The brain regulation mechanism of error monitoring in impulsive children with ADHD—An analysis of error related potentials

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A B S T R A C T

The objective of this study was to investigate the brain mechanism involved in the regulation of impulsivity in children with Attention Deficit and Hyperactivity Disorder (ADHD) through error detection as well as error monitoring. The subjects in this study included 7–11-year-old impulsive ADHD children as well as normal children and adult controls. Error related negativity (ERN) and error positivity (Pe) were measured. ERN peak latency from the children groups was delayed significantly when compared with the adult group; however, no significant difference in ERN amplitude was found among the three groups. Impulsive ADHD children had the earliest peak latency of Pe. In addition, the average Pe amplitude in impulsive children was significantly smaller than in adults (Cz and Pz), and smaller than in normal children (Pz). Late conscious cognitive processing of error is significantly weaker in impulsive ADHD children, suggesting a serious deficit of late error monitoring, rather than error detection.

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Impulsiveness traits are thought to be related to a lack of behavioral self-control [15]. Children with high impulsivity exhibit dysregulation of emotion and cognition [12]. Hyperactivity–impulsivity is the core symptom in children with Attention Deficit and Hyperactivity Disorder (ADHD) [1]. Individuals with ADHD, who tend to be more insensitive to errors, are more likely to make impulsive (commission) mistakes on continuous performance tests (CPT) than their normal counterparts [3]. Recent studies suggest that poor inhibitory response and deficient executive function related to error monitoring may play a crucial role in this disorder [2]. Error monitoring refers to online detection of errors and subsequent adjustment of performance [22].

Response inhibition is a key executive control process. The Go/No-Go task is a procedure in which response inhibition can be monitored. Studies have revealed that children with ADHD were slower to initiate the inhibitory response [3] and, thus, demonstrating deficiencies in error monitoring [22]. It has been suggested that ADHD individuals differ from normal developing individuals in terms of both error detection and behavioral adjustment to errors [22]. However, the correlation between error monitoring and inhibition was not evident in ADHD children [23]. It is logical to think that impulsive ADHD children tend to produce more errors, but short term behavioral tests, such as the hit test, may not be sensitive enough to assess their executive functions or their self-regulation.

Self-regulation of emotion and cognition has been mapped to the cortical regions (e.g. frontal lobe) of the brain, where activity can be easily detected [21]. Event-related potential (ERP) is a sensitive method to assess responses of the brain to stimulus. Error-related negativity (ERN), the negative wave after an incorrect response serving as the error detection system, and a subsequent positive potential (error positivity; Pe), the ‘remedial action system’ to compensate for errors, are two major components of ERP that are useful indices of self-regulation and executive function [10,11,26]. Falkenstein et al. proposed that ERN reflects response checking itself rather than error detection, and Pe associated with a later aspect of error processing or post-error processing might reflect the subjective assessment of an error [10]. The external feedback reward may enforce the individual’s self-evaluation [10,13,17,19]. Studies in adults have demonstrated that both ERN and Pe exhibit different styles in people with affective and behavioral problems, although Pe is a more sensitive index of regulation than ERN [20]. Low-socialized individuals who could not control their impulses had smaller ERN amplitude when negative consequences were involved [7]. ERN amplitude was also reduced in high-exteriorizing adults [14] and externalizing children [24]. Liotti et al. have shown significantly lower ERN for ADHD children when compared with normal children; however, Pe was not reported in this particular study [16]. Moreover, there is still a controversy regarding the change in ERN in ADHD children. For instance, Wiersema et al. did not find a signif-
We agree that impulsive children may not have impaired error detection; however, it is not clear yet which part of error monitoring is disrupted in the ADHD children. Therefore, we hypothesize that the inhibition deficit of impulsive children depends more on cognitive regulation after error detection rather than on error detection itself, which in turn results in the inability to adjust behavior even if they accurately detect the errors. Our study is to investigate the brain mechanism involved in regulating impulsivity through the use of indicators of error monitoring ERN and Pe in children with high impulsivity. We evaluated ERN and Pe in the condition of giving feedback after error response to reinforce the subjects’ awareness of error.

This research was approved by the local research ethics committee and was conducted in accordance with the Declaration of Helsinki. The subjects were divided into three groups: impulsive children with ADHD, normal children controls, and normal adult controls. The impulsive children with ADHD met the diagnosis criteria of ADHD hyperactivity–impulsivity according to the DSM-IV and more than two items of impulsivity criteria in ICD-10. Subjects with any psychopathological diseases were excluded. Sixteen children with ADHD, aged 7–11 years old, as well as sixteen normal children were recruited. The impulsive children and normal children were age- and sex-matched, and they had no significant difference on IQ (normal: 94 ± 15.1; ADHD: 92.9 ± 11.6; F = 0.053, P > 0.05). Each child’s full-scale intelligence quotient (IQ) was no less than 80 by the Wechsler Intelligence Scale revised for children. They were all right handed. The adult subjects were informed of the complete tests contents and informed consent was signed by each participant.

The average age of impulsive children and normal children were 7.5 (± 1.4) and 7.6 (± 1.8) years old respectively, and was not significantly different (F = 0.072, P > 0.05). Fifteen normal adult controls, representing mature individuals, were college students, medical students or acquaintances. The normal adult age ranged from 21 to 37 years old, averaged 26 years old. They were from the same geographical and demographic district, and their age-adjusted IQs were within normal range.

Parents filled out a questionnaire assessing their child’s self-regulation ability, which was modified from the Early Adolescents Temperament Questionnaire (EATQ, Parent Report) [5]; the following three factors were included in the study: Activation Control, Attention, and Inhibitory Control. We used these three factors as the index of effortful control. EATQ-R was provided by M.K. Rothbart and was translated into Chinese. Although the initial sample of EATQ-R was in adolescents aged 9–15 years old, the test was also suitable for children as young as six years old, as reported previously [4,8]. Cronbach alpha of the revised Chinese version of effortful control is 0.71, and the repeated reliability is 0.68. The average of the three factors is the index of effortful control. The higher the score, the greater effortful control is.

ERPs were recorded using the Brain-Product electroencephalography (EEG). EEG and VEOG signals were amplified 5000 times, and electrode impedances were maintained below 50 kΩ. VEOG was recorded using cup electrodes placed 1 cm above and below the right eye, with all electrodes referenced to the linked ears. The stimuli task was presented using E-Prime Version 1.1.

The Go/No-Go model was adopted into this experiment. In each trial, a five-letter (X, K, H, V, and Y) random array stimulus was presented at the center of a 14-in. screen. The letters were 56 font and green in color on a black background. Subjects were seated directly in front of the computer screen, with their eyes positioned approximately 60 cm from the screen and at the same level of the arrays. Each array, either has or do not have X, was presented randomly for 275 ms, then a blank black screen for 700 ms as a response window, and followed by a screen with a green ball as a fixation point for 500 ms. The occurrence probability of X (Go trials) and no X (No-Go trials) was 75% and 25%, respectively. The subjects were instructed to left-click on the mouse for Go trials, and not to press anything for No-Go trials. They were instructed to respond as quickly and accurately as possible using the index finger of their right hand. Each subject went through two blocks of trials, each with 160 trials. A Chinese character (meaning of error or right) was presented on the screening as feedback. Error feedback was given in No-Go trials at the instant incorrect button was pressed, and each lasts for 200 ms. Similarly, correct feedback was provided after a correct response in the Go trials.

The percentages of correct responses as well as the reaction time to press the correct button were analyzed. Lack of a response in 700 ms to a Go stimulus was recorded as a miss. The correct rate (CR) was calculated as the ratio between the number of correct responses and the total number of presentations in the Go trials. The reaction time (RT) of correct response was measured from the onset of the stimulus to the point when the button was pressed in response to the Go stimulus.

The sites Fz, Cz, and Pz on the midline were used for analyzing ERP. All data were filtered using a ranging FIR (0.1–30 Hz) bandpass filter. Epochs containing artifacts or amplitudes of eye movements exceeding ±100 μV were excluded. Baseline was adjusted to 200–400 ms before test began.

One-way ANOVA was used to analyze differences on CR, RT, and ERPs among the three groups, and significant effects were followed by post hoc (Fisher’s LSD) tests. Two boys in impulsive ADHD group were excluded because of excessive movement artifacts resulting in low trial counts for ERPs. Two of their normal counterparts were also excluded. The mean score of effortful control of the impulsive ADHD children was significantly lower than that of normal children (2.6 ± 0.5 vs. 3.2 ± 0.3; F1,26 = 14.70, P = 0.001). There was no significant difference on the RT among the three groups (impulsive children: 549.4 ms ± 99.4, normal children: 539.9 ms ± 96.8, adults: 493.5 ms ± 54.4; F2,40 = 2.15, P > 0.05). As expected, the CR for adult subjects (90.0% ± 5.9) was the highest (F2,40 = 40.15, P < 0.001), and post hoc tests showed that it was significant higher than normal children (71.7% ± 7.2) as well as impulsive children (67.1% ± 8.6) (all P < 0.001). However, there was not a significant difference in CR between impulsive and normal children (P > 0.05).

The ERN is represented as the largest negative wave occurring within 180 ms after an error key press response, while Pe is the largest positive wave before 400 ms.

From the grand view of the waves (Figs. 1 and 2), in the adults, ERN was invoked within 100 ms, and Pe reached its peak at approximately 390 ms. ERNs in normal and impulsive children were invoked within 200 ms after the error, and Pe appeared between 300 and 400 ms. In general, the amplitudes of ERN and Pe were smaller in children than in adults.

The data from ERN and Pe as well as the statistical analysis from the three groups are summarized in Table 1. In short, the latency of ERN peaks in the adults group was the shortest among the three groups (P < 0.001). The latency of ERN peaks was not significantly different between impulsive and normal children. In addition, there was no significant difference in ERN peak amplitude among the three groups (P > 0.05).

The latency of Pe peak in impulsive children was the earliest (P < 0.001) of the three groups. The average amplitude of Pe peak at the Cz and Pz sites was significantly greater in adults when compared to impulsive children (P < 0.001), while the amplitude of the
Fig. 1. Grand-average waveforms of ERN and Pe at Cz, Fz and Pz after incorrect responses for adults group in Go/NoGo trials. Vertical hashed line at 0 ms represent the time of the key press. ERPs are presented relative to a 200 ms baseline, 400–200 ms prior to the response.

Table 1
Comparison of ERN latency, Pe latency, and Pe peak amplitude among impulsive ADHD children and normal control groups (\(\bar{x} \pm s\)).

<table>
<thead>
<tr>
<th></th>
<th>Impulsive children</th>
<th>Normal children</th>
<th>Normal adults</th>
<th>F value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ERN latency (ms)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fz</td>
<td>165.3 ± 16.7</td>
<td>161.1 ± 37.6</td>
<td>42.1 ± 13.1</td>
<td>117.6</td>
<td>0.000***</td>
</tr>
<tr>
<td>Cz</td>
<td>165.7 ± 17.8</td>
<td>165.3 ± 38.8</td>
<td>45.7 ± 11.7</td>
<td>109.4</td>
<td>0.000***</td>
</tr>
<tr>
<td>Pz</td>
<td>187.5 ± 19.3</td>
<td>173.6 ± 52.2</td>
<td>74.5 ± 11.3</td>
<td>52.9</td>
<td>0.000***</td>
</tr>
<tr>
<td><strong>Pe latency (ms)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fz</td>
<td>269.7 ± 8.1*</td>
<td>291.9 ± 7.9</td>
<td>390.9 ± 15.6</td>
<td>481.4</td>
<td>0.000***</td>
</tr>
<tr>
<td>Cz</td>
<td>267.6 ± 9.4*</td>
<td>282.1 ± 8.9</td>
<td>397.1 ± 15.8</td>
<td>517.4</td>
<td>0.000***</td>
</tr>
<tr>
<td>Pz</td>
<td>278.7 ± 8.5*</td>
<td>330.7 ± 10.3</td>
<td>396.5 ± 14.6</td>
<td>383.2</td>
<td>0.000***</td>
</tr>
<tr>
<td><strong>Pe Peak ((\mu V))</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fz</td>
<td>3.5 ± 5.6</td>
<td>4.3 ± 6.9</td>
<td>6.3 ± 9.7</td>
<td>0.52</td>
<td>0.599</td>
</tr>
<tr>
<td>Cz</td>
<td>2.8 ± 4.7</td>
<td>5.1 ± 6.6</td>
<td>10.6 ± 5.4</td>
<td>7.93</td>
<td>0.001**</td>
</tr>
</tbody>
</table>
| Pz             | 1.5 ± 4.2*         | 6.5 ± 7.0       | 11.8 ± 5.1    | 12.67   | 0.000***     

**P < 0.01.**  
***P < 0.001.**  
* Comparing with normal children, post hoc tests showed the latencies of Pe were significantly shorter at the three sites (\(F_{(1,26)} = 17.59–212.7, P < 0.001\)), and peak amplitudes of Pe at Pz was significantly smaller in impulsive children (\(F_{(1,26)} = 5.34, P < 0.05\)).

Pe peak at the Pz site was significantly lower in impulsive children compared to normal children (\(P < 0.05\)) (Table 1).

Fig. 3 maps the ERPs 400 ms after errors occurring on No-Go tasks. In the adult group, the frontal–parietal area as well as a significant region of the occipital lobe has negative potential activation (representing active inhibition) from 0 to 100 ms. This was followed by positive potential activation (representing excitation) around 400 ms after the error response. In normal children, the frontal lobe was in low negative potential activation around 100 ms, and the positive activation occurred around 300 ms after the error response. Lastly, for impulsive children, the left temporal lobe and orbital frontal lobe were in low positive potential activation at the time of the error response, but lacking the negative activation representing the inhibitory control. Furthermore, the activation was lower between 300 and 400 ms at the pre-frontal cortex as well as the parietal cortex.

In this study, we demonstrated that the impulsive children with ADHD had a significantly lower score of effortful control, indicating that they exhibited low self-regulation. Surprisingly, even though the impulsive children have a trend of lower CR and RT than normal children, these parameters did not reach statistical significance. One possibility could be that measurements of brief temporal duration are less sensitive to the identification of the disorder and its associated cognitive deficits [3]. Barkley also pointed out that tests such as “hit rates” are limited in predicting ADHD, and thus will most likely underestimate the degree of actual impairment in an executive function as it is applied in a naturalistic setting across time [3].

Although the behavioral data did not reach statistical significance, ERP graphs did show difference between ADHD children and normal children. Consistent with previous studies, ERN and Pe in the adult group were significantly greater than the two children groups, suggesting a higher level of maturity in the adult group. The average ERN latency in children was later than the adults, ranging...

Fig. 2. Comparison of the grand-average waveforms of ERN and Pe at Cz, Fz and Pz after incorrect responses for normal children and impulsive ADHD children in Go/No-Go trials. Red line designates impulsive ADHD children group, and black line designates normal children control group. Vertical hashed line at 0 ms represent the time of the key press. ERPs are presented relative to a 200 ms baseline, 400–200 ms prior to the response.
Fig. 3. The topographical maps after incorrect key response for adults, control children, and impulsive ADHD children.

from 150 to 200 ms, indicating that children’s awareness of error was also slower than the adults.

The error reflection is presented by the Pe. Pe may consist of early and late positive wave components; the early positivity was thought to be a rebound from the ERN [9], while the late positivity may reflect conscious recognition of an error or emotional reaction to an error [10]. Compared with adults, children had a shorter latency of Pe peak, smaller Pe peak, and an earlier return of Pe back to the baseline. These results suggest that the Pe processing in children finished earlier, and the processing level was lower. The Pe of impulsive children was the smallest, especially at sites Cz and Pz, indicating that the impulsive children generally had lower activation level, especially in the parietal cortex and the central area. Taking together, our results suggest that impulsive children have weaker processing of conscious recognition or error reflection than normal children.

Self-monitoring of the consequence for an action is a crucial self-regulatory function. As expected, our results provide evidence that the adults have greater capability in the whole monitoring procedure. Our results also suggest that, although the impulsive children and normal children had similar level of detection and early monitoring, the impulsive children are deficient in later error monitoring processes associated with the emotional and conscious evaluation of the error rather than error detection. This may potentially be the cause of impulsive children’s inability in adjusting their behavior even if they are able to detect the error.

Error processing involves a wide region in the brain as shown in topographic maps. Efficiency in executing tasks is not only the result of active inhibition, but also activation of an error monitoring process. The inhibition and later error monitoring process in mature individuals (normal adult) appear in the proper time window and are represented by high-level activation in multiple cortex regions, with an emphasis in the midline area. This suggests that more regions in the brain in adults are involved in activation of inhibition and late monitoring of error. As expected, children display lower activation than adults. In addition, impulsive children exhibit an impaired activation. Specifically, activation of the prefrontal cortex and the frontal cortex were weak or lacking the time of or after the response; on top of that, inappropriate excitations of other regions of the brain were detected and might disrupt the efficiency of the monitoring process. The superficial and early completion of the Pe wave indicates a deficiency of brain activation for effective performance. Such deficiency is resulted from the lower level of brain development in certain areas, leading to low evaluation of error and an inability to avoid making mistakes continuously.

It has been suggested that the source generating ERN may be in the anterior cingulate cortex (ACC) [9]. During No-Go events, inhibitory control is the key function of pre-frontal cortex (PFC). It was observed that the brain activation related to response inhibition involved bilaterally the dorsolateral prefrontal cortex, the inferior frontal cortex, the premotor cortex, the inferior parietal lobule, and many others [18]. Lateral frontal/insular cortex regions and medial parietal regions have been shown to be involved in error processing [18]. In Davies’ study on the development of response-monitoring ERPs, subjects who are 7–25 years old showed an age effect on ERN but not on Pe [6]. The maximal amplitude of ERN usually occurs at fronto-central region while the maximal Pe occurs at centro-parietal region. It was found that the late Pe was maximal at a more posterior site and thought to be generated by the rostral ACC and the parietal cortex [25]. Consistent with this finding, we showed that the largest Pe was in the parietal cortex of normal adults and children, but the parietal Pe was the smallest in impulsive children. This suggests that the parietal cortex is important for the later cognitive processing, and the impulsive children may have serious deficiency in the parietal cortex.

Different from the report submitted by Liotti et al. [16], studies from our lab as well as Wiersema et al. demonstrated no difference in ERN between ADHD and normal children [16,26]. Rather, we found that impulsive ADHD children had smaller Pe than normal children. One possibility accounting for this inconsistency is the low sensitivity and unstable nature of ERN in children. If the symptoms are not severe, changes in ERN may not be easily detected. Another possibility is the heterogeneity within impulsive ADHD children. For some impulsive children, their major deficiency is later processing of cognition rather than error detection. We provided further evidence for this by including the error feedback system in
our experiments. In addition, we found that later monitor is more important than early detection in cognitive processing of error. The late monitoring procedure following the error, such as self-evaluation, emotional experience and prevention of future error occurrence, is necessary for proper inhibition control.

Conflict of interest statement

We declare no conflict of interest.

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