Brain State Before Error Making in Young Patients With Mild Spastic Cerebral Palsy

Elina Hakkarainen, MS¹, Silja Pirilä, PhD², Jukka Kaartinen, PhD³, and Jaap J. van der Meere, PhD⁴

Abstract
In the present experiment, children with mild spastic cerebral palsy and a control group carried out a memory recognition task. The key question was if errors of the patient group are foreshadowed by attention lapses, by weak motor preparation, or by both. Reaction times together with event-related potentials associated with motor preparation (frontal late contingent negative variation), attention (parietal P300), and response evaluation (parietal error-preceding positivity) were investigated in instances where 3 subsequent correct trials preceded an error. The findings indicated that error responses of the patient group are foreshadowed by weak motor preparation in correct trials directly preceding an error.

Keywords
Cerebral palsy, error making, event-related potentials

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Cerebral palsy is the term used for a group of nonprogressive disorders of movement and posture caused by abnormal development of, or damage to, the motor control centers of the brain.¹ The disorder is caused by events before, during, or after childbirth. The abnormalities of muscle control that define cerebral palsy are often accompanied by other neurological and physical abnormalities such as mental retardation, learning disabilities, behavior disorders, seizure disorders, visual impairment, hearing loss, speech impairment, and abnormal sensation and perception. It is obvious that the severity of the motor disorder together with the amount and nature of comorbidities determines, to a large extent, the quality of life in children with cerebral palsy.²,³ Whether cerebral palsy is associated with weak executive function abilities is a relevant issue. Broadly defined, executive function skills are the abilities to plan, organize, and manage the complex tasks the authors encounter every day. Strong executive function skills make it possible to live, work, and learn with an appropriate level of independence and competence.

Recent studies show altered performance in executive function tasks in children with cerebral palsy.⁴-⁶ Patients with mild spastic cerebral palsy scored significantly lower than a control group on a planning, attention, and inhibition task,⁶ with 30% to 50% of the cases in the clinical range. However, the executive function hypothesis in mild spastic cerebral palsy confined itself to outcomes in reaction time research, and it can therefore be challenged for 2 reasons. First, patients’ slow and inaccurate performance on executive function tests might be caused by their compromised motor system, instead of reflecting poor cognitive skills per se. Second, errors and slow reaction times in cognitive tasks are attributed to poor cognitive skills, with poor cognitive skills being marked by the occurrence of errors and slow performance.

All in all, measuring nonmotor functions (here executive function abilities) in motor disordered patients might be complicated, because tests also load motor aspects of the information processing system. As a result, symptoms of executive function deficits can go undiagnosed or misdiagnosed in children with mild spastic cerebral palsy. Using the event-related brain potential methodology in cognitive research on youth with mild spastic cerebral palsy provides 1 route out of the conceptual circularity, because the methodology is apt to break down reaction time performance into a cognitive-related part and a motor-related part.

In their earlier study,⁷ the authors investigated reaction time performance in youth with mild spastic cerebral palsy while carrying out a visual stimulus recognition task with increasing
complexity. During task execution, 2 event-related brain potentials were registered. The first was the positive parietal P300 amplitude and latency, indexing cognitive processes before motor execution takes place. The second was the amplitude of the frontal late contingent negative variation, also termed the readiness to respond potential or Bereitschaftspotential, indexing motor preparation/stimulus anticipation. The findings indicated that the mean correct reaction times of the patient group were slower compared to the control group, which was related to post-P300 processes (ie, motor execution). Patients’ cognitive processes related to stimulus intake, stimulus evaluation, and decision making and indexed by the amplitude and the latency of P3000 were intact. Besides being slow, patients committed many commission errors, which was associated with poor motor preparation, as indexed by the contingent negative variation before stimulus presentation. Hence, slow and inaccurate performance of the patient group was related to compromised motor processes, not to deficits in cognitive operations.

In a subsequent study, the authors tested whether patients were aware of their error making. To this end, characteristics of the response-locked error-related negativity were examined. This potential peaks about 50 ms after an error response has been executed, and reflects the activity of a neural network involved in action monitoring and error detection. Compared to the control group, it appeared that the peak was more pronounced in the patient group, suggesting that patients spontaneously realized that they have committed an error. This conclusion was validated by a performance analysis indicating that after error making, patients normalized their motor preparation, as indexed by the late negative contingent variation, and improved their reaction time performance.

In sum, the authors’ 2 event-related potential studies indicate that poor motor preparation 500 ms before the stimulus presentation is causally responsible for error making in the patient group, not action monitoring or error-detection mechanisms, subserved by the anterior cingulate cortex. The aim of the present study is to examine the patterns of brain activity preceding errors in the patient and control group. For this purpose, 3 event-related potential components will be examined in 3 successive correct trials before the actual error occurred. The late contingent negative variation indicates motor preparation before stimulus presentation and subsequent actual motor response. It is tested whether poor response preparation in the error trial is foreshadowed in earlier correct trials. Research on adults without cerebral palsy suggest that errors are associated with a significant relative reduction in the amplitude of the preceding P300, indicating a loss of sustained control over action seconds before the error occurs. The third physiological manifestation that can foreshadow error making in the patient group is the positive polarity after correct responses preceding errors. The error-preceding positivity component has been interpreted in terms of a neural index of transient deficiencies of the monitoring system prior to the actual execution of an error. Thus it is tested if errors are foreshadowed by weakened response-evaluation processes.

### Table 1. Group Characteristics.

<table>
<thead>
<tr>
<th>Patient</th>
<th>FIQ</th>
<th>VIQ</th>
<th>PIQ</th>
<th>GMFCS</th>
<th>MACS</th>
<th>Diagnosis</th>
<th>Lesion Site</th>
<th>Prematurity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>61</td>
<td>71</td>
<td>52</td>
<td>1</td>
<td>1</td>
<td>Diplegia</td>
<td>Bilateral</td>
<td>–</td>
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<tr>
<td>2</td>
<td>94</td>
<td>103</td>
<td>85</td>
<td>3</td>
<td>2</td>
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<td>Bilateral</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>117</td>
<td>133</td>
<td>100</td>
<td>1</td>
<td>1</td>
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<td>Bilateral</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>80</td>
<td>50</td>
<td>3</td>
<td>2</td>
<td>Hemiplegia</td>
<td>Unilateral</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>82</td>
<td>99</td>
<td>65</td>
<td>2</td>
<td>1</td>
<td>Hemiplegia</td>
<td>Bilateral</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>83</td>
<td>89</td>
<td>78</td>
<td>1</td>
<td>1</td>
<td>Diplegia</td>
<td>Bilateral</td>
<td>–</td>
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<tr>
<td>7</td>
<td>77</td>
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<td>Unilateral</td>
<td>–</td>
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<tr>
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<td>118</td>
<td>1</td>
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<td>Hemiplegia</td>
<td>Unilateral</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>68</td>
<td>56</td>
<td>3</td>
<td>2</td>
<td>Diplegia</td>
<td>Bilateral</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>83</td>
<td>100</td>
<td>68</td>
<td>3</td>
<td>1</td>
<td>Diplegia</td>
<td>Bilateral</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
<td>72</td>
<td>80</td>
<td>64</td>
<td>1</td>
<td>1</td>
<td>Diplegia</td>
<td>Bilateral</td>
<td>+</td>
</tr>
</tbody>
</table>

Abbreviations: FIQ, Full-Scale Intelligence Quotient; GMFCS, Gross Motor Function Classification System (1 = ambulatory, 2 = some limitations in walking, 3 = some assistive devices); MACS, Manual Ability Classification System (1 = average fine motor functionality, 2 = some limitations, 3 = pronounced limitations); PIQ, Performance Intelligence Quotient; VIQ, Verbal Intelligence Quotient. Intelligence was estimated using the Wechsler Intelligence Scale for Children–Third Edition.

### Methods

#### Study Population

Eleven patients (4 girls) with cerebral palsy (mean = 15 years 0 months, SD = 3 years 6 months, range 9-18 years) participated in the study. All were diagnosed with mild spastic cerebral palsy when they were between the ages of 1 year and 3 years. Brain magnetic resonance imaging data during the first year of life or later were used to check the lesion side. Patients were recruited through the Department of Pediatric Neurology at Tampere University Hospital in Finland. All had experienced peri/neonatal complications. Four patients were born preterm (birth weight < 1500 g) but none had severe visual or hearing impairments, or epilepsy. One child had hydrocephalus. The clinical characteristics of the patient group are shown in Table 1.

Twelve control children (6 girls) and adolescents (mean = 14 years 3 months, SD = 2 years 8 months, range 10-18 years) participated. They were recruited from mainstream elementary schools and upper secondary schools in the same city. The 2 groups did not differ significantly with respect to age, t(21) = 0.52, P = .61. The IQs of the control group were not measured, because IQs in the patient group were within a normal range. Data from the same participants have been examined in the authors’ earlier studies. Informed consent was
obtained from all participants. Ethical approval was obtained from the Regional Ethics Committee of Tampere University Hospital.

**Study Design**

The participants were seated in front of a monitor, about 80 cm from the screen. A variant of the Sternberg short-term memory scanning paradigm\(^\text{17}\) was employed. The task is probably the most used test in clinical, developmental, and psychophysiological research.\(^\text{18}\) All stimuli were white letters (consonants only), measuring 1.5 cm on a black background. A memory set was presented of 2 target letters, which the participants had to memorize temporarily. These letters were simultaneously shown on a single row in the center of the screen. Subsequently, a new set of 4 letters was presented, making up a square of 8 × 8 cm. One of the letters of the memory set or neither was presented in this set. A varied mapping procedure was followed: targets and distracters were randomly intermixed over trials.

Participants placed their dominant hand between 2 response buttons. When the target was present in the display set (positive set), participants pressed the yes button (on the left) with their dominant hand. When the target was not present (negative set), participants pressed the no button (on the right) with their dominant hand. The probability that the target was present in the display set was 0.5.

The letters in each trial were randomly selected with the restriction that no letter occurred as a target in 2 consecutive trials and that no more than 3 consecutive positive or negative trials occurred in sequence. In addition, it was ascertained that the frequencies were approximately equal for the target appearing in 1 of the 4 positions of the display set (left up, right up, left down, right down). All participants were presented the same random sequence of memory and display sets.

Starting from the appearance of the display set, participants had 4500 ms to respond. For each response, the interval between the onset of the display set and button-press was measured as the reaction time. The accuracy of the target identification was also recorded, including incorrect responses (button-press errors) and failure to press a button within 4500 ms (error of omission). Precipitate responses (reaction time < 200 ms) were excluded from the analysis. Participants were given a short practice period, which generally lasted about 2 minutes, until they completely understood the task. The experiment, including instruction and practice, lasted about 15 minutes. During the test, the researcher sat out of sight of the participant, and no interaction was allowed.

**Selection of Trials for Data Analysis**

In the present study, the authors were interested in the 3 successive correct trials before an error (E-3, E-2, and E-1). The sequence of 3 successive correct trials was isolated from an original sequence of 4 correct trials. This was done to ensure that the E-3 trial was not preceded by an erroneous trial.

**Electrophysiological Measures**

Electroencephalograms (EEG) were recorded by Neuroscan using Ag/AgCl electrodes at 9 electrode sites (F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4). The reference electrodes were placed on the mastoids. Four additional tin electrodes were attached for a bipolar recording of the vertical electrooculogram from above and below the left eye and for the horizontal electrooculogram from the outer canthi of both eyes. Impedances were kept below 5 kΩ at all electrodes. Digital data together with triggers marking specific events were stored on hard disk for later analysis.

Data were first digitally filtered with a high-pass filter of 0.1 Hz and a low-pass filter of 30 Hz at 12 dB/octave for the error-preceding positivity and P300 components. For the contingent negative variation, a high-pass filter of 0.01 Hz and a low-pass filter of 30 Hz at 12 dB/octave were employed. For each event-related potential component, the EEG from individual trials was visually inspected and corrected for horizontal and vertical eye movements using the Gratton, Coles, and Donchin algorithm\(^\text{19}\) before averaging the epochs.

**Contingent negative variation.** Data from Fz were epoched into 5700-ms segments starting 200 ms before the onset of the memory set. To investigate a change of the wave across the time, a baseline was set at 2500-2600 ms, and an average time window was created at 4400-4500 ms, 100 ms before the onset of the display set.

**P300.** Only the EEG associated with 3 successive correct trials before an error was analyzed. Signals were epoched offline with a window from 150 ms before to 900 ms after the onset of the display set. All event-related potentials were aligned to a prestimulus baseline of −50 to 0 ms before the onset of the display set. After averaging, components were scored in the event-related potentials based on inspection of the grand-average waveforms. P300 components were identified at Pz for each subject. The mean amplitude of the P300 component was determined over a time interval of 300 to 600 ms poststimulus.

**Error-Preceding Positivity.** The positive polarity at parietal scalp distribution was measured as a mean voltage from 0 to 150 ms after correct responses in each trial separately. A baseline of −50 to 0 ms before the response was employed.

Figure 1 shows an overview of the time windows of the event-related potentials under study and essential task parameters. It also illustrates that the brain potentials studied do not overlap in time.

![Figure 1](image-url)
Table 2. Mean Reaction Times (RTs) on 3 Correct Trials Before an Error.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patient (Mean RT in ms, SD)</th>
<th>Control (Mean RT in ms, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E – 3</td>
<td>1472 (402)</td>
<td>1191 (343)</td>
</tr>
<tr>
<td>E – 2</td>
<td>1570 (470)</td>
<td>1349 (449)</td>
</tr>
<tr>
<td>E – 1</td>
<td>1545 (524)</td>
<td>1312 (359)</td>
</tr>
</tbody>
</table>

Statistical Analyses

Mean reaction times, the contingent negative variation, P300 amplitudes, and the error-preceding positivity were analyzed using a repeated measures ANOVA, with Group (cerebral palsy and control) as the between-subject factor and response type (E-3, E-2, E-1) as the within-subject factor. An alpha level of .05 (2-tailed) was used for all statistical tests. An independent-samples t test was performed for group comparisons.

Results

In total, 41 sequences of 3 correct trials before an error were found in the patient group, and 47 in the control group.

Behavioral Data

The mean accuracy was .81 in the patient group and .88 in the control group. However, the difference between the 2 groups remained nonsignificant ($t = –1.86$, $P = .08$). Mean reaction times for 3 correct trials before an error are presented in Table 2.

Although the patient group was overall slower, the group effect was not significant, $F(1, 21) = 2.34$, $P = .14$. The trial number before error-making effect was $F(2, 42) = 1.95$, $P = .16$, indicating no tendency of response speed alterations before error making. The finding was the same in both groups: the interaction of trial number before error making by group was nonsignificant, $F(2, 42) = .11$, $P = .90$.

Contingent Negative Variation

Figure 2 presents the frontal late contingent negative variation 3 trials (E-3), 2 trials (E-2), and 1 trial (E-1) before error making. (Note: Data from 2 control subjects at the E-3 condition were noisy and they were therefore eliminated from the grand average figure.)

The omnibus test indicated no group differences, $F(1, 21) = 1.07$, $P = .31$, no trial number effect before error making, $F(2, 42) = 0.15$, $P = .86$, nor a trial number by group effect, $F(2, 42) = 1.26$, $P = .29$. However, the figure suggested altered motor preparation in the patient group 1 trial before an error, and a planned comparison with a t test confirmed that the contingent negative variation component of the patient group was less pronounced in the E-1 condition, $t(21) = 2.14$, $P = .045$, indicating weakened motor preparation directly before an error occurred. In addition, the Pearson correlation between contingent negative variation amplitude and accuracy was significant only in the E-1 condition ($r = –.68$, $P = .001$), indicating a connection between motor preparation 1 trial before an error and accuracy.

P300

Figure 3 shows grand-averaged waveforms for the parietal P300 in the patient group and in the controls.

Figure 4 shows the stimulus-locked P300 amplitudes for 3 correct trials before error making (E-3, E-2, and E-1).

The figure indicates that the P300 amplitude for correct responses diminished significantly before an error occurred: the trial number effect was $F(2, 42) = 3.68$, $P = .034$. This phenomenon was, however, equal for both groups: the group main effect was $F(1, 21) = 0.15$, $P = .70$, and the interaction of trial number before error making by group was $F(2, 42) = 0.79$, $P = .46$. Although the figure suggests a difference
between the groups in trial E-1, a planned comparison with a t test indicated no differences, \( t(21) = -1.02, P = .32 \), in P300 amplitude between the groups. Hence, attention lapses before error making as indexed by the P300 amplitude in trials before error making were the same in both groups.

**Error Preceding Positivity**

Figure 5 presents the averaged parietal mean values of positivity in 3 correct trials before the error.

There was no number of trial main effect, \( F(2, 42) = 2.05, P = .14 \), or trial number by group effect, \( F(2, 42) = 1.28, P = .29 \), indicating that the response-locked positivity was equal in all 3 error-preceding conditions. Although the figure suggests more positive deflections in the patient group, the group main effect remained nonsignificant, \( F(1, 21) = 0.22, P = .64 \). Neither did a series of planned comparisons per trial apart indicate any differences between the 2 groups. These results show that the groups did not differ in the quality of performance monitoring before an error occurred.

**Discussion**

The results of the present study indicate that exceeded erroneous responses in youth with mild spastic cerebral palsy are, in comparison to the controls, preceded by poor motor preparation already 1 trial before the actual error took place, as indexed by the frontal late contingent negative variation. That is, the motor preparation starts to weaken already before the last correct trial preceding the error. Whether their poor motor preparation mirrors a starting cognitive disengagement, which would indicate an executive failure to monitor, \(^{20} \) is dependent on the interpretation of the frontal late contingent negative variation, because agreement on the interpretation and source of the frontal late contingent negative variation is far from universal. \(^{21, 22} \) To date, the so-called lateralized readiness potential has been
seen to be a more suitable psychophysiological measure for motor preparation free of cognition than late contingent negative variation.\textsuperscript{23} However, the lateralized readiness potential is derived from an experimental procedure involving a choice between the 2 hands. In the target group, this choice was not feasible due to the motor limitations of the participants. Furthermore, the results indicate that error making was foreshadowed by a decrease in stimulus evaluation, as indexed by a decrease in the amplitude of the parietal P300, occurring 3 trials before the error trial appeared. However, the patient group did not differ from the control group in this phenomenon. In addition, the groups did not differ in cognitive monitoring control, as indexed by the positivity of the response-locked components for correct responses in the 3 trials before the error trial appeared. Based on these findings the authors can conclude that cognitive operations involved in response monitoring before error making were similar in both groups.

The authors’ earlier results\textsuperscript{10} indicated that the response-locked negativity after error making was more pronounced in the patient group than it was in the controls. In the present study, a positive response-locked component related to occasional failures of the action monitoring system\textsuperscript{14} was similar in both groups. Error-preceding positivity has previously been associated only with trials immediately preceding errors (E-1).\textsuperscript{13} The authors’ results, however, showed no such specificity. Altogether, the findings indicate high levels of cognitive control before and after error making in the patient group. In spite of these high levels, however, they made more errors of commission.

The authors’ research question was inspired by many studies carried out in other domains of clinical field, like Parkinson’s disease.\textsuperscript{24} Event-related potential components provide useful parameters for cognitive and motor processes when motor execution is impaired. At the electrophysiological level, the results of the present study provide evidence that the executive function hypothesis in spastic cerebral palsy could be based on a myth. That is, the poor performance on cognitive reaction time test is due to their motor impairments, not cognitive deficits. The outcome of the study by Stadsklev\textsuperscript{25} points into the same direction: when children with cerebral palsy instruct other persons with intact hands to carry out executive function tests they perform like controls.

Taken together, the results suggest that the weakened motor preparation can also be a sign of rivalry between cognitive and motor effort. Because motor control requires more effort in the patient group than it does in the controls, it can induce motor execution decline, as indicated by altered contingent negative variation, but leave the cognitive measures intact. It is certain, however, that perception, decision, and action are closely linked and that more research is needed to disentangle these interacting processes.

**Limitation of the Study**

The conclusions and interpretations are based on a small sample size and are therefore seen as preliminary. In addition, the results cannot be generalized to patients with more severe forms of cerebral palsy. In the present study, the authors measured event-related potentials and reaction times to study executive functions. In the future, other measures of executive functions could be studied together with psychophysiological measures in children with cerebral palsy.

**General Conclusion**

The purpose of this study was to investigate whether error making in the target group was associated with poor cognitive abilities. The answer is no. The source of their error making is connected with their compromised motor system, which results in spurts of weak ability to anticipate future events.

**Acknowledgments**

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**Author Contributions**

EH and SP contributed equally to this work. JK and JJV provided, as the senior researchers, the support and mentorship necessary for the success of the work.

**Declaration of Conflicting Interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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**Ethical Approval**

The Regional Ethics Committee of Tampere University Hospital approved the study.

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