal cortex during “positive”, “negative” and “neutral” task conditions and right frontal area during negative task condition, with wider concentration changes in the control group.

Previous studies comparing TD children and children with ADHD consistently found a lower activation of clinical groups during different neuropsychological tasks (Grazioli et al., 2019; Grazioli et al., 2019; Mauri et al., 2018; Ichikawa et al., 2014; Soloff et al., 2015). Moreover, in line with previous study, through NIRS we found peculiarities in cortical activation of individuals with ADHD to be localized in the right hemisphere (Mauri et al., 2018; Ichikawa et al., 2014; Köchel et al., 2015).

The right lateralization effect found in our study could be explained through an analysis of the e-CPT characteristics. This task determines subjects’ responses based on the affective context (i.e., negative, positive or neutral faces) and an additional attentional demand (presence of an “X” rather than an “A”). Hence, subjects are required to perform an attention-driven cognitive task that is directly related to emotional processing. Neurophysiology studies suggest that the right dorsolateral area activity is crucial in all emotions processing, specifically in top-down attentional control functions (Wyczesany et al., 2018). Hence, right lateralization in terms of greater activation found in control

Fig. 3. a. HbO activations in each ROI and condition. ADHD = Attention Deficit/Hyperactivity Disorder; TD = Typically Developing; Cond = Condition. Error bars represent 95% confidence intervals.
b. HbR activations in each ROI and condition. ADHD = Attention Deficit/Hyperactivity Disorder; TD = Typically Developing; Cond = Condition. Error bars represent 95% confidence intervals.
methodologies, Williams et al. (2008) found atypical neurophysiological responses related to a facial expressions identification task in children with ADHD. Similarly to the present study, their work identified a clinical profile characterized by impairment in the emotional domain and significant brain activity reduction in children with ADHD compared to TD peers. Williams and colleagues work, however, used event-related potentials (ERPs) on occipitotemporal brain systems. This study results suggested a reduction in occipitotemporal cortex activation in response to emotional faces across both right and left hemispheres. The results found in early neural pathways could possibly suggest an atypical emotional processing in ADHD related not only to cognitive control and the emotional processing of positive, negative and neutral valence stimuli.

However, given methodological differences, it is not possible to directly compare our results with those of previous studies. In fact, our participants were asked to perform active recognition of emotional stimuli and, at the same time, exert cognitive inhibition. Furthermore, we measured cortical activation in frontal and prefrontal cortices in order to evaluate neural correlates of cognitive control of emotional processing.

HbO concentration changes in the regions found activating differently between TD children and those with ADHD, were significantly negatively correlated with indexes of attention problems and rule-breaking behavior (CBCL/6–18) as well as with ADHD index (CPRS) and with behavioral performances at e-CPT. These findings suggest a relationship between atypical neural activation and clinical and behavioral peculiarities as well. Specifically, lower HbO activation was found being related to higher scores in clinical scales and worse performances in the behavioral task, thus confirming a possible relationship between peculiar brain metabolism in children with ADHD and the clinical and behavioral characteristics.

To summarize, considering a generally greater activation in the control group, we found altered NIRS performances in children with ADHD in all task conditions presenting a human face with or without emotional valence, also finding between-group differences in NIRS signal in blocks with “neutral” emotional value, but not emotional recognition alterations. It seems therefore that blocks comprising faces were easier to perform for TD children.

In our ADHD sample, we found atypical hemodynamic activation in the right prefrontal and frontal cortices while performing e-CPT. Thus, it is possible to hypothesize that these peculiarities are linked to cognitive control and the emotional processing of positive, negative and neutral valence stimuli.
Taken together, our results suggest that when cortical activation in areas linked to cognitive control is evaluated, children with ADHD do not show neural abnormalities specifically linked to difficulties in emotional processing of negative stimuli but these abnormalities are more likely related to a general deficit in dealing with complex tasks demanding behavioral inhibition. This point of view is also sustained by the fact that, when we considered cortical areas presenting statistically significant between-group differences in hemodynamic activations, we found that these areas (i.e., right prefrontal and right frontal cortices) are associated with symptoms of inattention, impulsivity and restlessness, measured both by CPRS and CBCL/6–18, but not with internalizing or emotional liability traits.

5. Limitations

For data interpretation, it is important to consider some limitations that our study presents. First, the limited size of our sample. It might be crucial to replicate our findings in an independent sample with a higher number of participants. Second, the use of a task previously implemented for fMRI acquisition in an fNIRS environment, in consideration of the limited compliance of our clinical patients. It is worth to note that, owing to the limited possibility of near infrared light to penetrate tissue, fNIRS can only measure Hb concentration changes in upper cortical areas.

Our study also presents some strengths. To our knowledge, it is the first study to investigate emotional processing in children and adolescents with ADHD using an “active” task which requires participants to deal with emotion recognition. Moreover, our study is the first in this field conducted on a completely drug-naïve sample, a condition necessary to exclude possible drug-related neurobiological effects.

Conclusion

In conclusion, our findings suggest the presence of deficits in emotional processing, as suggested by poor performances to e-CPT task, in children with ADHD as well as a peculiar sensitivity to emotional stimuli linked to atypical hemodynamics of right prefrontal and frontal cortical areas. Moreover, these peculiarities, which were seen both with positive and negative emotional stimuli, seem to be linked to behavioral inhibition deficits. While performing an emotional task that requires cognitive control, children with ADHD did not show abnormalities specifically linked with negative stimulus processing – contrary to what was previously reported in the literature (Ichikawa et al., 2014; Kochel et al., 2015) — but did show abnormalities related to a general deficit in behavioral inhibition.

Contributors

M.N. conceptualized the study design and methodology; S.B., E.G., E.R. and M.Ma. conducted the investigation; A.B., S.G., U.P. and M.Ma. contributed to the discussion of the results; all the authors agreed on the final version of the manuscript; M.N. and M.Mo. were responsible for findings acquisition.

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Declaration of Competing interest

None

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