Event-related brain potentials (ERPs) to auditory stimuli were recorded from 11 closed head injured (CHI) and 10 age-matched healthy adults. Auditory stimuli consisted of sequences of repetitive standard tones (600 Hz), occasionally replaced by deviant tones (660 Hz) or by natural novel sounds. Subjects were instructed to ignore auditory stimuli while concentrating on a demanding visuo-motor tracking task. CHI patients showed, in comparison to control subjects, significantly enhanced late P3a component in the ERPs to novel sounds. This suggests that novel stimuli cause greater distraction in CHI patients than in controls, demonstrating that ERPs provide a powerful tool to determine the physiological basis of attentional deficits in CHI patients. *NeuroReport* 10:2125–2129 © 1999 Lippincott Williams & Wilkins.

**Key words:** Attention; Audition; Closed head injury; Distractibility; Event-related brain potential (ERP); Mismatch negativity; Novel sounds; P3a

**Introduction**

Closed head injuries (CHIs) occur as a consequence of sudden movements and stretching of the brain tissue within the skull by external acceleration–deceleration forces commonly resulting in a predictable focal injury in the frontal poles and in a diffuse axonal injury (DAI) [1]. DAI essentially reduces connections between the frontal and other brain areas. However, the pathophysiological consequences of CHI, for instance DAI in its whole extent, are not detected by brain imaging techniques such as CT, MRI and SPECT [2].

The typical symptoms accompanying CHI include disorders in planning, initiation of motor or cognitive actions, and altered social–emotional and behavioral functioning, as well as forgetfulness, fatigue, slowness of information processing, distractibility and other attentional deficits [3]. Adaptive and psycho-social functioning may be altered even in the absence of measurable intellectual decline with routine neurocognitive examination [4,5]. The deficits in attention and speed of information processing in CHI appear to be caused by frontal lesions and DAI [6]. These deficits are essential from the point of recovery and psychosocial outcome [6,7]. However, the nature of the attentional deficits in CHI still is unclear because of difficulties in their objective measurement [8,9].

Recordings of human brain activity have revealed that the prefrontal cortex is crucial in controlling voluntary and involuntary attention [10,11]. For example, event-related brain potentials (ERPs) to task-irrelevant novel stimuli show decreased P3a responses (a positive ERP peaking at about 250–300 ms from stimulus onset with its maximum over the fronto-central scalp areas) in patients with dorsolateral prefrontal lesions, suggesting abnormal involuntary attention [11]. The P3a to novel sounds appears to have generator sources in several cortical areas, including prefrontal and auditory cortices [11–15].

The mismatch negativity (MMN), peaking over the frontal scalp areas 100–200 ms from stimulus onset is elicited by any discriminable deviant sounds occurring among repetitive standard stimuli and is probably associated with initiation of involuntary attention to auditory stimulus changes [10]. The MMN has its major generator sources bilaterally in the auditory cortices [15–18]. Since the MMN is
elicited even by slightly deviant stimuli occurring in an unattended auditory input, it evidently indicates automatic stimulus discrimination occurring in the auditory cortex [10]. In addition, the MMN appears to have a further contribution from the frontal cortex, as indicated by scalp-current density analysis of ERPs [17] and neuromagnetic recordings [18]. This frontal cortex MMN activity might be associated with the initiation of involuntary switching of attention to acoustic changes [10,17]. The important role of prefrontal cortex in MMN elicitation is also indicated by MMN attenuation in patients with lesions in the dorsolateral prefrontal cortex [19,20].

Several studies have shown increased reaction times (RT) and decreased numbers of correct responses to auditory or visual target stimuli following MMN- and P3a-eliciting task-irrelevant deviant or novel sounds [21–23]. These findings strongly support the role of MMN and P3a generators in the neural network of involuntary orienting of attention to changes occurring in the auditory environment outside the focus of attention. Therefore the purpose of the present study was to determine whether ERPs could be used to evaluate attentional problems of CHI patients, who are easily distracted and frequently complain about such problems. The present hypothesis was that MMN and P3a might indicate in CHI patients enhanced engagement of attention by changes in task-irrelevant sounds reflecting increased distractibility.

### Materials and Methods

ERPs were recorded in 11 male patients (Table 1) with chronic severe CHI (volunteers, age 23–47 years, mean 33 years) 1–3 years post-injury. Subjects with any history of psychiatric problems or alcohol or drug abuse were excluded. All patients were right-handed, had normal hearing, and normal or corrected-to-normal vision. In the patient group, the length of unconsciousness had varied between 10 min and 21 days, and the length of post-traumatic amnesia between 4 days and 3 months (Table 1). Structural changes detected by CT or MRI are described in Table 1. In two patients, no parenchymal changes were found on CT (Table 1). Since diffuse axonal injury, proportional to injury severity, seems to be a consistent feature of CHI, most patients can be suspected to have DAI. In every patient, typical neuropsychological deficits following severe CHI were reported, for example difficulties in attention, memory and behavioral changes. All patients were undergoing neuropsychological rehabilitation at the time of the study. All patients were psycho-socially independent, but only one of them (patient 7) was working on the previous level. The control group included 10 healthy men (age 22–41 years, mean 31 years).

Subjects were presented with auditory stimulus sequences consisting of 600 Hz standard tones (probability of occurrence, \( p = 0.85 \), 660 Hz deviant sounds.

### Table 1.

<table>
<thead>
<tr>
<th>Age</th>
<th>LOC</th>
<th>GCS</th>
<th>PTA</th>
<th>Radiological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>33</td>
<td>5 days</td>
<td>no data</td>
<td>3 weeks</td>
</tr>
<tr>
<td>2.</td>
<td>34</td>
<td>10 min</td>
<td>14</td>
<td>4 days</td>
</tr>
<tr>
<td>3.</td>
<td>47</td>
<td>6 h</td>
<td>7</td>
<td>3 weeks</td>
</tr>
<tr>
<td>4.</td>
<td>30</td>
<td>3 h</td>
<td>7</td>
<td>5 weeks</td>
</tr>
<tr>
<td>5.</td>
<td>23</td>
<td>13 days</td>
<td>7</td>
<td>3 weeks</td>
</tr>
<tr>
<td>6.</td>
<td>25</td>
<td>21 days</td>
<td>7</td>
<td>3 months</td>
</tr>
<tr>
<td>7.</td>
<td>41</td>
<td>12 h</td>
<td>14</td>
<td>4 days</td>
</tr>
<tr>
<td>8.</td>
<td>31</td>
<td>10 days</td>
<td>9</td>
<td>2 months</td>
</tr>
<tr>
<td>9.</td>
<td>33</td>
<td>2 h</td>
<td>10</td>
<td>1 week</td>
</tr>
<tr>
<td>10.</td>
<td>35</td>
<td>3 days</td>
<td>9</td>
<td>1 month</td>
</tr>
<tr>
<td>11.</td>
<td>27</td>
<td>5 days</td>
<td>9</td>
<td>1 month</td>
</tr>
</tbody>
</table>

DAI = diffuse axonal injury.
tones ($P = 0.075$), and complex novel sounds ($P = 0.075$) delivered in a random order, except that each deviant tone and novel sound was preceded by at least one standard tone. In each stimulus sequence, 400 stimuli were delivered binaurally through the headphones at a constant rate of 1/900 ms. Thus, each sequence had a duration of 6 min. There were six auditory stimulus sequences. The stimulus delivery was controlled by Stim software (NeuroScan Ltd., USA). Standard and deviant tones had sinusoidal waveforms, an intensity of 75 dB SPL at each ear, and duration of 200 ms including 10 ms rise and fall times. The novel sounds were drawn from a pool of 60 different digitized complex sounds (telephone ringing, electric drill, rain etc.) with a duration of 200 ms, including 10 ms rise and fall times, and a maximum intensity of 70–80 dB SPL at each ear. None of the novel sounds appeared twice within the same stimulus sequence.

Subjects were instructed to ignore sounds and to perform a visuo-motor tracking task. The visual display consisted of five small red circles moving on a yellow background with random speed and to random directions, one of them being a slightly differing target. Subjects were instructed to follow the target circle with a cursor circle controlled by a computer trackball manipulated by subjects with their right hand. The distance between the cursor and the target was continuously measured with a sampling rate of 500 Hz.

The EEG (DC-100 Hz) was continuously sampled at a rate of 500 Hz with SynAmps and Scan software (Neuroscan Ltd., USA) from 21 scalp sites with Ag/AgCl electrodes. Changes in electro-oculogram (EOG) due to eye movements or blinks were monitored with electrodes at the canthi of the right and left eye and at the forehead. All EEG and EOG electrodes were referred to an electrode attached to the tip of the nose. EEG epochs of 900 ms starting 100 ms before stimulus onset were averaged in each condition separately for the standard tones, deviant tones, and novel sounds. Epochs contaminated by ocular or muscle activity (EOG or EEG variation during an epoch exceeding $\pm 100 \mu V$) were rejected from averaging, as well as the epochs for the first five sounds of each sequence. Frequencies $> 30$ Hz were digitally filtered out from the averaged ERPs.

The ERP amplitudes were measured in relation to the mean voltage during a 100 ms pre-stimulus baseline. The peak latencies and amplitudes of the centrally maximal N1 and P2 deflections elicited by standard tones were measured in each subject at the central midline electrode (Cz). The peak latency and amplitude of the frontally maximal MMN elicited by deviant tones were measured from the difference waves obtained for the frontal midline electrode (Fz) by subtracting, in each subject, the ERP to the standard tones from that to the deviant tones. The peak latencies and amplitudes of the negativity to novel sounds (consisting of N1 and MMN [15]) and of the successive centro-frontally maximal P3a were separately determined for each subject at Cz from the ERPs to novel sounds. Moreover, the amplitude of the later portion of the P3a, after the P3a peak, was measured at Cz as a mean amplitude of the novel-sound ERP over a period 350–450 ms from stimulus onset. The significance of the between-group differences in ERP amplitudes and latencies were studied with $t$-tests.

**Results**

The performance in the visual tracking task (the mean distance on the screen between the target object and the cursor) did not significantly differ between the groups (average distance 31.6 mm, s.d. 7.2 in the patients and 25.4 mm, s.d. 5.1 mm in the controls), $t(19) = 1.96, p < 0.07$.

There were no significant between-group differences in the N1 and P2 peak amplitudes and latencies for standard tones (Fig. 1; mean N1 peak latency and amplitude: patients 102 ms and $-1.9 \mu V$; controls 105 ms and $-1.9 \mu V$; mean P2 peak latency and amplitude: patients 169 ms and $0.9 \mu V$; controls 167 ms and $0.7 \mu V$). Moreover, there were no significant differences in the MMN latencies or amplitudes to deviant tones between CHI patients and control subjects (Fig. 1; mean MMN peak latency and amplitude: patients 126 ms and $-4.0 \mu V$, controls 124 ms and $-3.3 \mu V$). The ERPs to novel sounds (Fig. 2) showed no between-group differences in the peak latency and amplitude of the negativity composed by N1 and MMN (the mean peak amplitude and latency: patients 101.5 ms and $-1.9 \mu V$; controls 105 ms and $-1.6 \mu V$) or P3a (the mean P3a peak amplitude and latency: patients 224 ms and 5.5 $\mu V$; controls 226 ms and 5.4 $\mu V$). However, as shown in Fig. 2, the amplitude of the later portion of the P3a, measured as the mean amplitude at Cz over 350–450 ms, was significantly larger in patients than in controls (mean $1.2 \mu V$ vs $-1.1 \mu V$; $t(19) = 2.64$, $p < 0.02$).

**Discussion**

There were no significant differences between CHI patients and controls in the N1 or P2 amplitudes or latencies in this study. This suggests that the early cortical processing of auditory stimuli [10] was not affected in CHI patients. The MMN indicates
sensory-memory related pre-attentive discrimination of auditory stimulus changes [10,24]. Since no significant difference was found in the MMN amplitudes or latencies between the groups pre-attentive auditory discrimination and sensory memory can be regarded as normal in the present patients. Interestingly, previous studies indicate that in focal dorsolateral prefrontal lesions the MMN amplitude is attenuated [19,20]. This difference in results may be explained such that mechanical forces causing frontal and temporal injuries and diffuse axonal injury in CHI [3] do not necessarily affect the dorsolateral prefrontal cortex.

The main result of the present study was that the later portion of P3a was enhanced in patients as compared with controls. P3a is probably associated with involuntary switching of attention to stimulus changes, its earlier portion being generated at least partly in the auditory cortex [15,23] and its later portion mainly in the frontal cortex attention mechanisms [11,14]. The increased later portion of the P3a component to novel sounds among unattended auditory stimuli in the present CHI patients suggests enhanced processing of distracting sounds [7]. This could indicate stronger involuntary switching of attention in the patient group because of their measured difficulties in suppressing of irrelevant stimuli.
Conclusion

The results of the present study are in concordance with previous studies. Attentional deficits form the basic problem in the sequelae of CHI and may lead to devastating dysfunctions. ERPs appear to provide a powerful tool for indicating these kinds of attentional problems. Thus measuring attentional deficits with ERPs might provide an additional method for making diagnostics as well as following recovery and rehabilitation. Further studies are needed to construct optimal ERP paradigms to reveal the exact nature of the attentional deficit in this patient group. Specific ERP paradigms might also be used for clinical purposes even when the related lesions are not detectable in CT or MRI scanning or suggested by neurobehavioral tests assessing cognitive functioning.

References


ACKNOWLEDGEMENTS: This research was supported by The Academy of Finland, the National Scientific Research Fund of Hungary (OTKA T02681), and the Spanish Ministry of Education and Culture (DGES UE96-0038). The authors wish to thank Ms Elena Yago and Dr Marie Cheour for their constructive comments during preparation of this report.

Received 12 April 1999; accepted 5 May 1999