

Cognitive deficits in patients with mild to moderate traumatic brain injury

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ABSTRACT

Traumatic brain injury (TBI) is one of the most frequent causes of brain damage. Cognitive deficits reported in the literature after moderate to severe TBI include memory, language, executive functions, attention and information processing speed impairments. However, systematic studies on patients with mild TBI are scarce although neuropsychological changes are present. **Objective:** To investigate the cognitive functioning of patients with mild to moderate TBI. **Method:** We evaluated 12 patients with mild to moderate TBI using a comprehensive protocol (PN01) of neuropsychological tests. **Results:** There were significant deficits of episodic memory including immediate and delayed verbal memory recall, verbal recognition, immediate and delayed visual memory recall, naming, verbal fluency and information processing speed. **Conclusion:** These results emphasize the importance of comprehensive neuropsychological assessments even in cases of mild TBI in order to identify impaired and preserved functions providing adequate managing including rehabilitation programs for each case.

Key words: traumatic brain injury, cognitive deficits, mild to moderate level.

Alterações neuropsicológicas em pacientes com traumatismo crânio encefálico leve-moderado

RESUMO

Traumatismo cranioencefálico (TCE) é uma das causas mais frequentes de lesão cerebral. São relatados na literatura déficits cognitivos após TCE moderado-grave relacionados à memória, linguagem, funções executivas, atenção e velocidade de processamento de informações. Estudos em pacientes com TCE leve são escassos embora alterações neuropsicológicas sejam encontradas nestes pacientes. **Objetivo:** Investigar o funcionamento cognitivo de pacientes com TCE leve e moderado através de um protocolo abrangente (PN01) de testes neuropsicológicos. **Método:** Foram avaliados 12 pacientes com TCE leve e moderado. **Resultados:** Foram identificados déficits graves de memória episódica verbal para evocação imediata, tardia e de reconhecimento, de memória episódica visuo-espacial para evocação imediata e tardia, nomeação, fluência verbal nominal e velocidade de processamento de informações. **Conclusão:** Os resultados do estudo argumentam a favor da importância de avaliação neuropsicológica abrangente mesmo em casos de TCE leve a fim de se identificar funções comprometidas e preservadas, proporcionando condutas e programas de reabilitação adequados a cada caso.

Palavras-chave: traumatismo crânio encefálico, déficits cognitivos, grau leve e moderado.

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To the World Health Organization (WHO), traumatic brain injury (TBI) is a public health issue¹, because it is one of the largest causes of brain injury, resulting

in high rates of morbidity and mortality²⁻⁴. However, with modern medicine and the progress of techniques for acute treatment of TBI victims, patient survival rate is in-

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creasing. Consequently, the number of patients who survive with cognitive impairment is growing³⁻⁵.

TBI severity (mild, moderate, severe) depends on a number of factors, including type of injury (diffuse or focal), extension and location, resulting in different patterns of damage². The Glasgow Coma Scale (GCS) is one of the most commonly used tools to evaluate the level of TBI severity⁶. It is based on the score for best motor and verbal response as well as minimum stimulus to cause eye opening (Severe Level: 3 to 8; Moderate Level: 9 to 12; and Mild Level: 13 to 15, according to the Advanced Trauma Life Support (ATLS), American College of Surgeons Committee on Trauma, Chicago, 2004).

The frontal lobes (especially the orbitofrontal region) and temporal lobes are particularly vulnerable to lesions caused by TBI^{2,5,7-9} due to their neuroanatomical localization. Bigler⁵ emphasizes mesial temporal lobe vulnerability, especially the hippocampus, with its connections to the fornix, associated to persistent post-concussional syndrome. This syndrome may occur in approximately 15% of mild TBI cases, with changes in attention, memory, information processing speed and presence of fatigue, headaches, nausea, and emotional instability, even when evidence of lesion is not present in brain imaging. Some authors argue for functional factors and others for organic factors as the cause of these changes⁵.

Amongst neuropsychological impairments caused by mild and moderate TBI, reduction of information processing speed^{7,10-12} is frequently reported in literature and it may contribute to deficits in attention^{10,11}, orientation and executive functioning^{7,10-12}. Impairments of executive functions affect mental flexibility, planning, self-monitoring, and problem solving². These impairments can compromise other abilities, such as attention and memory^{13,14}. After the period of post-traumatic amnesia (PTA), patients who experienced severe TBI may present memory disorders of variable intensity¹⁵; damages of short term and long term^{7,9-11,16, 17} memory.

Changes in behavior and personality may be associated to TBI, such as reduction in motivation and self-esteem, difficulty with empathy⁷, emotional processing, loss of insight, psychosocial difficulties⁸, post-traumatic stress disorder, depression, anxiety, and fatigue^{5,7,8,12,18,19}.

Around two to five years after experiencing mild to moderate TBI, most patients remain stable, even though some of them present some cognitive difficulties, which may be observed in daily life tasks⁷.

Considering damage variability in cases of TBI², neuropsychological assessment should be comprehensive allowing for a systematic analysis of various cognitive functions, and providing a background of global functioning of patients. Studies with systematic neuropsychological assessments in patients with mild-moderate TBI are rare.

Therefore, this study aimed at investigating the presence of cognitive changes in patients with mild to moderate TBI as well as associations between these changes and the localization of brain lesions.

METHOD

Subjects

The subjects were recruited from database that contains all neurological patients treated by the Neuropsychology staff at Hospital das Clinicas outpatient and ward. Sixteen patients were evaluated, but 4 were excluded because they did not correspond to the inclusion criteria: mild to moderate TBI and after 1 year of TBI.

The sample included 12 subjects with mild to moderate TBI. Patients with less than 1 year of TBI, with comorbidity or other neurological or healthy problems, including use of drugs and alcohol were excluded.

The Department of Neurology Ethics Committee FMUSP and CAPPesq (086/06) approved the project and all participants signed an Informed Consent Term.

Instruments

The main instruments consisted of clinical interview and neuropsychological tests. The aim of each one is described below.

PN-01 Protocol

Vocabulary (Wechsler Adult Intelligence Scale - Wais III)²⁰: To investigate verbal abilities and derivation of word meaning, which, together with Matrix Reasoning test, provides an estimate Intelligence Quotient (IQ)²¹;

Matrix Reasoning (Wechsler Adult Intelligence Scale - Wais III)²⁰: Non-verbal abilities and non-verbal logic reasoning, which provide an estimate IQ;

Hopkins Verbal Learning Test - Revised (HVLT - R)²²: Episodic memory with immediate, delayed recall and recognition of verbal information;

Brief Visuospatial Memory Test - Revised (BVMT - R)²³: Episodic memory with immediate, delayed recall and recognition of visual-spatial information;

Digits (Wechsler Adult Intelligence Scale - Wais III)²⁰: Short term memory and working memory;

Wisconsin Card Sorting Test (WCST-Nelson version)²⁴: Mental flexibility, abstraction and problem solving;

FAS (COWA - Controlled Oral Word Association)²⁵: Nominal verbal fluency, aspect related to executive functions, providing evidence of the ability to inhibit irrelevant responses;

Category - animals (COWA - Controlled Oral Word Association)²⁵: Categorization fluency associated to semantic memory;

Boston Naming Test (BNT)²⁵: Language function: naming;

Symbol Digit Modalities Test²⁶: Information processing speed;

Visual Object and Space Perception Battery (Vosp)²⁷: Visuoperceptive and visuospatial functions.

Procedure

All patients were evaluated at the outpatient clinic of University of São Paulo Neurology Division, Medical School using the PN-01 protocol. The main functions assessed included memory, language, information processing speed, visuospatial, visuoperceptive, executive and intellectual functions. The assessment lasted for two and a half hours and was carried out in one day.

Results were analyzed according to norms of each standardized test taking into account sample age, gender and years of education. Descriptive analyses were carried out using SPSS v. 10 (means and standard deviations) of percentiles obtained from the norms of each test. This is a descriptive study due to the very small sample, that would not allow for a robust statistical analysis.

RESULTS

Subjects aged between 25 and 68 years, mean (M)=39.75 and standard deviation (SD)=14.37, 2 to 13 years of formal education (M=8.33 and SD=3.39) were evaluated from November 2006 to May 2008.

All subjects were evaluated with the GCS (M=12.75 and SD=2.56), 6 subjects were classified as mild TBI (M=14.8 and SD=0.45) and 6 as moderate TBI (M=11.28 and SD=2.43). The subjects were evaluated between 12 and 19 months of TBI (M=14.08 and SD=2.02).

Amongst the patients studied, 8 presented left hemisphere and 4 right hemisphere lesions. The majority of the patients presented lesions to frontal region (50%), as described in Table 1.

The main results showed a significant impairment on their information processing speed (M=5.3 and SD=14). There were 10 patients showing this deficit accounting for 83% of the sample. The second most affected function was verbal episodic memory recognition, with 9 (75%) patients presenting significant deficits (M=9.85 and SD=19.9). Eight (67%) patients presented impairments in immediate verbal recall (M=10.2 and SD=21.9), delayed verbal recall (M=9.55 and SD=19.5) and naming (M=18.4 and SD=31.8). Seven (58%) subjects showed an impairment in visuospatial immediate recall (M=20.6 and SD=28.5) and nominal verbal fluency (M=8.4 and SD=15). Six (50%) patients presented deficits on visuospatial delayed recall (M=28.7 and SD=38.6). Results can be seen in Table 2.

In terms of the associations between cognitive changes and localization of brain lesions, most patients with left frontal lesions presented important impairments especial-

Table 1. Sample distribution according to the area and hemisphere of the lesion.

Lesion site		N	%
Parietal	R	1	8.33
Temporal	R	1	8.33
	L	1	8.33
Frontal	L	4	33.36
FT	R	1	8.33
	L	1	8.33
FTP	R	1	8.33
TP	L	1	8.33
PO	L	1	8.33
Total			100
Right hemisphere - total		4	33.36
Left hemisphere - total		8	66.64
Total			100

R: right hemisphere; L: left hemisphere; FT: fronto-temporal; FTP: fronto-temporo-parietal; TP: temporo-parietal; PO: parieto-occipital.

ly on verbal episodic memory (delayed recall and recognition) and presented normal performance on visuospatial episodic memory (recognition), short-term memory, non-verbal skills and Intellectual Quotient (Intellectual Functions) as described in Table 3.

Patients with right and left hemisphere temporal lesions presented moderate to severe deficits in most cognitive functions. The results can be seen in Table 4.

Significant impairments were observed on nominal verbal fluency, naming, and information processing speed in patients with left and right frontal-temporal lesions.

The patient with right parietal lesion showed moderate to severe deficits in most of the functions evaluated, with performance within an expected range only on naming and non-verbal intellectual abilities.

The patient with left temporal-parietal lesion presented severe deficits in verbal episodic memory (immediate, delayed recall and recognition), naming, categorical verbal fluency, information processing speed and normal performance on visuospatial immediate and delayed recall and recognition, short-term memory and visuoperceptive functions.

The patient with right frontal-temporal-parietal lesion had a moderate to severe impairment on all functions evaluated, except for visuoperceptive functions.

The patient with left parietal-occipital lesion showed a severe difficulty on information processing speed and nominal verbal fluency and moderate deficit on intelligence function. His memory, visuoperceptive and visu-

Table 2. Performance average percentiles and standard deviation for right and left hemisphere lesioned patients concerning cognitive functions and percentile of classified subjects in accordance to standard testing used.

Cognitive functions	Cognitive tests	Average of percentile (SD)	Right hem. Average of percentile (SD)	Left hem. Average of percentile (SD)	Classification performance - N (%)				
					Preserved	Mild deficit	Moderate deficit	Severe deficit	
Verbal episodic memory									
Immediate recall	HVLT-R	10.2 (21.9)	0.1 (0)	15.3 (25.8)	1 (8)	2 (17)	0	8 (67)	
Delayed recall	HVLT-R	9.55 (19.5)	3.08 (5.95)	12.8 (23.4)	2 (17)	1 (8)	1 (8)	8 (67)	
Recognition	HVLT-R	9.85 (19.9)	3.28 (4.55)	13.1 (24)	2 (17)	1 (8)	0	9 (75)	
Visuospatial episodic memory									
Immediate recall	BVMT-R	20.6 (28.5)	3.8 (6.81)	28.9 (31.8)	4 (33)	1 (8)	0	7 (58)	
Delayed recall	BVMT-R	28.7 (38.6)	3.75 (6.84)	41.2 (42.3)	4 (33)	2 (17)	0	6 (50)	
Recognition	BVMT-R	15 (10.74)	7.5 (2.88)	18.75 (11.39)	5 (42)	2 (17)	5 (42)	0	
Short-term memory									
Immediate and operational	Digits	35.5 (35.3)	12.8 (7.5)	46.9 (38.6)	4 (33)	4 (33)	3 (25)	1 (8)	
Language									
Naming	Boston NT	18.4 (31.8)	16.6 (33)	19.3 (33.4)	3 (25)	1 (8)	0	8 (67)	
Executive functions									
Nom. v. fluency	FAS	8.4 (15)	2.8 (3.6)	11 (19)	1 (8)	2 (17)	2 (17)	7 (58)	
Categ v. fluency	Category	18.7 (24.25)	3.42 (5.72)	26.34 (26.64)	6 (50)	1 (8)	2 (17)	3 (25)	
Mental flexibility	WCST	32 (29)	33 (36)	26 (28)	5 (42)	1 (8)	2 (17)	4 (33)	
IPS	Symbol Digit	5.3 (14)	0.1 (0)	7.9 (17)	1 (8)	1 (8)	0	10 (83)	
Intellectual functions									
Verbal skills	Vocabulary	22 (29)	14 (17)	28 (34)	4 (33)	2 (17)	2 (17)	4 (33)	
Non-verbal skills	Matrix reasoning	38 (37)	28 (36)	43 (39)	6 (50)	1 (8)	3 (25)	2 (17)	
IQ		24 (29)	11 (17)	30 (33)	5 (42)	0	5 (42)	2 (17)	
Visuo-perceptive functions									
Incomplete Letters	VOSP	44.8 (34.1)	25.8 (35.8)	54.3 (31.1)	10 (83)	0	0	2 (17)	
Position Discrimination	VOSP	44 (26.8)	23.6 (26.1)	54.3 (21.9)	8 (67)	2 (17)	1 (8)	1 (8)	

SD: standard deviation; Hem.: hemisphere; N: number; IPS: information processing speed; IQ: intellectual quotient; HVLT-R: Hopkins Verbal Learning Test - Revised; BVMT-R: Brief Visuospatial Memory Test - Revised; Boston NT: Boston Naming Test; Nom. V. fluency: Nominal verbal fluency; Categ. V. fluency: category verbal fluency; WCST: Wisconsin Card Sorting Test; VOSP: Visual Object and Space Perception Battery.

spatial functions, mental flexibility and categorical verbal fluency were preserved.

DISCUSSION

This study aimed at evaluating overall cognitive performance of patients diagnosed with mild to moderate TBI, by means of The PN-01, a systematic protocol. The main results showed significant deficits in information processing speed, memory (verbal and visuospatial), language (naming) and executive functions.

Episodic memory and executive processes related to encoding, storage and retrieval, together with strategy formulation, were the main altered cognitive functions. In the literature, these changes are observed especially in moderate to severe cases of TBI¹³.

Most patients presented some level of difficulty, from mild to severe, on the administered tests. Nevertheless, in two of the 16 functions evaluated, they showed normal performance including on visuo-perceptive and visuospatial functions. This finding can be possibly explained by

Table 3. Average percentile and standard deviation and classification performance of patients with left frontal lesions concerning cognitive functions.

Cognitive function	Average of percentile (SD)	Frontal left lesions			
		Classification performance - N (%)			
		Preserved	Mild deficit	Moderate deficit	Severe deficit
Verbal episodic memory					
Immediate recall	23.3 (35.9)	1 (25)	0	2 (50)	2 (50)
Delayed recall	6.9 (13.4)	1 (25)	0	0	3 (75)
Recognition	0.22 (0.25)	0	0	0	4 (100)
Visuospatial episodic memory					
Immediate recall	27.9 (33.6)	2 (50)	0	0	2 (50)
Delayed recall	34.8 (40.1)	2 (50)	0	0	2 (50)
Recognition	21.5 (11)	3 (75)	0	1 (25)	0
Short-term memory					
Immediate and operational	71.2 (38.3)	3 (75)	1 (25)	0	0
Language					
Naming	26.1 (43.1)	1 (25)	1 (25)	0	2 (50)
Executive functions					
Nominal verbal fluency	21.5 (22.6)	1 (25)	1 (25)	0	2 (50)
Category verbal fluency	14.8 (7.1)	2 (50)	1 (25)	0	1 (25)
Mental flexibility	28.8 (24.6)	2 (50)	1 (25)	0	1 (25)
IPS	15.1 (23.8)	1 (25)	1 (25)	0	2 (50)
Intellectual functions					
Verbal skills	43.7 (41.98)	2 (50)	1 (25)	0	1 (25)
Non-verbal skills	57.7 (40.1)	3 (75)	0	1 (25)	0
IQ	46.2 (39.3)	3 (75)	0	1 (25)	0
Visuoperceptive functions					
Incomplete letters	63.8 (24.5)	4 (100)	0	0	0
Position discrimination	46.5 (30.9)	3 (75)	0	0	1 (25)

SD: standard deviation; IPS: information processing speed; IQ: intellectual quotient.

the preservation of occipital and posterior brain areas in many of the patients.

Most patients had frontal and temporal lesions and these regions are known to be particularly vulnerable to cognitive deficits related to memory and executive functions^{2,5-8,14}. Patients with left frontal lesions presented more difficulties on verbal episodic memory, on both recognition and delayed recall, as well as, on executive functions.

Patients with right and left hemisphere temporal lesions presented a moderate to severe difficulty in most cognitive functions as patients with right parietal, left temporal-parietal and right frontal-temporal-parietal lesions.

In addition, cognitive impairments were observed on nominal verbal fluency, naming and information process-

ing speed in patients with left and right frontal-temporal and left parietal-occipital lesions. These findings are in line with the literature showing participation of frontal and temporal areas in processes such as encoding, storage, and retrieval of information, in addition to, strategy and information processing speed¹³.

One limitation of the study is the relatively small number of samples, which did not allow for a robust statistical analysis. In spite of the small sample, it was possible to demonstrate that even mild to moderate TBI patients may show a range of mild to severe deficits in a variety of cognitive functions. It is possible that, since PN01 is a detailed and systematic protocol, the current study was able to show a wide range of cognitive impairments in these subjects.

The current results also suggest that a systematic neu-

Table 4. Classification performance of patients concerning localization of brain lesions and cognitive functions.

Cognitive function	Classification performance concerning lesion localization (Percentile)							
	Parietal	Temporal		Frontal temporal		FTP	TP	PO
	Right	Right	Left	Right	Left	Right	Left	Left
Verbal episodic memory								
Immediate recall	Sev. (<1)	Sev. (<1)	Sev. (1)	Sev. (<1)	Mod. (8)	Sev. (1)	Sev. (<1)	Mild (21)
Delayed recall	Sev. (<1)	Sev. (<1)	Sev. (1)	Mild (12)	Mod. (8)	Sev. (1)	Sev. (<1)	Pres. (66)
Recognition	Sev. (1)	Sev. (2)	Sev. (1)	Mild (10)	Pres. (50)	Sev. (<1)	Sev. (<1)	Pres. (54)
Visuospatial episodic memory								
Immediate recall	Sev. (1)	Sev. (<1)	Sev. (1)	Mild (14)	Sev. (<1)	Sev. (<1)	Pres. (50)	Pres. (69)
Delayed recall	Sev. (<1)	Sev. (<1)	Sev. (1)	Mild (14)	Mild (10)	Sev. (<1)	Pres. (96)	Pres. (84)
Recognition	Mild (10)	Mod. (5)	Mod. (5)	Mild (10)	Mod. (5)	Mod. (5)	Pres. (27)	Pres. (27)
Short-term memory								
Immediate and operational	Mod. (9)	Mild (24)	Sev. (<1)	Mild (9)	Mild (24)	Mod. (9)	Pres. (50)	Mild (16)
Language								
Naming	Pres. (66)	Sev. (<1)	Sev. (<1)	Sev. (<1)	Sev. (<1)	Sev. (<1)	Sev. (<1)	Pres. (50)
Executive functions								
Nominal verbal fluency	Sev. (2)	Mod. (8)	Sev. (<1)	Sev. (1)	Sev. (<1)	Sev. (<1)	Mod. (3)	Sev. (<1)
Category verbal fluency	Mild (12)	Sev. (<1)	Mod. (7)	Sev. (<1)	Mild (24)	Sev. (<1)	Sev. (<1)	Pres. (46)
Mental flexibility	Sev. (<1)	Pres. (50)	Sev. (<1)	Pres. (75)	Mod. (9)	Sev. (2)	Mod. (9)	Pres. (75)
IPS	Sev. (<1)	Sev. (<1)	Sev. (<1)	Sev. (<1)	Sev. (<1)	Sev. (<1)	Sev. (2)	Sev. (<1)
Intellectual functions								
Verbal skills	Sev. (2)	Mild (14)	Sev. (<1)	Pres. (37)	Mod. (9)	Sev. (1)	Pres. (34)	Mod. (4)
Non-verbal skills	Pres. (37)	Sev. (<1)	Mod. (5)	Pres. (75)	Pres. (84)	Sev. (1)	Mod. (5)	Mild (21)
IQ	Mod. (5)	Mod. (3)	Sev. (2)	Pres. (37)	Pres. (37)	Sev. (<1)	Mod. (9)	Mod. (9)
Visuoperceptive functions								
Incomplete letters	Sev. (<1)	Sev. (<1)	Sev. (<1)	Pres. (27)	Pres. (76)	Pres. (76)	Pres. (76)	Pres. (27)
Position discrimination	Mild (14)	Mod. (4)	Pres. (62)	Pres. (62)	Pres. (62)	Mild (14)	Pres. (62)	Pres. (62)

FTP: frontal temporal parietal lesion; TP: temporal parietal lesion; PO: parietal occipital lesion; IPS: information processing speed; IQ: intellectual quotient; Sev.: severe; Mod.: moderate; Pres.: preserved.

ropsychological evaluation could be a relevant investigation tool complementing clinical and neuroimaging exams by showing the cognitive impairments and preserved cognitive functions in this patient population. Systematic neuropsychological evaluations such as the PN-01 protocol, may help to monitor changes on neuropsychological profiles of these patients and non-pharmacological treatments, such as neuropsychological rehabilitation, focused on specific cognitive domains. This protocol could be an important instrument to help on evaluation of patients after traumatic brain injury.

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