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Neuropsychological Deficits in Patients with Persistent Symptoms Six Months after Mild Head Injury

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There is much debate on the nature and duration of cognitive deficits and postconcussive symptoms (PCS) after mild head injury. Most studies performed so far have compared head-injured patients with subjects who had not suffered a concussion, instead of directly comparing patients with and without persistent PCS. The present study examined whether patients with PCS (n = 9) about 6 months after an uncomplicated mild head injury performed less well on selected neuropsychological tests than patients with mild head injuries who did not have PCS (n = 9) and healthy controls (n = 9). Patients with PCS were individually matched with controls for the time elapsed after the injury, age, sex, and education. We found that patients with PCS performed less well on tests of divided and selective attention than both patients without PCS and healthy controls. It is concluded that cognitive deficits may be present up to 6 months after mild head injury when symptoms persist. The findings indicate that patients with mild head injury and subjective symptoms may manifest demonstrable cognitive deficits. (*Neurosurgery* 30:692–696, 1992)

Key words: Attention, Mild head injury, Postconcussive symptoms

INTRODUCTION

The cognitive deficits and postconcussive sequelae caused by severe head injury have been well established (5). Mild head injury (MHI) is much more common than severe head injury, and many patients have subjective impairments as a result of their head injury (3). There has been much debate over the years as to whether minor head injuries result in significant persistent cerebral damage and, if present, whether this damage is demonstrable by objective methods. Neuropsychological investigations have been carried out over the past 20 years to evaluate behavioral and cognitive dysfunctions in patients with MHI. Whereas gross deficits in intelligence or memory have not been reported in conjunction with minor head injury (8, 10, 18), subtle impairments in the rate of information processing and attention have been found (12, 13, 15, 22). An important question is how long these cognitive deficits will persist. Neuropsychological and psychosocial difficulties persisting 3 to 6 months after minor head injury have been reported (2, 17, 26). The results of several other studies, however, do not indicate decreased cognitive functioning about 1 month after minor head injury (8, 10, 18). The conflicting results may be because of the heterogeneity of the subjects, the different time intervals after injury, the sensitivity of the selected cognitive tests in detecting posttraumatic brain dysfunction, and the appropriateness of the control group. Most studies performed so far have compared head-injured patients with subjects who had not suffered a concussion, instead of directly comparing patients with and without persistent postconcussive symptoms (20). Evidence is growing to indicate that cognitive deficits may be limited to a subgroup of MHI patients, for instance, those with subjective complaints (9, 10, 17).

The aim of the present study, therefore, was to test the hypothesis that patients with postconcussive symptoms 6 months after MHI have cognitive dysfunctions as compared with matched, symptom-free MHI patients and healthy control subjects. A specific impairment of attention after MHI has been shown by a number of studies (10, 11, 15). Therefore, tests that measure different aspects of attention were included in the test battery.

PATIENTS AND METHODS

Patients

Patients with persistent PCS (n = 9) were selected from a cohort of patients with MHI. The criteria for inclusion in the study were as follows: an interval of about 6 months since the injury, a period of posttraumatic amnesia not exceeding 60 minutes, a period of unconsciousness of less then 15 minutes, a Glasgow Coma Scale score (28) of 15 at admission, and no serious traumatic physical complication (including the absence of orthopedic injury). Patients who had drunk alcohol at the time of the trauma or who had a skull fracture were excluded. None of the subjects was involved in litigation or in seeking compensation, and none had a history of neuropsychiatric disorder. Consequently, 25 patients (7 female, 18 male) were excluded from the study. Forty-six patients (23 female, 23 male) with an uncomplicated MHI with no premorbid compromising condition were selected. The causes of the injury were traffic (n = 33), falls (n = 6), fights (n = 1), sports (n = 5) and accidents at work (n = 1). Six patients became unavailable for follow-up. There were 9 patients with persistent PCS at 6 months after the uncomplicated MHI (22%). The causes of the injury within the PCS group were traffic (n = 7), fights (n = 1), and sports (n = 1).

The MHI patients who had recovered completely and had no PCS 6 months after injury (n = 9) were selected from the same population on the basis of matching criteria with the patients with persistent PCS. The uninjured group (n = 9) was selected from a pool of healthy volunteers who had not suffered a concussion. Both the MHI patients without PCS and the healthy volunteers were individually matched with the patients with PCS for age (±6 years), sex, and education (±1 level) (29). The 7-point scale of Verhage (29) represents 7 different levels of educational achievement based upon the Dutch scholastic system. Each group consisted of 5 male and 4 female subjects. Mean age, time elapsed after the trauma, and the educational level are presented in Table 1. All subjects gave their informed consent.

Postconcussive symptoms

A checklist of postconcussive symptoms, which included headache, nausea, dizziness, difficulty with concentration and memory, fatigue, and sleep disturbances was completed for each subject. As these symptoms also occur in healthy individuals (8), the symptoms were scored

TABLE 1
Mean[a] Age, Time after the Injury, and Educational Level of Patients with Persistent Postconcussive Symptoms and Controls

	Patients with PCS[b] (n = 9)	Controls	
		Patients without PCS (n = 9)	Healthy Subjects (n = 9)
Age (yr)	30.4 (11.7)	28.5 (11.2)	30.1 (11.7)
Education[c]	4.7 (0.6)	4.9 (0.8)	5.0 (1.2)
Time after injury (mo)	5.89 (0.89)	6.17 (1.09)	

[a] The standard deviation is given in parentheses.
[b] PCS, postconcussive symptoms.
[c] Categories taken from Verhage R: *Intelligentie en leeftijd.* Doctoral dissertation. Assen, The Netherlands, 1964.

for the absolutely or relatively increased appearance of the symptom after the injury as compared with the pretraumatic condition. Of the 9 patients with persistent PCS, 8 complained of three symptoms or more, and one patient complained of two symptoms. By definition, patients without PCS did not report any symptom 6 months after the injury.

Psychometric tests

The following tests were used:

1. *Memory task.* A visual, computer-assisted version of the Auditory Verbal Learning Test (19) was presented on a portable microcomputer (4). The test consists of a list of 15 monosyllabic, meaningful words, which are presented for 1 second at 1-second intervals. At the end of the trial, the subjects recall the words. Five trials were carried out. The variable used in this study was the total number of correct words over all trials.

2. *The Stroop Color Word Interference Test.* This test consists of three subtasks (19). The tests examines the speed at which 100 color names (yellow, green, red, and blue) are read (Subtask I) and the speed at which 100 colored spots are named (Subtask II). Subtask III again involves 100 color names, but the printing ink is different from the color name; the speed at which the color of the printing ink of the words is named is taken as the test variable. The color word interference score—which can be taken as a measure of selective attention (14)—results from the subtraction of the time needed for Subtask II from that of Subtask III (III minus II), and was used as the cognitive parameter.

3. *The computerized divided attention task.* In this test, dots were presented at irregular time intervals within a fixed rectangular matrix measuring 6 – 10 on a monitor screen measuring 20 – 28 cm (Vienna test system, Schuhfried GmbH, Vienna, Austria). The subject was instructed to press a button when four dots formed a square (the signal). Each square was illuminated for three seconds while other dots appeared and disappeared. The maximum number of different points "moving" simultaneously was three. Sixty signals were presented during the total testing time of 12.5 minutes. The mean reaction time and the number of omissions were recorded and used as the cognitive measures.

Statistical analysis

The first step in the analysis was to assess by MANOVA (27) whether there was an overall difference between the two groups for all cognitive parameters together. This multivariate approach is particularly suitable for analyzing differences between groups when subjects are examined by more than one parameter, in that the same degree of protection against Type I errors as that for the general analysis is maintained for each comparison. In the second step, separate univariate analyses per cognitive parameter were carried out. Duncan's multiple range test was used as a post hoc test to evaluate significant main effects (27). Probabilities greater than 0.05 were considered nonsignificant. Ranks over all observations were calculated for scores that did not approximate a normal distribution (7).

RESULTS

Multivariate analysis yielded a significant "group" effect [Wilks lambda = 0.42; equivalent multivariate $F(8, 42) = 2.82$; $P < 0.05$]. Therefore, separate univariate tests per cognitive parameter were carried out. Mean data and F values are presented in Table 2. With respect to the verbal learning test, the ANOVA failed to achieve a significant difference between groups ($P < 0.1$). There was a significant overall group effect of the Stroop Color Word Interference Score (III minus II). Post hoc tests indicated that patients with PCS had significantly higher interference times than both control groups.

Analysis of the scores for the divided attention task revealed an overall significant group effect for the mean reaction time. Post hoc tests indicated that the patients with PCS were significantly slower than

TABLE 2
Results of the Neuropsychological Tests[a]

Test	Patients with PCS (n = 9)	Controls	
		Patients without PCS (n = 9)	Healthy Subjects (n = 9)
Divided Attention Task			
Omissions (F = 1.04)[b]	15.3 (9.1)	11.0 (6.4)	11.6 (4.6)
Reaction time (F = 5.92)[c]	1.49 (0.22)†‡	1.10 (0.35)†	1.18 (0.15)‡
Stroop Color Word Interference Test			
Subtask I	51.43 (19.01)	36.08 (4.46)	38.88 (3.14)
Subtask II	62.00 (18.73)	45.70 (4.89)	46.62 (4.59)
Subtask III	104.01 (37.06)	64.35 (6.75)	74.56 (11.27)
Subtasks III – II (F = 7.29)[c]	42.01 (20.57)†‡	18.65 (3.10)†	27.94 (8.92)‡
Verbal Memory Test			
Total score (F = 3.00)[d]	43.89 (9.73)	53.67 (11.88)	53.02 (5.72)

[a] All results are presented as means, with the standard deviation given in parentheses. F(1, 26) values (ANOVA) are given for each test. A common symbol (†, ‡) signifies a statistically significant difference according to the Duncan Multiple Range Test.
[b] Not significant.
[c] $P < 0.01$.
[d] $P < 0.1$.

the patients without PCS and the healthy controls. In contrast, there were no significant differences between the patients without PCS and the healthy control subjects. To check the possible biasing effects of fatigue, the mean reaction time of subjects in the first half of the test was compared with that in the second half. ANOVA revealed no significant group effect [$F(1.32) = 1.3$, nonsignificant], indicating that each group had about the same reaction times in both halves of the test. Although patients with PCS tended to make more omissions, there was no significant overall difference between the three groups for this parameter (Table 2).

DISCUSSION

There has been considerable debate about whether minor head injuries result in significant persistent cerebral damage and, if present, whether this damage can be demonstrated by using psychometric tests. There is accumulating evidence to indicate that even MHI may produce subtle cognitive deficits (15). These deficits appear selectively to impair functions of attention and information processing and are most consistently seen in conjunction with more complex and demanding tasks (11, 15, 22, 24). Studies in patients with MHI cover a heterogeneous population, as there are subgroups of patients who recover quickly, within days, whereas others have persistent PCS after the first weeks of recovery. It is possible that these subgroups represent varying degrees of posttraumatic brain dysfunction. It is important to compare a group of MHI patients experiencing PCS with both MHI patients without PCS and healthy subjects when seeking to establish a meaningful relation between MHI and PCS. The present study indicates that patients with persistent PCS 6 months after an uncomplicated MHI had neuropsychological deficits, as compared with MHI patients without PCS and healthy subjects. The present results are in accordance with those of Dikmen et al. (8) and Leininger et al. (17), and indicate that symptomatic MHI patients displayed significantly poorer performance than controls on several neuropsychological tests. Deficits were most evident on tests of divided and selective attention.

Although we only found a trend towards decreased performance on the verbal memory tests, Leininger et al. (17) found that MHI patients symptomatic 1 to 22 months after injury had decreased scores on a verbal memory test. The Stroop Color Word Interference Test has been used to measure selective attention in patients with head injury (14). Results consistently indicate that head-injured patients have no specific difficulty in focusing on the color dimension of the ambiguous stimuli when data are aggregated at a group level without reference to the persistence of PCS (1, 6). In contrast, McLean et al. (23) found a significant interference effect on the Stroop test only in the subacute stage after injury. We found that patients with persistent PCS at 6 months had more difficulties with the Stroop Color Word Interference measure than asymptomatic patients and healthy controls. Recently, Gentilini et al. (11) reported further evidence for deficits in selective attention in mildly head-injured patients.

Patients with PCS reacted significantly slower on the divided attention task than the asymptomatic patients and healthy controls. Fatigue can be discarded as a causative factor, because the cognitive deficits were already present in the first half of the task. Although these impairments in attention may appear to be subtle, they may have very disabling consequences. Impaired attention and information processing may adversely affect performance in a vocation that entails decision making or stress (15). Patients are less efficient in the processing of information under time pressure and in demanding situations. Moreover, the demands placed on a mildly head-injured patient at a given point in time after injury are greater than that placed on a victim of severe head injury (25). The real-life consequences of slight disturbances in complex information processing in MHI patients have not been investigated as yet.

With respect to the persistence of symptoms following MHI, Gronwall and Wrightson (12) reported that information processing functions were impaired during the first weeks, with recovery occurring by 35 days, unless the posttraumatic symptoms persisted. These authors suggested that a reduction in the rate of information processing is an important factor in the genesis of the postconcussion syndrome. Similarly, Jakobson et al. (16) were able to predict behavioral recovery 1 month after minor head injury by using a reaction time task. In contrast, MacFlynn et al. (22) found no relationship between measures of reaction time and behavioral sequelae. Whether cognitive deficits underlie or contribute to the behavioral sequelae has to be considered in the perspective of different factors, such as the selection of a particular cognitive test, the environmental demands placed upon a patient (21), and the nature of particular postconcussive symptoms. For example, MacFlynn et al. (22) demonstrated that patients with a symptom cluster of vomiting, vertigo, and diplopia had neurophysiological abnormalities, but did not differ in mean reaction time from patients without this symptom cluster.

The critical question is whether the lower neuropsychological performance of symptomatic patients was caused by the injury or whether neuropsychological dysfunctions were already present before the injury. Given the small sample size and lack of information on the patients' premorbid condition, no firm conclusion can be drawn. Patients were, however, strictly matched on educational level. In addition, none of the patients was unemployed because of the trauma. The presence of symptoms was scored for their appearance after the injury in comparison with the pretraumatic condition. Despite the persistence of symptoms, all patients had resumed their work within 3 months after the injury, with one patient being forced to stop working for a second time. Although none of the patients experienced a symptom-free interval within the first period after the trauma, the resumption of work was a common cause of aggravation of their symptoms.

There is a complex relation between head injury and depression. It is now widely believed that depression may occur after head injury (20), and may compromise cognitive functioning (30). Therefore, symptoms of pre- or posttraumatic psychopathology need to be considered in the evaluation of patients with cognitive dysfunction. Patients with a neuropsychiatric history were excluded from the study. Although postconcussive patients may demonstrate depression, none of the patients with an uncomplicated MHI developed symptoms of a depressive syndrome or posttraumatic stress disorder in the present study.

In summary, the subgroup of MHI patients who report PCS at 6 months after an uncomplicated MHI may demonstrate deficits on tests of attention and information processing. The present findings provide an objective basis for the sometimes vague complaints and symptoms of patients after an uncomplicated MHI. In contrast, patients who had recovered from an uncomplicated MHI did not differ in cognitive functioning from healthy control subjects. The less adequate neuropsychological functioning of symptomatic patients is important and warrants further investigation. Further research should be aimed at a more integrated approach using a combination of cognitive and neurophysiological or neuroimaging measures, to investigate whether MHI patients with persisting PCS may have evidence of structural brain damage.

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COMMENTS

The persistence and pathogenesis of postconcussional symptoms after an uncomplicated mild head injury continue to generate controversy. The contributions of this study include the direct comparison of patients exhibiting postconcussional symptoms at 6 months after a mild head injury versus patients sustaining apparently similar injuries whose symptoms resolved by 6 months. Using experimental tests of attention, the investigators were able to show that the symptomatic patients had a residual cognitive impairment relative to the asymptomatic patients and a normal control group. Other assets of the study include exclusion of patients with preexisting neuropsychiatric disorders and the use of multivariate statistics. The authors acknowledge the possibility that depression may have contributed to the attention deficit of their patients; however, without assessment of depression and evaluation of the patients at an earlier time after injury, the potential role of depression cannot be determined.

A second explanation for the persistence of symptoms and attention deficits in 9 of the 46 patients is the possibility of heterogeneity in injury. A recent study by Williams et al. (1) showed that patients with Glasgow Coma Scale scores of 13 to 15 who had evidence of a brain lesion on a computed tomographic scan exhibited more severe neuropsychological sequelae and residual disability than other patients with mild impairment of consciousness who had normal computed tomographic findings. In the present study, the authors do not report computed tomographic findings. Consequently, it is unclear whether the symptomatic patients may have sustained a brain lesion similar to the complicated patients reported by Williams et al. In any case, Bohnen and co-workers provide further evidence for heterogeneity in the mild head injury population. Elucidation of the basis of this heterogeneity in outcome awaits further research.

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If repeated knock-outs by blows to the head lead to subsequent mental deterioration (1), does one transient knock-out produce any mental decline? Monkeys subjected to a solitary blow with momentary loss of consciousness suffer disruption of axons in their brain (2). Somewhat more severe but classifiably mild head injuries do appear to produce long-term mental deficits (3). Such considerations suggest that head injuries producing brief (e.g., seconds, an hour) loss of consciousness can produce detectable long-term decrements in mental performance.

The current manuscript is a welcome addition to an emerging body of evidence that suggests that such "minor" head injuries may have long-term sequelae. Bohnen, Jolles, and Twijnstra offer us data indicating that such is the case, and provide an informative review of the literature. Their data concern patients who incurred transient loss of consciousness of no more than 15 minutes. They compare the patients who complained of two or more postconcussive symptoms 6 months later with those who did not. Additional comparison is made with a group selected to be matched controls. Patients with persistent symptoms at 6 months did less well than either of the other groups on a small, predetermined group of neuropsychological tests. The results suggest that minor head injuries can result in longer term mental performance deficits.

The caveats to this study are well discussed. They include the possibility that the symptomatic postconcussive group was already emotionally and/or cognitively different before the head injury. Furthermore, it is possible that neuropsychological test performance was diminished by the patients' symptoms or some other related noncognitive factor. It must also be noted that none of the patients studied appears to have had computed tomographic scans done at the time of injury.

If, indeed, such minor head injuries prove to be capable of producing measurable deficits, we will have to grapple with the functional costs and implications of these findings in the areas of head injury prevention and rehabilitation.

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