Electrophysiological correlates of active and passive attentional states after severe traumatic brain injury

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Summary

We aimed to investigate attentional resources distribution in traumatic brain injury (TBI) patients. Auditory event-related potentials (ERPs) were recorded from 35 severe TBI patients in post-acute care, and 35 age- and gender-matched controls using an auditory oddball paradigm under passive (ignore stimuli) and active (count deviants) conditions. Six components (P1, N1, P2, N2, P3, N3) in four waveforms were studied, i.e., the waveforms elicited by standard and by deviant tones in the passive and active task, respectively. In addition to alterations of latency and/or amplitude of single components, particularly of the late components N2 and P3, we observed in patients a different response pattern to task condition. We found evidence of deficits in the early stages of information processing and allocation of attentional resources. The analysis of the response to standards was crucial for detecting new aspects of attentional impairments.

KEY WORDS: attention, auditory oddball, ERP, P300, traumatic brain injury.

Introduction

Auditory event-related potentials (ERPs) have been widely investigated as an index of cognitive function during recovery from severe brain injury. However, experimental data in these patients are still not sufficient to allow standardization of their indications in clinical practice (1).

The oddball paradigm, which includes presentation of a series of stimuli, with one frequently repeated stimulus (standard), and one infrequent stimulus (deviant), has often been used to this end. All published studies have reported significant differences between patients and controls in at least one ERP parameter, but the pattern of deviant parameters varies considerably between studies (2-18) (Table I, see over). Comparison between studies is made difficult by the fact that, apart from differences in subjects and test paradigms, studies have focused on different aspects of the ERP waveforms. As a result, a full set of parameters from early to late potentials (P1/N1 to P3/N3) has not yet been reported. Moreover, most authors examined only the waveforms elicited by deviant stimuli, neglecting those elicited by standard stimuli (Table I). Recording methods and data analysis also differ considerably among studies, and may also contribute to discrepant results.

Given that the late evoked potentials are thought to be sensitive to cognitive processes, the waveform differences obtained manipulating a subject’s attention might be a source of further information, but this approach has very seldom been used in clinical groups.

Campbell (13,19) was the first and one of the very few authors to test different task conditions. The patient and control groups each included only eight subjects. However, the author analyzed only the N1 and the P3 components, interpreting the attenuation of the N1 as a correlate of slight hearing loss in the patients. Subsequently, three other studies have investigated the ERPs of traumatic brain injury (TBI) patients, manipulating their attentional state.

The first study (20) compared a neutral task, i.e., a run of standard stimuli, with an active oddball paradigm run. However, whereas the N1 and P2 components were measured in ERP curves reflecting processing of the standard tone both in the active and in the neutral condition, N2 and P3, on the contrary, were measured only in ERP curves reflecting processing of the deviant tone in the active condition. Therefore, a direct comparison of attention shifts on the same component was not possible in this study. In the second study (5), passive ERPs were measured when patients were still in coma, and active ERPs (mental count of the deviants) were measured later in those patients who awoke from coma and became collaborative. Data analysis was restricted to the waveforms elicited by deviants, whereas the waveforms elicited by standards were neglected. The third study (3) compared auditory ERPs in a simple reaction time task, a go/nogo reaction time task, and a choice reaction time task. In this study, too, the waveforms elicited by the standard stimuli were not investigated.

To our knowledge, there exist no studies of electrophysiological correlates of different attentional states in TBI subjects that have investigated a greater number of components in the waveforms elicited both by frequent and by rare stimuli. Therefore, we carried out the present investigation.
Materials and methods

Subjects

Thirty-five inpatients in post-acute rehabilitation in our clinic, 23 males and 12 females, mean age 35.7±14.8, range 17-66 years, and 35 age- and gender-matched healthy volunteers from hospital staff and their families took part in the study after giving their informed consent. Subjects with a prior history of substance abuse, brain injury, central nervous system pathology, or major mental illness were not included in this study.

All patients had sustained a severe to very severe TBI (initial Glasgow Coma Scale score < 8). In the majority of patients the injury was caused by a motor vehicle accident, and in a minority of cases it was sustained in a fall. Most of the patients had also suffered secondary brain injury (intracranial haematoma, subarachnoid haemorrhage, brain swelling, raised intracranial pressure), and 18 had needed surgery. Cranial computed tomography showed that 14 patients had their main lesions in the left brain hemisphere, 11 in the right hemisphere, and nine in both hemispheres; in one patient there was no clear lesion, only severe diffuse axonal damage. 23 of the 35 patients presented frontal damage. The mean time elapsed from the event was 190±186 days (range: 25-763 days); 31 patients were tested within 12 months of injury, four patients, whose recovery had been very slow, were tested within 12-24 months. Mean Functional Independence Measure (21) score was 97.8±21.5 points.

Eight patients were taking carbamazepine (daily dose 150 mg), four patients were taking amantadinesulphate (daily dose: 100 mg), two were taking haloperidol (daily dose: 5 mg), and one was taking propranolol (daily dose: 80 mg). The subjects were also involved in a larger project requiring neuropsychological, psychophysiological, psychophysical, and electrophysiological assessment. As a result, part of these data, including the description of the patient group, have already been published (22,23). For neuropsychological testing...

<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th>TBI patients (severe, mild)</th>
<th>Time elapsed from TBI (y, m, d)</th>
<th>Controls Examined (d, s)</th>
<th>Filtering curves (Hz)</th>
<th>Channels Reject (EOG)</th>
<th>Number of targets</th>
<th>Task (press, count)</th>
<th>Main results in patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (2004)</td>
<td>–</td>
<td>0.5-3 y</td>
<td>11</td>
<td>2 (N1/N2)</td>
<td>2</td>
<td>20</td>
<td>press</td>
<td>reduced and prolonged P3</td>
</tr>
<tr>
<td>3 (2003)</td>
<td>9</td>
<td>&gt; 2 y</td>
<td>16</td>
<td>0.01-100</td>
<td>11</td>
<td>EOG</td>
<td>press</td>
<td>reduced N1/N2; prolonged N2/P3</td>
</tr>
<tr>
<td>4 (2001)</td>
<td>–</td>
<td>1-3 y</td>
<td>12</td>
<td>0.5-30</td>
<td>4</td>
<td>EOG</td>
<td>?</td>
<td>reduced P3; normal N1/P2/N2</td>
</tr>
<tr>
<td>5 (2001)</td>
<td>10</td>
<td>y</td>
<td>11</td>
<td>0.2-30</td>
<td>3</td>
<td>?</td>
<td>28 count yes*</td>
<td>reduced N1; in passive condition prolonged N1, reduced P2/P3</td>
</tr>
<tr>
<td>6 (2001)</td>
<td>24</td>
<td>0-5 y</td>
<td>24</td>
<td>0.03-30</td>
<td>9</td>
<td>50 µV</td>
<td>press</td>
<td>trend to increased N2; increased N4</td>
</tr>
<tr>
<td>7 (2000)</td>
<td>–</td>
<td>1-10 y</td>
<td>27 (N1/N2 s N2/P3 d)</td>
<td>0.16-30</td>
<td>19</td>
<td>100 µV</td>
<td>40 count</td>
<td>reduced P2/N2; prolonged and reduced P3</td>
</tr>
<tr>
<td>8 (1996)</td>
<td>54</td>
<td>30 h-22 m</td>
<td>27</td>
<td>s/d</td>
<td>20</td>
<td>EOG</td>
<td>13 count</td>
<td>increased P1/P2/N2; reduced P3/N3</td>
</tr>
<tr>
<td>9 (1995)</td>
<td>16</td>
<td>4-12 y</td>
<td>20</td>
<td>0.5-30</td>
<td>4</td>
<td>75 µV</td>
<td>40 press</td>
<td>prolonged and reduced P3</td>
</tr>
<tr>
<td>10 (1993)</td>
<td>16</td>
<td>&gt; 6 m</td>
<td>16</td>
<td>s/d</td>
<td>11</td>
<td>EOG</td>
<td>45 press</td>
<td>prolonged N2/P3; more negative-going potentials; targets N1 larger</td>
</tr>
<tr>
<td>11 (1992)</td>
<td>7 (? )</td>
<td>1-5 y</td>
<td>10 (N1/P2 s+d N2/P3 d)</td>
<td>0.03-100</td>
<td>3</td>
<td>85 µV</td>
<td>17x3 press</td>
<td>reduced P2/N2; N2 shorter for targets; no P3 effects; normal N1</td>
</tr>
<tr>
<td>12 (1991)</td>
<td>10</td>
<td>2 d</td>
<td>103</td>
<td>0.2-100</td>
<td>19</td>
<td>EOG</td>
<td>20x5 count*</td>
<td>prolonged/reduced P3; P3 improves with recovery from PTA</td>
</tr>
<tr>
<td>13 (1990)</td>
<td>8</td>
<td>1-3 y</td>
<td>8</td>
<td>?</td>
<td>5</td>
<td>EOG</td>
<td>40 count yes*</td>
<td>P3 only in active condition; reduced N1; prolonged and reduced P3</td>
</tr>
<tr>
<td>14 (1988)</td>
<td>19</td>
<td>&gt; 6 m</td>
<td>19</td>
<td>0.03-32</td>
<td>9</td>
<td>EOG</td>
<td>47 press</td>
<td>prolonged/larger N2; reduced P3; standards N1 longer; targets P3 larger</td>
</tr>
<tr>
<td>15 (1988)</td>
<td>20</td>
<td>4 d</td>
<td>20</td>
<td>1.0-30</td>
<td>1</td>
<td>EOG</td>
<td>60 count</td>
<td>prolonged/reduced P3; normal P3 at retest</td>
</tr>
<tr>
<td>16 (1986)</td>
<td>8</td>
<td>10 in PTA</td>
<td>13 (N1/P2s, P3d)</td>
<td>?</td>
<td>7</td>
<td>EOG</td>
<td>? count</td>
<td>prolonged P3; normal N1/P2</td>
</tr>
<tr>
<td>17 (1984)</td>
<td>4</td>
<td>14 in PTA</td>
<td>7</td>
<td>s/d</td>
<td>1</td>
<td>50 µV</td>
<td>100 – yes*</td>
<td>prolonged P3; normal N1/P2</td>
</tr>
<tr>
<td>18 (1980)</td>
<td>11</td>
<td>14 after PTA</td>
<td>11</td>
<td>0.15-100</td>
<td>15</td>
<td>?</td>
<td>32 press</td>
<td>N2 larger; 50% severe TBI no P3; targets: P1-N3 larger, N2 shorter</td>
</tr>
</tbody>
</table>

* a larger number was investigated. We only consider patients investigated with active paradigm after coma; cutoff point: 12 dB; +50 Hz notch filter; + loud count; + press a button to all stimuli; ignore stimuli.

Examined curve: d=deviants, s=standards ?: not specified. Other abbreviations: y=years, m=months, d=days, h=hours, PTA=post-traumatic amnesia.

Table I - Long-latency auditory evoked potentials studies in traumatic brain injury (TBI) patients (1980-2005).
Attentional ERPs after TBI

we used a reaction time task, and it was carried out on the day after recording of the ERPs. Simple and choice reaction times to pairings of visual, auditory and tactile stimuli were measured, and found to be highly significantly prolonged (p<0.0001) in the patients (23). These results indicated severe attentional impairments in the patient group.

For the purpose of this study, only procedures for obtaining the auditory threshold and the auditory evoked potentials will be further described.

Stimuli and procedure

Evoked potentials were recorded by means of a Toennies Multiliner (Toennies, Würzburg, Germany). This is a clinical device that was developed primarily for making diagnostic neurophysiological recordings (VEPs, SEPs, AEPs, EMG), not for research purposes. It does not allow multichannel recordings, and does not have EOG channels. Artifacts are detected and rejected automatically on-line by the computer program.

All the control subjects and patients underwent a gross measurement of their auditory threshold and a basal recording of brainstem auditory evoked potentials (BAEPs) to verify the integrity of the peripheral and brainstem auditory pathways. BAEPs were recorded monaurally from Cz referred to mastoid. ERPs were recorded binaurally from Cz referred to linked mastoids with an earlobe ground. Impedance was kept less than 3 kW. Filter bandpass was 0.1-70 Hz, ISI 1,000 ms. The cut-off point for artifact rejection was set at ±20 μV.

All the subjects were investigated in two experimental conditions: the first with a passive, the second with an active odd-ball paradigm. Four hundred stimuli at 80 dB SPL (50 ms plateau, 0 ms rise/fall) were delivered in each run. Standards were 1,000 Hz, deviants were 2,000 Hz tones with a 20% occurrence probability. Subjects were informed that tones would have different pitches. This was done: i) to minimize any surprise effect of the deviants, ii) to reduce any uncertainty regarding the correct functioning of our apparatus which produced “irregular” tones, and iii) to produce a condition in which standards and deviants had the same context relevance. In the passive run, the subjects were instructed to ignore the tones; in the active run, they were asked to count silently and later to report the number of deviants. The passive task was always presented first. This was done to avoid inducing a response to the deviant stimulus during the passive task, which may have occurred had the active task been presented first.

Data analysis

Standard and deviant stimuli were separately averaged by the Multiliner computer. Thus, two traces were obtained for each task condition. Peaks were empirically defined according to their sequential contingency (e.g., P2 must be more positive than N1 and must follow N1 in time, N2 must follow P2, etc.), whereas crossing of the baseline was not a necessary requirement. The latter, rather tolerant criterion was applied to take into account, as far as possible, eventual peculiarities of the heterogeneous patient group. The consistency of the identified peaks was statistically tested a posteriori within each group, on the assumption that artificial peaks would not vary coherently between task conditions. Therefore, the number of 35 matched subjects in each group was chosen, which makes it possible to detect amplitude differences of 50% between groups or conditions with a test power of 95% (β=0.05) at an a probability level of 1% (p=0.99).

Latencies and amplitudes were measured setting the cursor on the screen manually. In each trace we measured the latency and amplitude of six components: P1 (maximal positivity in the 30-70 ms interval after the stimulus), N1 (maximal negativity between 70-120 ms), P2 (positive peak between 150 and 250 ms), N2 (maximal negativity preceding the P3), P3 (the largest positive-going peak occurring between 250-400 ms), and N3 or P3-endpoint (the point where the negative-going limb of the P3 intersects the baseline). The latency was calculated from stimulus onset to maximal peak of the wave. The amplitude was defined as the difference of potential relative to the previous component. Latency and amplitude calculations for all statistical purposes were obtained from each subject separately. Grand-averages of each trace across the 35 patients and the 35 controls were also computed.

Statistical analysis

A pre-analysis of data showed that peak latencies and amplitudes were significantly nonnormally distributed. As the skewness was positive for some variables and negative for others, a correction by non-linear transformation was not possible. Therefore, we analyzed data by non-parametrical methods. We calculated the 10th, 25th, 50th, 75th and 90th percentiles for graphical purposes. Differences between patients and controls were tested using the Mann-Whitney test. Differences between conditions were first checked for overall effects using the Friedman test. If the Friedman test showed significant differences, we tested separately the Count/No-count and Deviant/Standard pairs using the Wilcoxon tests. Cut-off probability level was set at p 0.02. Statistical dependencies were analyzed using Spearman rank correlation coefficients. All statistics were performed using SPSS 10.1 for Windows.

Results

Psychophysical data

The auditory threshold was significantly higher in the patient group (better ear: patients 31.0±6.8 dB, controls 23.9±8.0; worse ear: patients 41.0±16.3, controls 27.7±6.5).

The correlation between ears was higher in the control group: Spearman-Rho=0.804, p=0.01 for controls; Spearman-Rho=0.654, p=0.01 for patients. In the control group there was a significant correlation between auditory threshold and age (Spearman-Rho=0.576, p=0.01 for the worse ear; Spearman-Rho=0.411, p=0.05 for the better ear). In the patient group there was no significant correlation between auditory threshold and FIM score but we found, as in the control group, a positive correlation with age
(Spearman-Rho=0.424, p=0.05 for the worse ear; Spearman-Rho=0.644, p=0.05 for the better ear).

**Short-latency auditory evoked potentials**

BAEP latencies were similar in both groups, and no significant difference between patients and controls was found in any of the five peaks. In both groups, the latencies of the peaks III and V correlated with auditory threshold and with age (p<0.05).

**Behavioural data**

In the control group, all subjects reported the correct number of deviants. In the patient group, five subjects reported a smaller number of deviants (between 50 and 74), all the other subjects counted correctly. Simple and choice reaction times did not correlate with any of the ERP components, either in controls or in patients.

**Event-related potentials**

In all the subjects, the first wave complex (P1-N1-P2) was present, in the two task conditions, both in the response to standards and in the response to deviants. In the waveforms elicited by standard stimuli, the later components (N2, P3, N3) were present in 85.7% of the controls in the passive, and in 80.0% of the controls in the active task. The N2 was present in 97.1% of the patients in the passive, and in 94.3% of the patients in the active task. P3 and N3 were present in 65.7% of the patients in the passive task and in 60% of the patients in the active task. In the waveforms elicited by deviant stimuli, the N2 was missing in one control and in two patients, the P3 in two controls and in two patients, and the N3 in two controls and in one patient in the ignore condition; in the count condition, the three components were present in all the subjects. Figure 1 shows the grand-average across all controls and patients. Because of inter-individual latency jitter, the averaged components appear smaller and their duration longer. This is particularly true in the patient group, because patients have a greater inter-individual variance. The late components of the standard curves and of the deviant no-count curve disappear because of smoothing effects. Only the classic P3 peak elicited by counted deviants can still be observed. As an effect of averaging, the P3 peak appears strongly enhanced in the controls, and attenuated in the patients. Traces obtained from a patient (bottom) and from his matched control subject (top) are shown in figure 2. Many significant differences were found between TBI patients and their age- and gender-matched controls, and these are illustrated in figures 3 and 4. These differences can be considered from two perspectives: as single component differences between the two groups, and as single component differences between the two task conditions. The results are summarized in Table II (see over). Only those with a statistical significance of at least 2% are reported. The formation of patient clusters on the basis of location of the main lesions, medication use, FIM score, and time elapsed from the accident, did not give any statistically significant results. To avoid repetitions, a more detailed description of the results is combined with their discussion, in the next section.
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Figure 3 - Amplitude and latency of the early components P1, N1, P2. Boxes represent the quartiles, circles the medians, lines the 10\textsuperscript{th} and 90\textsuperscript{th} percentiles. SN=standards/no-count; SC=standards/count; DN=deviants/no-count; DC=deviants/count.

Figure 4 - Amplitude and latency of the late components N2, P3, N3. Boxes represent the quartiles, circles the medians, lines the 10\textsuperscript{th} and 90\textsuperscript{th} percentiles. SN=standards/no-count; SC=standards/count; DN=deviants/no-count; DC=deviants/count.
Discussion

The differences between controls and TBI patients can thus be considered in terms of single component differences between the two groups, or as a different electrophysiological response to the task condition between the two groups. We shall discuss these two perspectives separately.

Single components: patients vs controls

The results are presented in Table II. The latency of the first three components, P1, N1 and P2, did not show any significant difference between patients and controls. This result is in agreement with previous studies (4,7,8,13,16,18).

The amplitude of the P1 was generally larger in patients than in controls. The difference reached statistical significance in the standard waveforms in count condition. Increased P1 has already been reported. Ford and Khalil (8) interpreted the P1 increase as due to cortical irritability or hyperresponsivity resulting from local neuronal injury, or from a release of frontal inhibition over adjoining sites due to neural injury in the prefrontal area, or to disruption in the frontal cortex-brainstem reticular system due to brainstem injury.

An alternative hypothesis for our finding is a deficit of habituation mechanisms in TBI patients probably related to deficits of attention and working memory. P1 has already been used as an indicator of sensory gating in clinical studies (24). Adler (25) reported that in normal subjects the amplitude of P1 in the second stimulus of a pair was suppressed when the interval between the two stimuli was regular, whereas in schizophrenics this suppression did not occur, probably because of a defect in the sensory gating system. P1 non-suppression has also been reported in TBI patients; the authors, referring to similar findings in psychiatric patients, related it to impaired cholinergic function in the hippocampus (26).

A third hypothesis is that the P1 increase in patients was an artifact due to an overlap with Pa, the middle-latency AEP wave that precedes P1 by about 30 ms. A delay or suppression of the Pa might result in an enhancement of the P1. The neural source of P1 is likely to be in the ascending reticular activating system (27). Patients who respond slowly, might not be able to activate the reticular system effectively, and hence Pa would be taken as P1. Future oddball studies, paying more attention to the middle-latency AEPs, might help to clarify this point.

Literature data on N1 and P2 amplitude, on the contrary, are rather inconsistent. Decreased N1 has been reported by some investigators (3,5,13) but not by others (10,16). Some authors found a reduced P2 (7,11), but other authors reported an increment of this component (8) or its normality (4). We found no significant difference in N1 or in P2 amplitude between patients and controls.

Table II - Results.

<table>
<thead>
<tr>
<th>Effects of task condition</th>
<th>Differences between controls and patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency</td>
<td>Amplitude</td>
</tr>
<tr>
<td>Controls</td>
<td>Patients</td>
</tr>
<tr>
<td>S</td>
<td>D</td>
</tr>
<tr>
<td>P1</td>
<td>NC</td>
</tr>
<tr>
<td>N1</td>
<td>NC</td>
</tr>
<tr>
<td>P2</td>
<td>NC</td>
</tr>
<tr>
<td>N2</td>
<td>NC</td>
</tr>
<tr>
<td>P3</td>
<td>NC</td>
</tr>
<tr>
<td>N3</td>
<td>NC</td>
</tr>
</tbody>
</table>

Abbreviations: NC / CO = no count / count; S / D = standard / deviants; C / P = controls / patients.
**Attentional ERPs after TBI**

The last three components showed strong differences between patients and controls, especially in the active task. The N2 was prolonged in patients in both conditions, in standards as well as in deviants. This is in agreement with previous findings (3,7,8,14,18). The N2 wave has been interpreted as a sign of effortful, controlled stimulus processing, with a peak latency that correlates with the time taken to categorize the eliciting stimulus (28-30). We can therefore interpret a delay of this component as a sign of inefficiency or slowing of information processing in TBI patients. Compared with controls, patients showed, in the count condition, a significantly higher N2 amplitude, to standards as well as to deviants. Fitzgerald and Picton (28) and Näätänen and Picton (29) suggested an association between N2 amplitude and the allocation of cognitive effort, reflecting the conscious allocation of attentional resources to stimuli indicated as salient by pre-attentive processes: the greater the effort, the higher the N2. Increased N2 amplitude to deviants in TBI patients has been reported by Rugg, who interpreted it as an index of greater levels of effort required by patients to perform the task adequately (14). Our data support and extend these findings: whereas Rugg, in his study, used only the count condition, we used both the passive and the active paradigm and found that the N2 amplitude was significantly higher in our patients than in controls only in the active task. We can take this as evidence of the patients’ enhanced conscious attentional effort.

P3 and N3 were also altered in the patient group. The P3 latency to standards did not show any significant difference, whereas the P3 latency to deviants was significantly prolonged in patients in both conditions. The N3 latency was significantly prolonged only in the standard waveform and only in the count condition. P3 and N3 amplitudes in the standard waveforms were similar in patients and controls. In response to deviants, P3 and N3 were also altered in the patient group. The P3 latency to standards did not show any significant difference, whereas the P3 latency to deviants was significantly prolonged in patients in both conditions. The N3 latency was significantly prolonged only in the standard waveform and only in the count condition. P3 and N3 amplitudes in the standard waveforms were similar in patients and controls. In response to deviants, P3 and N3 were also smaller in patients, especially in the count condition.

Changes in P3 parameters (latency or amplitude) in TBI patients have been widely reported, but the results are discrepant among studies (Table I). Besides methodological differences between the studies, which could account for the discrepancy of the results, there are physiological factors which probably contribute to instability of this component. Studies with repeated testing found progressive shortening of the P3 latency and a positive correlation of this shortening with improvement of neuropsychological test scores (12,15,16,18,31), and there is general agreement on the sensitivity of P3 latency to deviants as well as to standards, patients showing a significantly higher latency to deviants than to standards, whereas this trend was not significant in the controls. This suggests that the attentional processes are regulated at a very early stage of auditory information processing. In addition to the above-mentioned theories explaining the P1 increase in patients, we could interpret this increase as a result of deficient information processing, i.e., severe TBI patients can cope with task demands only through excessive cognitive effort (Van Zomeren’s “coping hypothesis”) (32). This may apply even in a task as undemanding as an auditory oddball detection.

The results are presented in Table II. Several findings of interest emerge from the comparison of the responses to the task condition. Many components were sensitive to manipulation of arousal state and specific attention. As mentioned before, the patients in the count condition showed a larger P1 amplitude than the controls. In the patients, moreover, the P1 was significantly greater in response to deviants than to standards, whereas this trend was not significant in the controls. This suggests that the attentional processes are regulated at a very early stage of auditory information processing. In addition to the above-mentioned theories explaining the P1 increase in patients, we could interpret this increase as a result of deficient information processing, i.e., severe TBI patients can cope with task demands only through excessive cognitive effort (Van Zomeren’s “coping hypothesis”) (32). This may apply even in a task as undemanding as an auditory oddball detection.

In the no-count condition, the controls showed a longer N1 latency to deviants than to standards, whereas this trend was not significant in the controls. Although N1 mainly reflects exogenous processes modulated by the physical characteristic of the stimulus, it has been suggested that this component also reflects “a widespread transient arousal” and the orienting of attention towards novel stimuli (33).

Therefore, the prolonged N1 latency to deviants shown by the control group may be due to the superimposition of a mismatch component, which the patients did not exhibit. The N1 amplitude to standards was, in both groups, larger in the no-count than in the count condition, which seems to indicate that the N1 amplitude may be influenced by task relevance and voluntary resource allocation. This could explain why, in both groups, the N1 amplitude to standards was larger in the no-count than in the count condition. In the no-count condition, deviants and standards had equal task relevance; therefore, attentional resources were similarly distributed between the two stimuli. In the count condition, on the other hand, the standard stimuli were task-irrelevant, and voluntary attentional resources were concentrated on the deviant, task-relevant stimuli.

In the patients, P2 latency to deviants was significantly shorter in the count condition, whereas in the controls this was a non-significant trend. P2 amplitude to standards was, in both groups, higher in the passive than in the active task, while P2 amplitude to deviants did not show any significant change between task conditions. Little is known about the functional significance of the P2. It has been suggested that it represents the beginning of a central process responsible for stimulus identification and the initiation of decision making. As previous studies showed, in healthy subjects, P2 latency is inversely related to reaction time, while P2 amplitude decreases as the difficulty in making an auditory discrimination increases (34). Our data support this view.

N2 latency to deviants was, in both groups, significantly shorter in the count condition. In the no-count condition there was no significant difference between N2 latency to standards and N2 latency to deviants in either group. In the count condition, however, controls and patients showed an opposite effect: in
the controls, the N2 latency was shorter to standards than to deviants, whereas in the patients the N2 latency was shorter to deviants than to standards. Also, the N2 amplitude variations differed markedly between controls and patients. In the controls, the N2 amplitude to standards was significantly larger in the no-count than in the count condition, whereas in patients there was no significant difference. Patients, unlike controls, showed in the count condition a larger N2 amplitude to deviants than to standards. These results indicate an abnormal distribution of voluntary attentional resources between task-relevant and task-irrelevant stimuli in the patients, since the main differences between patients and controls were found in the active task.

P3 latency to deviants as well as to standards was not influenced by the task condition either in patients or in controls, i.e., P3 latency was independent of the task relevance of the stimuli and only reflected the closure of a perceptual epoch. P3 amplitude and the P3-N3 slope were larger in response to deviants than to standards in both groups and conditions. In the controls, amplitudes to deviants were significantly larger in the active task, while in patients this was only a trend. On the one hand, this confirms that, in addition to attentional allocation (35,36) and updating of one’s model of the environment (37), the salience of the stimulus to the subject strongly contributes to P300 amplitude (38,39). On the other, it fails to clarify why the patients, in the active task, did not produce significantly greater P3 and N3, as the controls did. Indeed, in the active task the stimulus was as relevant to the patients as to the controls. The counting performance was as good in the patients as in the controls. The effort in terms of attentional allocation was probably higher in the patients than in the controls, as also shown by the higher N2 in patients. One explanation, therefore, could be that the P3 is only partially a strictly event-related component, and more a reflection of general attentional capacity (40), i.e. the amplitude of the P3 at least partially reflects the limit or total amount of attentional resources that can be allocated. This amount, although reduced in patients, sufficed to complete the task required of the subjects in our study, i.e. counting the deviants, but it is likely that patients will not be able to complete more complex tasks.

The aim of the present study was to explore the effectiveness of auditory ERPs as a tool for assessing, in clinical practice, the distribution of attentional resources in TBI patients. A better understanding of the long latency EP components could be of great help in monitoring therapy or medication. Normative data could constitute objective criteria for insurance purposes.

Our study set out to contribute to the reaching (not as yet achieved) of these desirable goals. We used the simplest recording technique, which is relatively inexpensive and available in any clinical lab. We are aware that our conclusions must be considered preliminary until they are replicated with a more standard research setup, but we think that our results are encouraging with a view to the routine implementation of cognitive ERPs.

References
20. Rappaport M, Clifford JO, Winterfield KM. P300 response un-
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34. Lindholm E, Kothath JJ. Analysis of multiple event related potential components in a tone discrimination task. Int J Psychophysiol 1985;5:121-129