Introduction

Traumatic Brain injury (TBI) is one of the most common neurological injuries. The World Health Organization estimates its incidence at 600 / 100,000 population in the world (1)little is known about outcome following mild TBI (mTBI and annual costs exceed US $ 500 billion in the United States of America (USA; (2). In the USA, 1.7 million people are diagnosed with TBI and 75% of them are classified as mild (3,4). Automobile accidents are the main cause in developing countries and falls from their own height are the main cause of TBI in underdeveloped countries (5). In Colombia, TBI frequency reaches up to 70% in the emergency room. Traffic accidents (51.2%) are the main cause, of which 43.9% are caused by motorcycles (6). According to the National Registry of Disability, 13% of people with disabilities are due to TBI from traffic accidents (7).

TBI can cause persistent physical, cognitive, and emotional sequels in the short and long term (2,3,5), but cognitive impairment is one of the most disabling sequelae. The main cognitive problems are alterations in verbal and non-verbal communication (8), problems of memory, attention, adaptive and emotional functioning (4), alterations in executive functions (9)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 and corticosensory and motor skills (10). Its evolution during the first year of trauma is fundamental to know the long-term prognosis of these patients (4) thus, early diagnosis is a key aspect to change the curse of these symptoms.

The degree of cognitive impairment of these patients is heterogeneous and depends on the type and severity of the injury (11). Several authors performed different studies to determine the profile and trajectory of cognitive deficits presented by TBI patients during the first year after trauma (8). Unfortunately, in Latin America cognitive performance studies use non validated neuropsychological tests for the sociodemographic characteristics of the population. This leads to misdiagnosed patients, who cannot get treatment sooner, and probably affecting their quality of life.

Despite of the development of cognitive performance assessments since the 70s (12), in Colombia the impact on quality of life among TBI patients is poor (10). Just recently, it was possible to use neuropsychological tests with normative data adjusted to the sociodemographic characteristics of the Colombian population (13) to assess cognitive performance. However, its usefulness and predictive value remains unknown. For this reason, this article aims to a) compare cognitive performance of a group of TBI patients and healthy-controls, and b) to address the accuracy of each of the test-scores contained in the large set of neuropsychological battery, to detect the most sensible ones to discriminate between TBI patients and healthy-controls.

Method

Participants

The sample consisted of 228 healthy controls (HC) and 228 participants with TBI from Colombia. Sixty-eight percent of the healthy sample were men, the mean age was 32.3 (SD=10.8), and the mean years of education was 12.5 (SD= 3,9). Among clinical sample, 73.2% were men, the mean age was 32.1 (SD=9.6), and the mean years of education was 12.1 (SD= 3,0). Forty-three percent (n=100) of the clinical sample have mild TBI, 38,6% (n=88) moderate TBI, and 17,5% (n=40) severe TBI. The two groups were matched by age, education, and sex (see Table 1).

To be eligible for the study, patients must meet the following inclusion criteria: (a) had a diagnosis of TBI, b) age 18 or older, c) be one-year post injury, d) have the TBI related to motorcycle accident. The healthy control group was selected from a multicenter data study that was done to get normative data in a study previously done in various cities of Colombia. The inclusion criteria of the

Table 1. Sample distribution by age, education, and gender.

Variable	Group	Mean (SD)	Median	Min - Max	U / X^2	p value
Age	HC	32,3 (10,7)	29.0	18.0 - 66.0	25485.0	.718
	TBI	32,1 (9,6)	29.0	18.0 - 66.0		
Education	HC	12,5 (3,9)	12.0	2.0 - 20.0	23850.0	.124
	TBI	12,1 (3,0)	12.0	2.0 - 19.0		
Gender	HC	Female 72 (31.6%); Male 156 (68.4%)			1.284	.303
	TBI	Female 61 (26.8%); Male 167 (73.2%)				

* *Note.* HC= Healthy Controls; TBI= patients with traumatic brain injury.

HC subject on that study were: a) Individuals between 18 to 95 years of age, b) spoke Spanish as their native language, c) had completed at least one year of formal education, d) were able to read and write at the time of evaluation, e) scored ≥23 on the Mini-Mental State Examination (MMSE) (14), f) scored ≤4 on the Patient Health Questionnaire–9 (PHQ-9) (15), and g) scored ≥90 on the Barthel Index (16). For further information regarding HC recruitment, see (17).

Individuals with TBI and Healthy controls were excluded if they: (a) had a history of neurological conditions, serious psychiatric disorders, alcohol and drug abuse, or developmental or learning disabilities.

Measures

The following neuropsychological test were used for this study:

Rey-Osterrieth Complex Figure Test (ROCF) (18). The ROCF is a measure of visual perception, visual-spatial constructional ability, and visual memory (18). The ROCF includes 18 elements, and two trials (Copy and three minutes Delayed Recall). The maximum score for each trial is 36. Two points are given when the element is correctly reproduced, 1 point when the reproduction is distorted, incomplete but placed properly, or complete but placed poorly; 0.5 point is credited when the element is distorted or incomplete and placed poorly. A 0 score is given when the element is absent or is not recognizable (19). The Spanish-language ROCF manual scoring guidelines were followed (20).

Modified Wisconsin Card Sorting Test (M-WCST) (21). The M-WCST consists of four stimulus cards and 48 response cards. Each card varies in shape (cross, circle, triangle or star), color (red, blue, yellow or green), and number (one to four). The first participant's response is always considered right, and during the administration, the examiner informs him/her whether their response is correct or incorrect until the participant accurately classifies six consecutive cards in each category. The test continues until all six categories are classified or until having used the whole card deck (21,22). Number of Categories, Perseverations, and Total Errors were analyzed for this study.

Trial Making Test (TMT A-B) (23). The TMT is a timed measure consists of two parts: TMT-A and B. In the TMT-A the participant must draw a line, as quickly as he/she can, connecting 25 numbers in ascending order, which are circled and randomly distributed on a sheet of paper. The task requirements are similar for the TMT-B, except that the person alternates between numbers and letters (1-A, 2-B, 3-C, etc.), the latter being significantly more difficult (24)education, and gender and to establish normative data.\nBACKGROUND: Prior research has suggested that these derived indices provide purer measures of the executive skills required to complete TMT-B. It has also been suggested that these scores can be effectively used to detect cognitive impairment, and that they are relatively free from the impact of age.\nMETHOD: Difference scores (B minus sign A. The score is the time that an individual takes to finish the task in each test. The time limit (maximum score) for TMT-A is 100 seconds and 300 seconds for TMT-B.

Phonological and Semantical Verbal Fluency Test. Verbal fluency tests (VFT) are commonly used measures both in clinical practice and research due to their sensitivity to brain damage. There are multiple variations of the VFT, but the two more commonly used paradigms measure letter and semantic fluency. In the letter VFT, participants are asked to produce as many words as possible beginning with a certain letter (in this study, the letter F/A/S/) within a 60 second time limit. In the semantic VFT, participants are required to produce as many words as they can belonging to a category (in this study, animals, fruits, and occupations), within the same 60 second timeframe. Participants are told to avoid proper names, augmentatives, and diminutives. The total score consists of the total correct answers per letter or category (25).

Symbol Digit Modalities Test (SDMT) (26). SDMT is a timed measure that requires participants to covert symbols (shaped geometric figures) into numbers, as quickly as possible. This study collected data for the written forms. When administering the test, confirmation that the subject is marking the answers in the order given and without skipping any lines is necessary. The subject's score is the number of correct substitutions made at an interval of 90 seconds (26).

Hopkins Verbal Learning Test - Revised (HVLT-R) (27). The list applied in the study was form 5, which contains a list of 12 semantically related words in three categories (professions, sports, and vegetables). Three trials of successive learning are presented where a list is read to the participant and the answers of each learning trial performed are recorded. Total Recall is the sum of words recalled correctly in the three trials. After 20-25 minutes, the Delayed Recall phase occurs where the subject is asked to recall all the words from the initial list that they can remember. Immediately before, Recognition phase starts, where the individual is prompted to determine which of the 24 words (12 target words and 12 false-positive) have appeared during the learning trial (27,28).

Procedure

Individuals with diagnosis of TBI were recruited from 5 Healthcare Institutions (IPS) in the Metropolitan Area of Medellín, Colombia. Initially, 10,203 medical records at these facilities were review it to see which patients were diagnosed with head trauma (codes S00-S09), according to the latest version of the International Classification of Diseases (ICD-10). Only 3,644 out of the 10,203 patients have complete medical information and confirmed diagnosis of TBI. Of these 3,644 individuals, only 642 have TBI due to a motorcycle accident and were selected to participate on the study. Of these 642, only 213 could be contact by telephone and 101 decide to participate on the study. A comprehensive battery of neuropsychological test including was administered to those participants that met the inclusion criteria. The administration of the tests was carried out by undergraduate psychology students under a supervision of a neuropsychologist. The Ethics Committee of the CES university approved the study.

Regarding HC, the sample came from a larger multi-center study to generate normative data for a neuropsychological battery for Colombian adult population (for further detailed information, see (17). Briefly, the University of Deusto (Bilbao, Spain) was the coordinator institution and the study was approved by its Ethics Committee. Participants underwent a neuropsychological battery in a single day. Before testing administration, each participant completed and signed an informed consent. Clinical sample was matched with HC sample according to sex, age and education, with a ±2 years of difference in the continuous variables. Thus, almost a completed match was reached (see table 1).

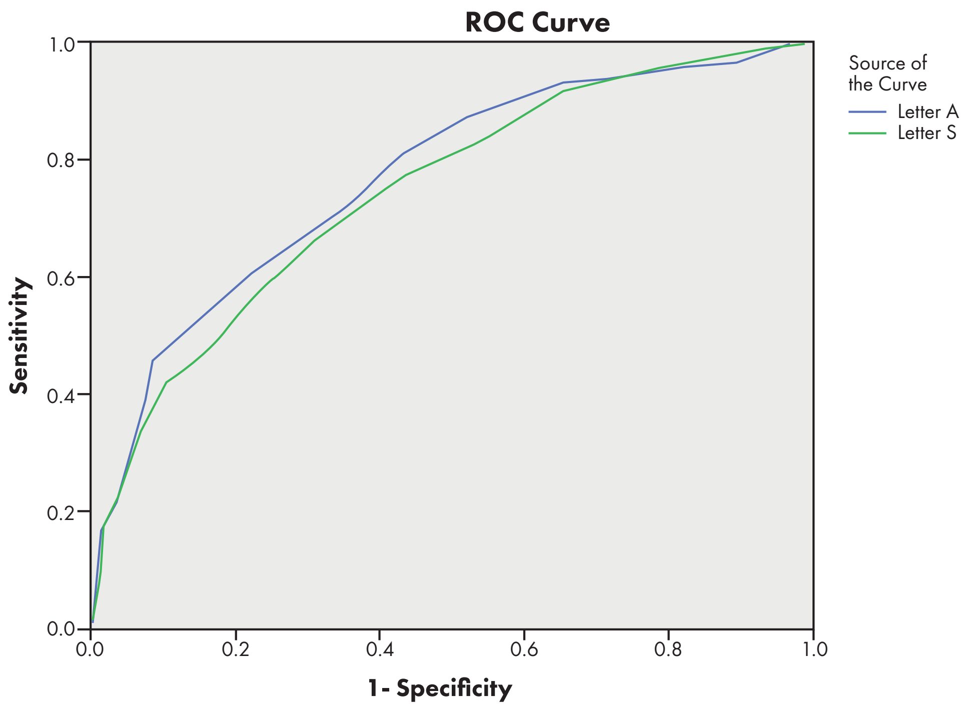

Figure 1. Area Under the Curve for Letters A and S.

Statistical Analyses

Kolmogorov Smirnov (KS) test was used to evaluate normality on the scores. If the scores had a normal distribution, t-test were run for group comparisons; and Mann–Whitney U test in absence of normal distribution. Since the sample size was large, Cohen r effect size was calculated for significant group differences in neuropsychological scores, with the cutoff point of .10 established as small, .30 as medium, and .50 as large effect size (29).

To determine which test-scores discriminate best between individuals with TBI and HC Receiver Operating Characteristics (ROC) analysis was conducted. The Area Under the Curve (AUC) was calculated as a measure of accuracy or precision (30,31) where the higher the value of the AUC, the better the instrument is at distinguishing the disease or phenomenon. Precision estimates based on this value are as follows: high accuracy if the value is 0.9 or higher, moderate accuracy if the value is 0.7 to 0.9, and low accuracy if the value is 0.5 to 0.7 (31,32).

Results

K-S analyzes showed that the scores did not have a normal distribution (*p's* <.05). Due to the lack of normality, nonparametric Mann–Whitney U test statistic was used. A series of Mann–Whitney U test showed that there were statistically significant group differences in the scores, where patients with TBI achieved lower scores that healthy participants in M-WCST Categories, ROCF – Memory, TMT – B, Letter F, Letter A, Letter S, Animals, Fruits, Profession, SDMT, HVLT-R Total Recall, Delayed Recall, and Recognition (*p's*<.001). No significant group differences were found in ROCF – Copy and TMT - A scores (*p's*>.05; see Table 2).

ROC curve showed different AUC levels. Letter A (AUC=.76), and letter S (AUC=.74) of the Phonological Verbal Fluency Test demonstrated moderate accuracy levels, while the rest of test-scores low accuracy levels (AUC's<.70), suggesting that scores in A and S letters have high accuracy to distinguish between individuals with and without TBI (see Figure 1).

Table 2. Difference between groups and Ander Under Curve values.

								Interval
M-WCST Categories	HC	6.0	0.0	6.0	19808.0**	0.192	.619**	(.567 - .671)
	TBI	4.0	0.0	6.0				
M-WCST Perseveration	HC	2.5	0.0	34.0	18343.5**	0.231	.646**	(.596 - .696)
	TBI	6.0	0.0	42.0				
M-WCST Total Errors	HC	9.0	0.0	41.0	20787.0**	0.177	.600**	(.548 -.652)
	TBI	12.5	0.0	43.0				
ROCF – Copy	HC	35.0	4.0	36.0	24796.5	0.035	.523	(.470 -.576)
	TBI	34.0	3.0	36.0				
ROCF – Memory	HC	23.0	2.0	36.0	16499.0**	0.306	.683**	(.634 - .732)
	TBI	17.0	0.0	34.0				
TMT -A	HC	46.0	17.0	100.0	25163	0.034	.515	(.462 - .568)
	TBI	47.0	18.0	100.0				
TMT – B	HC	85.5	33.0	300.0	19305.0**	0.191	.627**	(.576 - .678)
	TBI	107.0	24.0	300.0				
Letter F	HC	12.0	2.0	25.0	16091.0**	0.318	.690**	(.642 -.739)
	TBI	9.0	0.0	27.0				
Letter A	HC	13.0	3.0	25.0	12101.5**	0.458	.767**	(.724 - .810)
	TBI	9.0	0.0	23.0				
Letter S	HC	11.0	1.0	25.0	13313.0**	0.419	.744**	(.699 - .788)
	TBI	8.0	0.0	22.0				
Animals	HC	20.0	5.0	31.0	15906.5**	0.328	.694**	(.646 - .742)
	TBI	16.0	2.0	32.0				
Fruits	HC	15.0	1.0	23.0	17414.5**	0.281	.665**	(.616 - .714)
	TBI	13.0	2.0	25.0				
Profession	HC	14.0	2.0	25.0	17502.0**	0.295	.663**	(.614 - .713)
	TBI	12.0	0.0	24.0				
SDMT	HC	46.0	1.0	93.0	19261.0**	0.223	.629**	(.579 - .680)
	TBI	38.0	4.0	71.0				
HVLT-R Total Recall	HC	22.5	11.0	32.0	18252.0**	0.272	.649**	(.599 -.699)
	TBI	20.0	7.0	31.0				
HVLT-R Delayed Recall	HC	8.0	0.0	12.0	16064.5**	0.344	.691**	(.643 -.739)
	TBI	6.0	0.0	12.0				
HVLT-R Recognition	HC	12.0	8.0	12.0	16048.5**	0.365	.691**	(.643 -.740)
	TBI	11.0	3.0	12.0				

**Note.* HC= Healthy Controls; TBI= patients with traumatic brain injury.

Discussion

The objectives of this study were a) to compare cognitive performance of a group of TBI patients and healthy-controls, and b) to address the accuracy of each of the test-scores contained in the large set of neuropsychological battery, to detect the most sensible ones to discriminate between TBI patients and HC. . The results showed that people with TBI had significantly lower scores in all neuropsychological test scores, except for ROCF Copy and TMT-A scores. Moreover, according to the effect size, clinically relevant significances were found in ROCF-Memory, Letter A, S, and F, Animals category, and HVLT-R Delayed recall and Recognition. Furthermore, Phonological Verbal Fluency Test (letters A and S) showed the greatest ability to discriminate subjects in both groups.

The results matched the evidence in the current literature in regard to cognitive outcomes after TBI. These patients usually present sequelae in executive functions (6), processing speed (2,5,9), attention and concentration (5), and verbal and visual memory (9,12)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 which are considered the main sequels of TBI. However, other studies have also reported sequelae in other cognitive areas, which were not assessed in this study, such as visuoperceptive skills (3), complex language tasks (e.g. writing, making inferences, listening comprehension, oral expression, figurative language (4), prospective memory (1) little is known about outcome following mild TBI (mTBI, and complex work memory tasks. Importantly, it should be noted that patients from this study did not receive any kind of cognitive rehabilitation, so comparisons with other studies is thoughtful since is not usual to find clinical sample without receiving at least some kind of rehabilitation service.

Among cognitive processes, executive functions, especially phonological verbal fluency tests (letters A and S), seems to be the most relevant scores to discriminate HC or TBI patients. Verbal fluency tests, specifically phonological, are highly sensitive to brain damage since they require the correct functioning of executive functions (e.g., flexibility, organizing strategies, inhibition) and frontal lobe functions (33–35). Focal lesions in TBI tend to occur more frequently in the frontal and temporal lobes (36), so it is not surprising that the phonological verbal fluency test turns out to be sensitive to brain damage (8). Thus, verbal fluency test, must be frequently use at clinical settings and be included as part of neuropsychological assessment of TBI patients

This study has important implications from a clinicians and researchers since it allows to know the profile of cognitive performance in people with TBI during the first year after the injury that did not receive cognitive rehabilitation services. This is fundamental to be able to implement adequate rehabilitation programs in order to help these people to improve their cognitive functioning and, hopefully, improve their quality of life and, lastly, their social, family and work reintegration.

The results of this study should be interpreted in light of the following limitations. 1) The neuropsychological profile found in the present study is related to the cognitive areas evaluated by the set of tests used. For this reason, it is unknown if people with TBI in this study have deficits or low scores compared to control subjects in other non-evaluated cognitive areas such as intelligence, language (e.g. comprehension, naming, repetition), working memory, motor operation and praxis, among others. Future studies should include this type of tests to see the functioning of these patients in each of these areas. 2) The results of this study cannot be generalized to people with TBI in other parts of Colombia where the sociodemographic and trauma characteristics of the patients, as well as the type of medical services received in both the acute phase and during the first year may vary. 3) The sample of TBI patients was composed mainly of people with mild

TBI, for this reason the results should be evaluated with caution when generalizing these to patients with moderate and severe TBI. 4) People with TBI who participated in the present study did not receive cognitive rehabilitation, for this reason the results cannot be extrapolated to people who have received rehabilitation. 5) Due to the neuropsychological evaluation of these patients was performed during the first year after the trauma, it is possible that the profile of cognitive performance found may remain stable, worsen or improve beyond the first year. However, as this is a transversal study, it is not possible to determine this.

In conclusion, TBI is one of the main causes of disability and death in young adults in Colombia. TBI patients scored lower than controls in attention and concentration, memory, executive functions and verbal fluency tests. The letters A and S were the scores with the greatest capacity to detect people belonging to the group of TBI patients compared to controls. Having valid and reliable neuropsychological tests, such as those found in this study, it is useful for clinicians to easily assess the presence or absence of cognitive deficits in their patients. By identification of these impairments, clinicians can implement cognitive rehabilitation programs to impact on the quality of life of TBI patients.

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