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Cognitive control deficits in pediatric frontal lobe epilepsy

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A B S T R A C T

Executive dysfunction and behavioral problems are common in children with epilepsy. Inhibition and shifting, both aspects of cognitive control, seem related to behavior problems and are thought to be driven mainly by the frontal lobes. We investigated if inhibition and shifting deficits are present in children with frontal lobe epilepsy (FLE). Secondly, we studied the relationship between these deficits and behavior problems. Thirty-one children were administered the Stroop Color Word Test and a digital version of the Wisconsin Card Sorting Test (WCST). Parents completed the Behavioral Rating Inventory for Executive Function (BRIEF) and the Achenbach scale (Child Behavior Checklist (CBCL)). About 20% of the children displayed significant low results on the Stroop Effect. About 60% showed shifting problems on the WCST. Parents reported cognitive control and behavioral deficits in about a third of the children. Also, behavioral problems and deficits in inhibition and shifting in daily life (BRIEF) seem to be related. There were no correlations between questionnaires and the Stroop and the WCST. Only in the group of children with many perseverative errors there were especially high correlations between Inhibit of the BRIEF.

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1. Introduction

Executive function (EF) deficits in children with epilepsy have been frequently reported by parents on, for example, the Behavioral Rating Inventory for Executive Function (BRIEF) [1–4]. These deficits have also been demonstrated using validated neuropsychological tasks [5–8]. Although these studies support the EF hypothesis, the EF domain remains very broadly defined comprising various functions. This makes effective assessment of EF difficult. As executive dysfunction seems to be a major contributor to poor quality of life in children with epilepsy [9], proper identification of this is critical to provide appropriate support and interventions [1,10,11]. Therefore, the aim of the present study was to pinpoint more precisely the assumed EF deficit by investigating an important element of EF: cognitive control.

Cognitive control refers to the higher-level processes that regulate lower-level processes needed to remain goal-directed, especially in the face of distraction [12]. The cognitive control model comprises three well-established subcomponent processes: shifting, updating, and inhibition [13,14]. Updating is defined as the ability to maintain and actively manipulate the contents of working memory. We do not investigate ‘updating’ in this study because this has already been investigated in a separate study on the same sample [15]. Results of this study imply that updating seems relatively intact in children with frontal lobe epilepsy (FLE). Also, updating is suggested to have a distinct role in the “cognitive control” model [16]. Furthermore, ‘Inhibit’ and ‘Shift’ are both parts of the Behavioral Regulation Index (BRI) of the BRIEF [17–19], whereas ‘Working memory’ is a subscale of the Metacognition Index of the BRIEF, suggesting different cognitive control functions. The present study, therefore, focuses on the other elements of cognitive control: shifting and inhibiting.

The first component, shifting, involves moving between multiple tasks, operations, and mental sets and is positively correlated with intelligence [20]. It is closely related to cognitive flexibility [21], broadly defined as the ability to flexibly adjust behavior to the demands of a changing environment [22]. The second component, inhibiting, is the ability to deliberately lower the interference of unwanted stimuli or responses.

In general, deficits of these cognitive control processes may lead to weak attentional switching [21,23], poor sustained attention [23], impulsive behavior [24], and behavioral problems [11]. From a neurological perspective, a complex circuit is involved in the number of different processes necessary for successful response inhibition and shifting, both in real life and in the laboratory. The neuroanatomical basis has been suggested to be in different cortical and subcortical regions, specifically in the prefrontal cortex [21,22,24]. Consequently, frontal lobe dysfunction and thus children with FLE, could be at risk of developing cognitive control deficits. Therefore, the present study aimed firstly to investigate whether these deficits are associated with pediatric FLE and hoped to elaborate on a number of recent studies on this subject [5,15,25].
We used two common EF tests to assess cognitive control in a clinical setting: the Wisconsin Card Sorting Test (WCST) assessing shifting and cognitive flexibility and the Stroop Color Word Test (Stroop Test) assessing the inhibition of cognitive interference expressed as the ‘Stroop Effect’ [26]. Only few reports on the use of these tests in pediatric FLE are available. With regard to the WCST, results are inconclusive [27]: Some prior studies show reduced WCST performance, also in comparison with children with temporal lobe epilepsy [28]. In contrast, there are also investigations concluding that the WCST is relatively insensitive to EF in children with epilepsy [27,29] or that WCST performance is reduced on a specific item [30]. For the Stroop Test, prior research in pediatric epilepsy shows that epileptic activity negatively affects performance on the Stroop Test [31,32].

Because cognitive control deficits are linked to externalizing and internalizing behavioral problems [1,11,15], the second aim of the study was to link scores of EF tests with questionnaires measuring problem behavior with the Achenbach Scales [33–35] and EF in daily life as displayed by the BRIEF.

Based on the existing literature on patients with frontal lobe dysfunction, we hypothesize that children with FLE will display deficits in inhibition and shifting as assessed with the WCST and the Stroop Test and reported by parents on the BRIEF. Secondly, we hypothesize that cognitive control dysfunction will be related to behavioral problems in our sample.

2. Design

2.1. Sample

Children with FLE were referred for a broad neuropsychological assessment by the pediatric neurologist at a tertiary center. All parents were asked to complete questionnaires about perceived behavioral problems and executive functioning while their children were being tested. Assessment of EF with validated and normative tests is possible from the age of eight. Cognitive flexibility skills begin to develop in early childhood, with a sharp increase in abilities between 7 and 9 years of age. Cognitive flexibility and inhibition skills are largely mature around the age of 10 [21,36]. Previous work [37] has also shown significantly poorer performance in children with FLE aged 8–12 years compared with children with other epileptic syndromes. Therefore, inclusion criteria were age between 8 and 12 years and Intelligence quotient (IQ) > 70 or school achievement scores above C level (Dutch CITO) in math and language. Children who would become 8 years old in the next two months were also invited to participate. Exclusion criteria were health and/or psychiatric problems, which could influence the neuropsychological assessment, except for attention-deficit and hyperactivity disorder (ADHD), which is common in children with epilepsy [38]. Thirty-one children met the inclusion criteria. All parents completed both questionnaires. Epilepsy diagnosis was based on the International League Against Epilepsy criteria and confirmed by an Electroencephalogram (EEG) recording. The study was approved by the Ethical Committee of MST Enschede, and parents gave their informed consent.

2.2. Measures

2.2.1. Wisconsin Card Sorting Test

The WCST (classification) of the computerized test battery FePsy [39] was used to assess set shifting and cognitive flexibility. It consists of 128 digital cards to categorize on the color of its symbols, the shape of the symbols, or the number of the shapes on each card. The only feedback is whether the classification is correct or not. Outcome is the quantity of categories (with a maximum of 6), total errors, and perseverative errors. Unfortunately, no clinical cutoffs are available for the number of categories and amount of errors. More than 16 perseverative errors are considered as significantly elevated.

2.2.2. The Stroop Color Word Test

The Stroop Color Word Test, Dutch version [40], was used to assess inhibition. Subjects are required to read three different cards as fast as possible. Two of them represent the “congruous condition” in which subjects are required to read names of colors printed in black and name different color patches. In the third table, color-words are printed in an inconsistent color ink (for instance the word “green” is printed in red ink). Thus, in this “incongruent condition”, patients are required to name the color of the ink instead of reading the word. In other words, the patient is required to perform a less automated task (naming ink color) while inhibiting the interference arising from a more automated task (reading the word). This difficulty in inhibiting the more automated process is called the ‘Stroop Effect’ [41]. Working pace is measured in seconds and then computed into a normative score. A score of decile 1 (low) and 10 (high) is considered statistically significant for all cards.

2.2.3. The BRIEF and CBCL

Parents completed the Child Behavior Checklist (CBCL) and the BRIEF. This analysis focuses on the externalizing and internalizing scale of the CBCL and the two subscales Shift and Inhibit and the BRI of the BRIEF to assess more daily life behavior. The BRIEF has good psychometric properties that include appropriate construct validity. Internal consistency is strong, and the test–retest reliability is also high [42]. A score 1.5 Standard deviation (SD) (≥ percentile 93) above average is considered statistically significant for the indices. The CBCL is a well-established behavioral questionnaire with good psychometric properties [35], also for children with epilepsy [34]. A score 1.33 SD (≥ percentile 90) above average is considered statistically significant for the main scales.

2.3. Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (IBM SPSS Statistics 23.0). The data, corrected for age, were compared with normative data of the Dutch population. For the digital WCST, we did not use normative data because those were not available. In the analysis, we compared scores according to age. To explore group differences based on perseverative errors and the Stroop Effect, we categorized into few (<16 errors) vs many (≥16 errors) perseverative errors and Stroop effect (decile 1 vs no Stroop effect (decile 2).

Differences in normally distributed scores between the cohort with FLE and the reference values were tested with one-sample t-tests or, in not normally distributed data, with nonparametric tests. The association between the tests and the questionnaires was investigated. As sample sizes are relatively small, effect sizes are shown when appropriate using Cohen’s d.

3. Results

Patients’ demographic characteristics are presented in Table 1.

Fig. 1 shows the results of the Stroop Test. Working pace on card 1 (reading words) is significantly low (decile 1) in a third (n = 10) of the sample and slowest of all three cards. Sixteen percent (n = 5) scored

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic and epilepsy variables.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
<td>Value</td>
</tr>
<tr>
<td>N</td>
<td>31</td>
</tr>
<tr>
<td>Participants</td>
<td>18:13</td>
</tr>
<tr>
<td>Gender (male:female)</td>
<td>9.2 ± 1.6</td>
</tr>
<tr>
<td>Mean age (±SD) in years at assessment</td>
<td>4.6 ± 2.8 years</td>
</tr>
<tr>
<td>Age at seizure onset</td>
<td>4.6 ± 2.7 years</td>
</tr>
<tr>
<td>Duration of epilepsy</td>
<td>4.6 ± 2.8 years</td>
</tr>
</tbody>
</table>
significantly lower on the ‘Stroop effect’ compared with the normative sample.

In Fig. 2, the results of WCST are displayed controlling for age. It shows that task performance was not related to age: mean errors, mean perseverative errors, and the number of categories remained stable with age. More than 60% of the children scored in the clinical range (≥16 errors) for perseverative errors.

About a third of the parents reported behavioral and cognitive control (inhibit and shift) problems on the CBCL and the BRIEF (Fig. 3).

Except for one scale, correlations between the CBCL and the BRIEF questionnaires were moderate (Table 2), indicating that cognitive control (shifting and inhibiting) in daily life is associated with behavior as reported by parents. In contrast, the parent proxy reports did not correlate with the neuropsychological performance (the Stroop Test and the WCST) (Table 3) in the total group. However, especially in the group with many perseverative errors (on the WCST), these correlations were moderate between the Inhibit of the BRIEF and the Stroop Test.

The mean scores between age groups on the CBCL appeared to show huge variations, and we, therefore, conducted post hoc comparisons. This indicated that the mean score for internalizing problems of children aged 10 to 12 years (M = 82.00, SD = 18.59) was significantly different (p = .02) than the mean score of children aged 8 to 10 years (M = 58.94, SD = 31.80). There was no significant difference on externalizing problems between the ‘older’ children (M = 70.43, SD = 30.68) and ‘younger’ children (M = 65.71, SD = 26.03).

4. Discussion

This study focused on two aspects of cognitive control, namely inhibiting and shifting in children with FLE. Impaired response inhibition, as measured by the Stroop Test, was found in about 20% of the participants when the conservative cutoff level was used (−2SD). Performance on the Stroop Test (or the almost similar Color-Word Interference Test of the D-Kefs) has hardly been investigated in children with (frontal lobe) epilepsy. Nevertheless, our data seem to replicate the findings of a limited number of studies [43–45]. Furthermore, our data are consistent with several studies suggesting that people with frontal lobe dysfunction are impaired to some extent on different tasks of inhibition [45–47].

Furthermore, children displayed slowness on the Stroop Test, which was most pronounced on card 1 of the Stroop Test, but was also present on card 2. Psychomotor speed problems and general slowness are often reported in children with epilepsy [48,49]. It could therefore be argued that poor performance on the Stroop Test in our sample might be related to an attention problem and/or a problem in (processing) speed rather than a specific impairment in response inhibition [43,44].

For the WCST, the large amount of perseverative errors in 60% of the participants indicates weak shifting, which concurs with other studies [28,37,44]. Age factor was not associated with shifting abilities, which is in contrast with many developmental studies, showing that EF skills normally improve with age and brain maturation [21,50]. An explanation for this could be that in our group with frontal disturbances, the development of shifting skills levels off with age, whereby executive dysfunction emerges over time [50,51], resulting in long-term developmental “lagging behind”.

In concordance with the results on test assessment, parents’ reports on the BRIEF show inhibit and shifting deficits in about a third of the
sample. Parents also reported behavioral problems to the same extent. These reported cognitive control deficits on the BRIEF seem to be related to the reported behavioral problems on the CBCL. This concurs with other studies [1,11,25,37], suggesting that having cognitive control deficits places a child at risk for developing behavioral problems. However, significant connections between our neuropsychological measurements and the questionnaires including the BRIEF are low. This finding replicates the results in this sample on working memory [15] and previous findings [27,52,53]. When considering children with shifting problems only, we did found associations between Inhibit of the BRIEF and the Stroop Test. The sample size is small, but this might indicate that children with poor shifting skills also show other executive dysfunction.

Post hoc analysis yielded that parents of the children aged 10 to 12 years reported far more internalizing problems compared with children age 8 to 10 years. As longer duration of epilepsy is considered to be a risk factor for psychopathology [54–57], this could be expected. We could, however, not confirm this same finding for externalizing problems; these problems were reported to the same extent in both age groups. The perceptibility of mood and anxiety problems (so called internalizing problems) is low in young children [58], which might indicate that these problems are underreported. Therefore, it might be worthwhile to take unreliable proxy report into consideration when interpreting results [59,60].

The study has several limitations. Firstly, it is not controlled. Comparison with normative data gives information for clinical use, but a larger group (clinical and nonclinical) enables further comparisons, for example, based upon subgroups with epilepsy. Epilepsy variables can be taken into account in identifying people who are particularly at risk for developing cognitive deficits and behavioral problems. Secondly, because of setting, there is a selection bias as children were referred by a pediatric neurologist. The results can therefore not be fully generalized to a broader sample with epilepsy. Thirdly, inhibiting and shifting components of cognitive control are separable but also correlated [14]. Thus, indexing these abilities solely with experimental measures in children with FLE. These are also frequently reported by parents on daily life level, to the same extent as behavioral problems.

The WCST might not be fully reliable, and we failed to confirm this same finding for externalizing problems; these problems were reported to the same extent in both age groups. The perceptibility of mood and anxiety problems (so called internalizing problems) is low in young children [58], which might indicate that these problems are underreported. Therefore, it might be worthwhile to take unreliable proxy report into consideration when interpreting results [59,60].

5. Conclusions

Inhibition and shifting deficits are found with performance-based measures in children with FLE. These are also frequently reported by parents on daily life level, to the same extent as behavioral problems.

Table 3

<table>
<thead>
<tr>
<th>Total group (n = 30)</th>
<th>Inhibit</th>
<th>Shift</th>
<th>BRI</th>
<th>Int</th>
<th>Ext</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interference</td>
<td>.26</td>
<td>.13</td>
<td>.15</td>
<td>.06</td>
<td>.10</td>
</tr>
<tr>
<td>Card 1</td>
<td>.40*</td>
<td>.25</td>
<td>.30</td>
<td>.04</td>
<td>.14</td>
</tr>
<tr>
<td>Card 2</td>
<td>.35</td>
<td>.27</td>
<td>.31</td>
<td>.01</td>
<td>.09</td>
</tr>
<tr>
<td>Card 3</td>
<td>.34</td>
<td>.29</td>
<td>.26</td>
<td>.02</td>
<td>.17</td>
</tr>
<tr>
<td>Total categories</td>
<td>.21</td>
<td>.17</td>
<td>.19</td>
<td>.03</td>
<td>.07</td>
</tr>
<tr>
<td>Total perseverative errors</td>
<td>.31</td>
<td>.04</td>
<td>.20</td>
<td>.03</td>
<td>.23</td>
</tr>
<tr>
<td>Total errors</td>
<td>.08</td>
<td>.06</td>
<td>.00</td>
<td>.21</td>
<td>.22</td>
</tr>
<tr>
<td>Few perseverative errors (n = 11)</td>
<td>.02</td>
<td>.19</td>
<td>.23</td>
<td>.04</td>
<td>.11</td>
</tr>
<tr>
<td>Card 1</td>
<td>.11</td>
<td>.36</td>
<td>.27</td>
<td>.40</td>
<td>.05</td>
</tr>
<tr>
<td>Card 2</td>
<td>.44</td>
<td>.63*</td>
<td>.52</td>
<td>.52</td>
<td>.28</td>
</tr>
<tr>
<td>Card 3</td>
<td>.25</td>
<td>.66*</td>
<td>.48</td>
<td>.29</td>
<td>.05</td>
</tr>
<tr>
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<td>.60</td>
<td>.51</td>
<td>.62*</td>
<td>.36</td>
<td>.46</td>
</tr>
<tr>
<td>Total perseverative errors</td>
<td>.02</td>
<td>.06</td>
<td>.16</td>
<td>.40</td>
<td>.46</td>
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<tr>
<td>Total errors</td>
<td>.36</td>
<td>.36</td>
<td>.65*</td>
<td>.47</td>
<td>.36</td>
</tr>
<tr>
<td>Many perseverative errors (n = 19)</td>
<td>.54*</td>
<td>.21</td>
<td>.29</td>
<td>.06</td>
<td>.08</td>
</tr>
<tr>
<td>Interference</td>
<td>.56*</td>
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<td>.33</td>
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<td>.04</td>
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<tr>
<td>Card 1</td>
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<td>.13</td>
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<tr>
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<td>.54*</td>
<td>.20</td>
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<tr>
<td>Card 3</td>
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<td>.11</td>
<td>.12</td>
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<tr>
<td>Total categories</td>
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<td>.08</td>
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<tr>
<td>Total perseverative errors</td>
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<td>.02</td>
<td>.10</td>
<td>.19</td>
<td>.09</td>
</tr>
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</table>

Table 2

<table>
<thead>
<tr>
<th>Correlation between the questionnaires.</th>
<th>Internalizing</th>
<th>Externalizing</th>
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<tbody>
<tr>
<td>Inhibit</td>
<td>.34</td>
<td>.62***</td>
</tr>
<tr>
<td>Shift</td>
<td>.65***</td>
<td>.41</td>
</tr>
<tr>
<td>BRI</td>
<td>.60***</td>
<td>.64***</td>
</tr>
</tbody>
</table>

Correlations are shown using Spearman’s rs.

* p ≤ .05.

** p < .00.
Cognitive control in daily life and behavior seems related, whereas performance-based measures of cognitive control and behavior seem less related. Shifting problems might indicate the presence of other executive dysfunction.

Declaration of competing interest

The author(s) declare(s) that there is no conflict of interest.

References