

Neuropsychological and neurophysiological evaluation of cognitive deficits related to the severity of traumatic brain injury

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Abstract. – **OBJECTIVES:** Cognitive impairment is a common permanent sequela of traumatic brain injury (TBI). Its objectivization is based on neuropsychological and neurophysiological assessment. Neuropsychological evaluation requires a test battery, whereas for neurophysiological assessment the most significant is application of P300 Event-Related Potentials (ERPs).

The aim of the study was to determine whether it is possible to differentiate between degrees of severity of TBI on the basis of neuropsychological and neurophysiological parameters.

PATIENTS AND METHODS: A total of 90 patients with closed TBI were evaluated at least one year after trauma. Subjects were classified into three groups according to severity of TBI: mild, moderate and severe. In all subjects the Intelligence Test, the Wisconsin Card Sorting Test (WCST) and P300 ERPs were performed.

RESULTS: General intelligence measures did not prove sensitivity enough to differentiate levels of severity of TBI, whereas the number of achieved categories on the WCST significantly discerned patients with mild and moderate TBI from patients with severe TBI. Perseverative errors significantly separated patients with mild TBI from patients with moderate and severe TBI. Non-perseverative errors significantly differentiated only patients with mild TBI from patients with severe TBI. Finally, P300 latency (EPLAT) significantly differentiated patients with mild TBI from patients with moderate and severe TBI.

The results show that the applied test battery can discriminate between different levels of severity of TBI and emphasize the importance of P300 ERP in the evaluation of patients with brain injury.

CONCLUSIONS: Our findings indicate that the WCST and ERP P300 latency have a significant role in the assessment of cognitive deficit related to TBI.

Key Words:

Traumatic brain injury, Cognitive disturbances, Neuropsychological testing, Event related potentials (P300).

Introduction

Cognitive impairment is a frequent consequence of traumatic brain injury (TBI) that most frequently manifests as deficits in attention, information processing speed, speech, conceptual thinking, memory, in particular episodic and working memory, executive functions, and visuospatial processing¹⁻⁴.

For long-term impairment after a severe TBI the evidence is clear, whereas for a moderate TBI the evidence is only suggestive⁴. The difference in the strength of evidence is mainly due to inconsistency of diagnostic criteria for moderate TBI employed in different studies. As regards long-term cognitive impairment following a mild TBI there is little evidence and numerous dilemmas complicate the research of this problem, such as subtlety of manifestations of cognitive deficits and the presence of various factors that may mimic or mask cognitive deficits⁵.

Assessment of cognitive function following a TBI involves neuropsychological and neurophysiological objectivization of impairment. For the purpose of adequate neuropsychological assessment, neuropsychological test batteries are used. General measures of cognitive function, such as intelligence tests, are frequently insufficient, because they can only partially assess severity of injury. Therefore, they are recommended to be used only as part of a more comprehensive neuropsychological battery⁶. The neuropsychological functions most impaired in TBI are executive functions. The impairment of executive functions is manifested in difficulties in formulating goals, planning and organizing goal-directed activities, and consequently in inability to efficiently and completely carry out an activity or control an activity and correct possible observed errors⁷. Furthermore, executive dysfunction involves impairment of the abstract think-

ing, perseverance and inability to apply available cognitive skills. Therefore, assessment of the cognitive status after a brain trauma requires assessment of executive functions⁸.

Neurophysiological studies have shown that reduced information processing speed is a fundamental cognitive deficit that may result in impaired attention and memory⁹. This is known as the cognitive slowing theory^{10,11}. For the purposes of explaining the pathophysiological basis of this theory, Event-Related Potentials (ERPs) have often been used, because their latency is considered to reflect the basic time of central information processing. According to the theory of cognitive slowing, P300 latency, the most frequently used ERP, is usually prolonged in patients with TBI¹²⁻¹⁸. Thus, P300 latency may be considered a diagnostic or screening test for cognitive dysfunction.

The aim of this study was to assess the possibility of differentiating severity of TBI on the basis of psychological and neurophysiological parameters. The following measures were compared in subjects with severe, moderate and mild TBI: global intellectual function (global, verbal and manipulative IQ), subtests of the intelligence test that are considered the most sensitive to organic injury (Digit Span and Block Design), the Wisconsin Card Sorting Test, and P300 cognitive evoked potentials. Since all of these tests are sensitive to age, and all psychological measures are dependable on education, our objective was to control age and education, in order to determine the potential power of the stated diagnostic methods, independently of the effects of these relevant variables.

Patients and Methods

Sample

The study included 90 patients who suffered a closed craniocerebral trauma, initially observed

or hospitalized at the Clinic for Surgery, Clinical Center of Vojvodina in Novi Sad. The neuropathological lesion was verified by brain computerized tomography (CT). Assessment of cognitive deficit was in all subjects performed at least one year after trauma. Sample included subjects of both genders, aged 18-60 years. Subjects with repeated TBI, neurological or psychiatric disease or a severe chronic illness were excluded from the study.

Patients were classified into three groups with regard to severity of TBI assessed according to the initial Glasgow Coma Scale scores, duration of loss of consciousness, and duration of post-traumatic amnesia^{19,20}. There were 41 patients with mild trauma, 27 with moderate trauma, and 22 with severe trauma. Age and education level for the three groups are shown in Table I.

In all patients a neuropsychological testing (Intelligence Test and the WCST) and P300 event-related potential recording were performed. Written informed consent was obtained from all subjects prior to the study. Approval for this research was obtained from the local Ethics Committee.

Methods

The Intelligence Test, developed according to Wechsler's paradigm and standardized on the Serbian population was administered²¹. Five scores from the test were used in the research: global IQ, manipulative IQ, verbal IQ, the score on the Digit Span subtest that measures attention, concentration, mental control, and the score on the Block Design subtest that measures problem solving, visuospatial and motor skills. These two subtests were chosen as the best indicators of cognitive deterioration due to organic brain pathology.

The Wisconsin Card Sorting Test²² is used in the evaluation of mental flexibility, i.e., ability to maintain and shift mental sets, perseverance and

Table I. Means and standard deviations for age and education in the three groups of patients with different severity of trauma.

	Age (year)		Education (years)		N
	Mean	SD	Mean	SD	
Mild TBI	35.24	13.43	11.00	2.33	41
Moderate TBI	42.11	12.64	10.81	3.44	27
Severe TBI	38.82	12.49	10.73	2.85	22
All groups	38.18	13.17	10.88	2.80	90

TBI = traumatic brain injury; N = number; SD = standard deviation

concept formation. In our study we used the following scores: perseverative errors, non-perseverative errors, and number of categories achieved.

Evoked Potentials Recordings and Analysis

P300 event-related potential (ERP) recording was carried out at the Clinic for Neurology of the Clinical Center of Vojvodina, by means of a 4-channel system for evoked potentials (EPs), type "Mystral" (Medelec Ltd, Surrey, UK). The classic auditory "odd-ball" paradigm (stimuli of two different frequencies) was used. A high-frequency tone (3000 Hz) was the "target" stimuli (probability: 15%) and a low frequency tone (1000Hz) was the "non-target" stimuli (probability: 85%) at 70dB sound pressure level (SPL). The frequent-rare sequence was randomly applied. All patients were instructed to count the "target" stimuli mentally. The subject had to tell the examiner the number of "target" tones heard upon completion of the task.

P300 were recorded from a scalp electrode placed on Cz (defined in "10-20" International system), ground electrode was placed at Fz and reference electrodes were placed at ear lobes at position of A1 and A2 (linked). One hindered twenty eight artifact-free potentials following the "target" stimuli were averaged. P300 amplitude and latency were measured for analysis.

In our study P300 latency was identified (at Cz) as the largest positive peak (range: 250-450 ms) occurring after the N1, P2 and N2 ERP components obtained from the "target" stimulus presentation. Amplitude (μV) was quantified using peak-to-peak (N2-P3) measurement.

Statistical Analysis

Analysis of covariance (ANCOVA) was performed for comparison of mean achievements on psychological and physiological measures in the three groups with different TBI severity, while controlling for age and education. Scheffe test was used for contrasting of single mean results of all dependent measures. Descriptive statistics (means and standard deviations) was used for presentation of the dependent measures, as well as age and education. $p < 0.05$ was considered statistically significant.

Results

Three groups of patients with different severity of trauma were compared on different diag-

nostic measures using Analysis of Covariance (ANCOVA); age and education were entered as covariates.

Both covariates were significantly related to dependent variables (for age, $F(10, 76)=5.52, p < 0.001$; for education, $F(10,76)=2.85, p < 0.001$), but groups with different trauma severity still differed significantly ($F(20,152)=2.28, p = 0.003$).

Univariate tests indicated that the covariate age was significantly related to Digit Span, Block Design, all three measures on the WCST, and evoked potential latency (EPLAT). The other covariate, education, was significantly related to all measures, except the evoked potential (EP) measures. Finally, when controlling age and education, the groups with different levels of trauma severity still differed, but only in the three WCST measures and EPLAT.

Scheffe test of post hoc comparisons was used to reveal which groups could be differentiated through which test indicators. Results suggested that the number of categories achieved on the WCST differentiated those with mild and moderate trauma from those with severe trauma (moderate vs. severe $p = 0.007$; mild vs. severe $p < 0.001$). The difference between the groups with mild and moderate trauma was not significant ($p = 0.06$). On the contrary, perseverative errors on the WCST differentiated those with mild trauma from those with moderate and severe trauma (mild vs. moderate $p = 0.009$; mild vs. severe $p < 0.001$). The third WCST measure, non-perseverative errors, differentiated only those with mild from those with severe trauma ($p = 0.02$).

Finally, P300 ERPs latency (EPLAT) differentiated the group with mild trauma from the other two groups (mild vs. moderate $p = 0.004$; mild vs. severe $p = 0.03$). Table II shows descriptive results for all dependent measures.

Discussion

The overall results of testing the differences between the studied groups show that the applied test battery can differentiate between different levels of severity of TBI. However, different measures within the battery showed different levels of sensitivity.

As expected, there was a significant effect of age on all variables, and a significant effect of education on psychological tests. Despite this, some measures showed sufficient sensitivity in differentiation not only between mild and severe

Table 1. Means and standard deviations for age and education in the three groups of patients with different severity of trauma.

	Mild TBI		Moderate TBI		Severe TBI	
	Mean	SD	Mean	SD	Mean	SD
IQ global	103.32	16.82	104.22	14.59	103.73	14.02
IQ verbal	99.93	16.76	100.11	14.36	100.05	14.55
IQ manip.	106.93	16.47	107.96	17.83	103.68	21.76
Digit span	8.71	3.14	6.78	2.29	7.59	3.23
Block design	10.51	3.26	9.63	2.68	9.91	3.52
Categories	4.95	1.55	4.00	2.13	2.50	2.18
Perseverative	6.39	9.60	18.96	21.47	26.00	21.70
Non perseverative	30.98	14.01	34.00	14.53	41.14	15.55
EPAML (μ V)	14.02	7.61	11.22	5.66	11.55	4.81
EPLAT (ms)	326.83	36.76	355.67	42.32	350.55	31.71

Note: EPAML = amplitude of P300 ERP; EPLAT = latency of P300 ERP

TBI, but also in finer differentiation between mild, moderate and severe TBI.

General intelligence measures did not prove sufficiently sensitive for differentiating between levels of impairment. As regards global IQ indicators, this result is not surprising since these measures are composites of different specific indicators, some of which are known to be stable in relation to organic factors and may even be associated with compensatory mechanisms used by patients with organic injury to overcome their deficits. The absence of significant differences in global intellectual functions between the groups is, on the other hand, a good basis for comparison of the groups with regard to other features, since this result indicates that there were no differences in the general intellectual level between the groups.

A surprising finding was that specific intelligence subtests did not show sensitive even for differentiation between severe and mild injury. Digit Span is a subtest that was shown to be sensitive enough to differentiate between patients with organic injury and subjects without damage in many studies. For example, the Vocabulary and Digit Span proved applicable in differentiating patients with moderate and severe TBI from persons with financially compensable mild TBI²³. However, in a study by Cicerone and Azulay²⁴ comparing abilities of several attention measures to differentiate between persons with and without TBI, Digit Span showed poor classifying characteristics (sensitivity, specificity, efficacy, positive and negative predictive value and diagnostic accuracy) related to the most of the other measures. Our study indicated that measures based on processing speed, i.e. central executive aspect of working memory have

a considerable advantage in this kind of diagnostics. Since Digit Span does not belong to this group of tests, but places demands primarily upon selective-inhibitory aspects of attention, it proved, similarly as in our study, insufficiently sensitive to discriminate between different levels of severity of TBI. Also noteworthy is the significant effect of age on this subtest, which if not controlled may produce significant differences that are not real differences in attention and memory function.

In our work, the Block Design subtest did not show the ability to differentiate between groups with different levels of severity of TBI, either with or without controlling the variables age and education. This result is surprising since Wechsler's test is considered a measure of executive function. Different sensitivities of Wechsler's test and the WCST for detection of cognitive deficits in TBI speak in favor of the theories that propose the existence of a number of executive functions rather than a general one, as suggested by some factorial and neuroimaging studies²⁵. In our report, this test was not only unable to differentiate between levels of severity of TBI, but its result indicated that patients with TBI were not significantly impaired in cognitive functions measured by Block Design, since their performance was at the average level.

On the other hand, the WCST showed the ability to discern between different levels of severity of TBI, even with its less specific indicators such as number of categories achieved. Although significantly associated with both age and educational level as an indicator of premorbid intellectual function, this test showed the ability to differentiate more subtle differences in TBI severity, when these two variables are controlled.

The number of categories achieved on the WSCT significantly separated patients with mild and moderate TBI from patients with severe TBI. Patients with severe TBI formed almost two times fewer categories than patients with mild TBI and 1.6 times fewer than patients with moderate TBI.

Perseverative errors on the WSCT significantly differentiated patients with mild TBI from patients with moderate and severe TBI, with patients with mild TBI making three times fewer perseverative errors compared with patients with moderate TBI and four times fewer perseverative errors compared with patients with severe TBI. This means that patients with moderate and severe TBI show considerably higher mental rigidity and inability to form a new conceptual unit. Perseverative errors proved to be a more sensitive parameter than number of categories and non-perseverative errors, since a significant number of perseverative errors occurred already in mild trauma.

Non-perseverative errors differentiated significantly only patients with mild TBI from patients with severe TBI, and the number of non-perseverative errors was higher for one third in patients with severe TBI. It can be concluded that subjects with severe TBI showed prominent mental rigidity, i.e. inability to form and maintain a mental set, difficulty in concept formation, and perseverance.

On the basis of the statistically significant differences between the groups in number of categories achieved, perseverative and non-perseverative errors, it may be concluded that subjects with severe TBI show characteristics that may be explained as part of a more comprehensive dysexecutive syndrome. This involves primarily executive function deficits, difficulties in setting goals, planning, carrying out and controlling an activity. These results agree with the findings that activation of regional blood flow increased circulation in the prefrontal area in healthy subjects and decreased blood flow in the lower part of the left frontal lobe in patients with closed brain injury²⁶.

Our study emphasizes the importance of P300 ERP in the evaluation of patients with brain injury, because of its sensitivity in the detection of specific and subtle cognitive disturbances. Although both amplitude and latency were used, the latter was more sensitive. Whereas decreased amplitude was the only measure that indicated cognitive impairment, a prolongation of P300 latency is also sensitive to the degree of deficit. The results of our study are in line with those of Cooper

et al²⁷ reporting the existence of changes in P300 amplitude and latency in patients with cognitive deficit after brain concussion. These changes were found in all cases, regardless of the severity of injury. The most frequently reported effect of closed head injury on ERPs was a reduction in the amplitude of auditory P300²⁸. A majority of studies have also reported prolonged auditory P300 latencies. Moreover, there is evidence that more severe damage is associated with greater delays in the latency of P300²⁹⁻³¹. Increases in P300 latency have been reported to be proportional to the severity of injury³¹.

Conclusions

As regards neuropsychological assessment of cognitive deficits, our data show that the WCST has a great significance for detecting cognitive impairment, as well as for assessing the severity of TBI. As regards neurophysiological assessment, our results confirm the significance of ERP P300 in terms of a significantly increased response latency that correlates with severity of TBI.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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