Late neurobehavioural symptoms after mild head injury

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The present study examined whether patients (n = 11) with post-concussional symptoms (PCS) 12–34 months after mild head injury (MHI) performed less well on selected neuropsychological tests than patients with MHI without PCS (n = 11) and healthy controls (n = 11). Patients with PCS were individually matched with controls for the time elapsed after the injury, age, sex, education and IQ. There were no overall gross differences between the groups in cognitive functioning, except for an isolated deficit on a sustained attention task. Post-hoc analysis of results obtained with two behavioural rating scales showed that patients with higher ratings on a post-concussive/cognitive complaints scale performed less well on a sustained attention task than subjects with lower ratings.

Introduction

Neuropsychological investigations have been carried out over the past 20 years to evaluate behavioural and cognitive dysfunctions in patients with mild head injury (MHI). Whereas gross deficits in intelligence of memory have not been reported in minor head injury [1, 2], subtle impairments in the rate of information processing and attention have been found [3, 4]. An important question is how long these cognitive deficits persist. Although most patients may show substantial recovery on cognitive measures 1–3 months after MHI, isolated neurobehavioural defects may occasionally persist for longer [3]. For example, Leininger et al. [5] reported that MHI patients who complained of post-concussional symptoms (PCS) displayed a significantly poorer performance than uninjured controls on several neuropsychological tests. Deficits were most evident on tests of reasoning, information processing and verbal learning. In addition, Dikmen et al. [6] found differences in cognitive functioning between head-injured patients with different levels of PCS at about 1 month and 1 year after injury. In contrast, MacFlynyn et al. [7] found no relationship between measures of reaction time and behavioural sequelae.

The conflicting results may be because of difficulties in quantifying PCS. The subjective complaints, which persist in the absence of neurological abnormalities, preclude reliable assessment of the degree of post-traumatic disability, and impede the differentiation between symptomatic patients who are really impaired and those who are merely inconvenienced by their symptoms [8].
The aim of the present study, therefore, was to test the hypothesis that patients with persistent PCS after MHI have cognitive dysfunctions in comparison with matched, symptom-free MHI patients and non-concussed control subjects. In addition, the nature and intensity of the PCS reported by patients were investigated by means of two newly developed behavioural rating scales (one with post-concussive/cognitive complaints and a second with emotional/vegetative complaints) in order to investigate whether the nature and/or intensity of certain types of complaints adversely affect cognitive performance. Patients with a post-traumatic interval of more than 1 year were selected to better study the nature of the persistent post-concussion syndrome.

Subjects and methods

Subjects

Patients (n = 11) with persistent PCS were selected from a larger population of patients with MHI. The criteria for inclusion in the study included a post-traumatic interval of about 12–34 months (median 21 months), a post-traumatic amnesia not exceeding 60 min, a period of unconsciousness of less than 15 min, a Glasgow Coma Score (GCS) of 15 on admission, and no serious traumatic physical complication (including the absence of orthopaedic injury). Patients who had drunk alcohol at the time of the trauma, or who had a skull fracture, were also excluded. One subject was involved in a litigation-compensation affair, but none had a history of neuropsychiatric disorder. No patients were receiving medication at the time of testing, and none suffered from severe perceptual (visual or auditory) or motor problems. The control patients (n = 11), who had recovered completely and had no PCS at the corresponding time after injury, were selected from the same population on the basis of matching criteria with the patients with persistent PCS. Although most of these patients had endorsed symptoms for 1–3 months after their injury, all were free of symptoms after the first months of recovery.

The uninjured group (n = 11) were selected from a pool of non-concussed volunteers. Both the patients without PCS and the healthy volunteers were individually matched with the patients with PCS for age (± 6 years), sex, education (± 1 level [9]; and IQ (± 8 IQ points). Levels of IQ were measured with the Groninger Intelligence Subtest [10]. Each group consisted of six males and five females. Age, time elapsed after the trauma, and educational level are presented in Table 1. All subjects gave their informed consent.

<table>
<thead>
<tr>
<th>Group</th>
<th>Group 2</th>
<th>Group 3</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>27.2 ± 10.2</td>
<td>27.4 ± 10.1</td>
</tr>
<tr>
<td>Time after trauma</td>
<td>22.6 ± 7.0</td>
<td>22.9 ± 7.5</td>
</tr>
<tr>
<td>Educational level</td>
<td>4.6 ± 1.3</td>
<td>5.1 ± 1.2</td>
</tr>
<tr>
<td>IQ</td>
<td>105.3 ± 11.3</td>
<td>110.1 ± 8.2</td>
</tr>
</tbody>
</table>

Procedure

A checklist of post-concussive symptoms was completed, which included items of headache, nausea, dizziness, difficulties with concentration and memory, fatigue, and sleep disturbances. As these symptoms also occur in healthy individuals, the symptoms
were scored for the absolutely or relatively increased appearance after the injury in comparison with the pretraumatic condition [11]. Six patients with persistent PCS \((n = 11)\) complained of three symptoms or more, and five patients complained of one or two symptoms. By definition, patients without PCS did not report any symptom at the time of the study.

The patients were examined on a battery of cognitive tests and completed two newly developed behavioural rating scales together with the Zung Self Rating Depression scale (see below). Results of salivary cortisol sampling of the patients will be presented elsewhere.

**Psychometric tests**

The following tests were used:

1. In the computerized sustained attention task a small spot, which was moving in a stepwise fashion around an imaginary circle (diameter 11 cm), was presented on a monitor screen at 20 × 28 cm (Vienna test system, Schuhfried GmbH, Austria). The spot made 50 small regular steps (7.2 degrees) per round, randomly interspersed with a double step (14.4 degrees/5 double-steps per round). The total time per step was 1 s. The subjects were requested to press a button when a double-step occurred (= the signal). One hundred signals were presented in the total testing time of 12.5 min. Each session was preceded by a practice session of 2.5 min. The mean reaction time was used as the cognitive parameter.

2. Memory task: a visual, computer-assisted version of the Auditory Verbal Learning Test [12] was presented on a portable microcomputer [13]. The tests consist of a list of 15 Dutch monosyllabic meaningful words, which are presented for 1 s at 1-s intervals. At the end of the trial the subjects recall the words. In addition, auditory verbal interference was given by the experimenter (one monosyllabic word) during the interval time between the visual presentation of each word. Five trials were carried out. The variable used in this study was the total number of correct words over all trials.

3. The Stroop Colour Word Interference Test [12] consists of three subtasks. The tests examine the speed at which 100 colour names (yellow, green, red and blue) are read (subtask I) and the speed at which 100 coloured spots are named (subtask II). Subtask III again involves 100 colour names, but the printing ink is different from the colour name; the speed at which the colour of the printing ink of the word is named is taken as the test variable. The colour word interference score is obtained by subtraction of the time needed for subtask II from that of subtask III, and was used as the cognitive parameter.

4. In the computerized divided attention task, dots were presented at irregular time intervals within a fixed 6 × 10 rectangular matrix on a monitor screen of 20 × 28 cm (Vienna test system, Schuhfried GmbH, Austria). The subject was instructed to press a button when four dots formed a square (= the signal). Each square was illuminated for 3 s, while other dots appeared and disappeared. The maximum number of different points ‘moving’ simultaneously was three. Sixty signals were presented in the total testing time of 12.5 min. The mean reaction time was used as the cognitive measure.
Patterns of behavioural dysfunction

We have recently developed two behavioural rating scales derived by factor analysis of data from questionnaires completed by a consecutive series of patients with MHI (n = 71) about 10 days after the trauma [14]. The questionnaire consisted of 26 items regarding a number of post-concussive and cognitive-energetic complaints, as well as a series of emotional and vegetative complaints. Principal-components analysis (with varimax rotation) revealed two factors [15]. To minimize mis specification, factor loadings were considered relevant if they achieved a value of ± 0.45 or more. Factor I (post-concussive/cognitive complaints) consisted of 11 high-loading items of typical PCS, such as headache and items indicating problems with decreased work capacity. Factor II (emotional/vegetative) included 14 high-loading items of rather aspecific psychovascular functional symptoms, such as complaints of heart palpitations, wet hands, dyspnoea, flushing, as well as items of depression and emotional liability. Cronbach’s alpha for the first group (11 items) was 0.92, and 0.86 for the second group of 14 items. Total scores were calculated by summing the original scores for the selected items of each scale [16]. The response to each question was scored according to the severity or intensity of the complaint (1–4).

Table 2. Results of the cognitive tests (means ± SD). F(1,32) values are presented in the last column of the table

<table>
<thead>
<tr>
<th></th>
<th>Patients with PCS (n = 11)</th>
<th>Patients without PCS (n = 11)</th>
<th>Non-concussed controls (n = 11)</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sustained Selective Attention Task</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction time</td>
<td>0.58 ± 0.10*</td>
<td>0.51 ± 0.08</td>
<td>0.50 ± 0.08</td>
<td>3.20*</td>
</tr>
<tr>
<td><strong>Divided Attention Task</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction time</td>
<td>1.26 ± 0.31</td>
<td>1.12 ± 0.31</td>
<td>1.16 ± 0.23</td>
<td>1.01, ns</td>
</tr>
<tr>
<td><strong>Stroop Colour Word Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SI</td>
<td>50.22 ± 16.73</td>
<td>39.93 ± 7.79</td>
<td>40.69 ± 4.98</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>64.08 ± 23.57</td>
<td>49.89 ± 9.38</td>
<td>52.12 ± 6.50</td>
<td></td>
</tr>
<tr>
<td>IIII</td>
<td>107.11 ± 40.29</td>
<td>73.59 ± 17.24</td>
<td>84.39 ± 14.52</td>
<td></td>
</tr>
<tr>
<td>IIIII</td>
<td>43.02 ± 27.70</td>
<td>23.70 ± 9.71</td>
<td>32.26 ± 13.85</td>
<td></td>
</tr>
<tr>
<td><strong>Word Learning Test</strong></td>
<td></td>
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<tr>
<td>Total</td>
<td>45.72 ± 9.91</td>
<td>53.09 ± 6.96</td>
<td>48.09 ± 13.19</td>
<td>1.45, ns</td>
</tr>
</tbody>
</table>

A common superscript signifies a statistically significant difference according to the Duncan multiple-range post-hoc test.

*p < 0.05.

Depression scale

The Dutch version of the Zung Self Rating Depression Scale (SRDS [17]) was used to quantify depressive symptoms.

Statistical analysis

The first step in the analysis was to assess, by MANOVA, whether there was an overall difference between the two groups for the four cognitive parameters together, i.e. the mean reaction times of the sustained and the divided attention task, the Stroop
interference score, and the total number of words of the memory task [15]. The second step was to assess the influence of the scores on the two behavioural rating scales on cognitive functioning. Pearson correlation coefficients were calculated between the ratings on the behavioural scales and the scores on the Zung depression scale. Ranks over all observations were calculated for scores that did not approximate a normal distribution [18]. One-tailed significance levels were applied according to the unidirectional hypothesis that patients with higher endorsement of PCS had a decreased cognitive performance.

Results
The results of the cognitive tests are presented in Table 2. Multivariate analysis yielded no overall significant group effect (Wilks lambda = 0.64 with a multivariate $F(8,50) = 1.52$ n.s.).

MANOVA is particularly suitable for analysing differences between groups when subjects are examined in more than one test, in that the same degree of protection against type-1 errors as that for the general analysis is maintained for each comparison. However, an enhanced protection corresponds to a diminished power of the method. Given this consideration, and because the poorer scores of the group of patients with PCS were in the same direction, we repeated the same comparisons by means of separate univariate analyses. In this manner the performance of patients with PCS was found to be significantly lower only on the sustained attention task (see Table 2).

Post-hoc analysis
In order to test the hypothesis that patients with persistent PCS represent a heterogeneous group in terms of the intensity and particular nature of PCS, a post-hoc analysis was performed for the sustained attention task within the group of MHI patients with persistent PCS ($n = 11$). Median split distributions of this group were obtained on the basis of the scores for the emotional/vegetative and the post-concussive/cognitive complaints scale. Wilcoxon rank sum tests indicated that patients with PCS who had higher ratings on the emotional/vegetative scale did not differ from their lower rating counterparts in the mean reaction time of the sustained attention task ($0.60 \pm 0.09$ versus $0.56 \pm 0.11$; $z = 0.38$; n.s.). In contrast, patients with higher ratings on the post-concussive/cognitive complaints scale reacted significantly slower in the sustained attention task ($0.64 \pm 0.09$ versus $0.53 \pm 0.08$; $z = 1.71$; $p < 0.05$) than symptomatic patients with lower scores on this scale.

Interrelationships between the Zung depression scale and the two behavioural rating scales
There was a significant correlation ($R = 0.71$; $p < 0.05$) between the scores on the Zung depression scale and the emotional/vegetative behavioural rating scale within the group of patients with PCS ($n = 11$). In contrast, there was no significant correlation between the scores on the post-concussive/cognitive scale and the scores on the Zung depression scale ($R = 0.38$; n.s.); see also Table 3.
Table 3. Mean scores (± SD) on the behavioural rating scales (postconcussive/cognitive and emotional/vegetative scale) and the Zung depression scale

<table>
<thead>
<tr>
<th></th>
<th>Patients with PCS (n = 11)</th>
<th>Patients without PCS (n = 11)</th>
<th>Non-concussed controls (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zung</td>
<td>44.82 ± 10.28</td>
<td>25.60 ± 4.35</td>
<td>32.87 ± 7.67</td>
</tr>
<tr>
<td>Post-concussive/cognitive</td>
<td>29.55 ± 5.82</td>
<td>15.09 ± 2.81</td>
<td>17.64 ± 3.26</td>
</tr>
<tr>
<td>Emotional/vegetative</td>
<td>27.00 ± 4.45</td>
<td>16.18 ± 2.93</td>
<td>17.18 ± 2.75</td>
</tr>
</tbody>
</table>

Discussion

Gronwall and Wrighton reported that information processing functions are impaired during the first weeks after MHI, with recovery from this impairment occurring by 35 days unless the post-traumatic symptoms persist [19]. These authors suggested that a reduction in the rate of information processing is an important factor in the genesis of PCS. Leininger et al. found that symptomatic MHI patients displayed a significantly poorer performance than controls on several neuropsychological tests 1–22 months after injury [5]. The present results indicate that there were no overall gross differences in cognitive functioning between MHI patients with PCS 12–34 months after MHI. Although it has been reported that cognitive deficits after MHI are subtle, and appear selectively to impair functions of divided attention and information processing, we did not observe a difference in divided attention between the two groups [3, 20, 21]. In contrast, we found a subtle isolated deficit on the sustained attention task. The contrasting differences in effect size between our study and the study of Leininger and co-workers could be related to the fact that Leininger et al. examined referred patients, whereas our patients were selected from a larger survey of MHI patients.

Few studies have described relationships between subjective complaints and test performance. Barth et al. found that cognitive deficits and behavioural dysfunctions were only somewhat related in MHI patients [22]. This may simply indicate that the consequences of MHI are manifested differently in different individuals. For example, minor head trauma may cause considerable emotional dysfunction without causing significant cognitive disability in some patients. Although there are reports of a positive relationship between cognitive deficits and emotional symptoms, we did not observe a relationship between emotional/vegetative complaints and cognitive functioning in the subgroup of symptomatic MHI patients [23]. In contrast, patients with higher ratings on the post-concussive/cognitive scale displayed a poorer performance on the sustained attention task than those patients with lower ratings on this scale.

It can be summarized that a subgroup of MHI patients who reported PCS 12–34 months after an uncomplicated MHI demonstrated no overall gross differences on tests of attention and information processing.

References

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