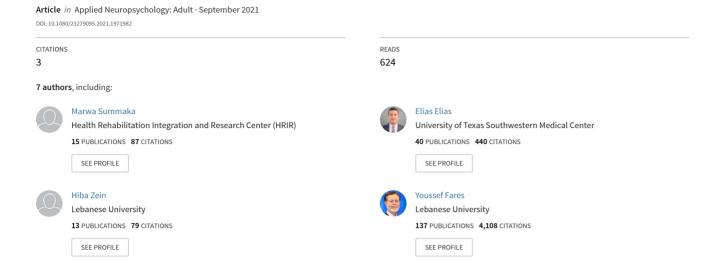
Computed tomography findings as early predictors of long-term language impairment in patients with traumatic brain injury







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ABSTRACT

This study aims to assess the relationship between computed tomography (CT) findings, during the acute phase of hospitalization, and long-term language impairment in people with traumatic brain injury (TBI). Another aim was to assess the receptive and expressive abilities of subjects with TBI based on the location of the injury. This is a retrospective observational study including 49 participants with TBI due to war injuries. The Arabic Diagnostic Aphasia Battery (A-DAB-1) was administered to the participants and the Helsinki CT score was computed to quantify brain damage. The results showed that the Helsinki CT score was negatively correlated with the total score of the A-DAB-1 (r = -0.544, p-value < 0.0001). Simple linear regression supported such findings and reflected an inversely proportional relationship between both variables (p-value < 0.0001). When compared with subjects having right hemisphere damage, subjects with left hemisphere and bilateral brain damage performed more poorly on language tasks respectively as follows: A-DAB-1 overall score (92.08-66.08-70.28, p-value = 0.021), Content of descriptive speech (9.57-6.69-7.22, p-value = 0.034), Verbal fluency (6.57-3.54-3.89, p-value = 0.002), Auditory comprehension (9.71-7.54-7.78, p-value = 0.039), Complex auditory commands (9.71-7.65-7.56, p-value = 0.043), Repetition (9.75-7.08-7.61, p-value = 0.036), Naming (9.93-7.15-8.11, p-value = 0.046). Following TBI, CT findings on admission can significantly predict long-term language abilities, with left side lesions inducing poorer outcomes.

KEYWORDS

Computed tomography; language impairment; Lebanon; rehabilitation; speech-language pathology; traumatic brain injury

Introduction

Traumatic brain injury (TBI) is identified as an alteration in the typical function of the brain due to an external force exerted on the head leading to brain insult or damage (Menon et al., 2010). The severity of TBI is classified by the injury characteristics and location indicated by the computed tomography (CT), along with the clinical severity and duration of symptoms (Pervez et al., 2018). Recently, CT scoring systems were implemented to guide the interpretation and quantification of brain injury (Stenberg et al., 2017). The clinical outcomes following TBI comprise deterioration in consciousness, alteration in mental state, physical weakness or paralysis, and cognitive communicative disorders (Pervez et al., 2018). On a long-term basis, TBI consequences might persist representing the residual of the head trauma, leaving the survivors with permanent physical (McLafferty et al., 2016; Rosenbaum et al., 2018; Tsyben et al., 2018), cognitive (Eshel et al., 2019; Marsh et al., 2016) and linguistic disabilities (Chabok et al., 2012; Sainson et al., 2014). Although physical impairment following TBI is apparent, communicative-linguistic disorders may be underestimated.

Communication involves the processing of cognitive, social, linguistic, and pragmatic skills to be operative and effective, which are well documented to be disrupted among subjects with TBI (Byom & Turkstra, 2017; Rigon et al., 2016; Sainson et al., 2014). A study conducted in Iran on 60 participants, within the acute phase of TBI hospitalization, reported that their sample exhibited poor auditory comprehension skills, weak narrative skills, reduced verbal fluency, and restricted semantic processing (Chabok et al., 2012). Moreover, a Canadian study was conducted in 2006 to explore the relationship between injury severity, demographic variables, and language impairments during the acute phase following TBI (Leblanc et al., 2006). Results showed that TBI severity, measured by the Glasgow Coma Scale (GCS), along with the educational levels of participants significantly predicted performance on tests of confrontation naming, auditory comprehension, and verbal reasoning (Leblanc et al., 2006). The same Canadian group indicated in 2014 that impairments in conversational discourse are related to the severity of TBI; hence as the severity increases, conversational discourse impairments become worse (LeBlanc et al., 2014). In addition to that, they identified problems of discourse as "acute predictive variables"

Table 1. The Helsinki CT scoring system.

Variable	Score
Mass lesion type(s)	
Subdural hematoma	2
Intracerebral hematoma	2
Epidural hematoma	-3
Mass lesion size >25 cm ³	2
Intraventricular hemorrhage	3
Suprasellar cisterns	
Normal	0
Compressed	1
Obliterated	5
Sum score	−3 to 14

Table reprinted from Raj et al. (2014).

following TBI, so that, they can significantly predict global outcomes, duration of hospitalization, and the need to be referred for speech-language pathology services (LeBlanc et al., 2014).

Similarly, previous studies reported parallel findings several months and years post-TBI (Elbourn et al., 2017; Hammond et al., 2004; Ponsford et al., 2014). Studies conducted 12-month post-TBI reported that participants demonstrated discourse deficits and slow speech rate (Byom & Turkstra, 2017; Elbourn et al., 2017). Another French study assessed the communicative-linguistic deficits in individuals with TBI, during the chronic phase (>12 months), and reported that the communication skills of the participants were characterized by difficulties in producing fluent and comprehensible language, adjusting conversation adaptively according to the discourse of the conversation and implementing pragmatics appropriately (Rousseaux et al., 2010).

Moreover, regarding the impact of topographic location of TBI on language skills, limited studies investigated this topic. Literature is abundant on the location of brain damage in cases of language deficits resulting from strokes. Research on subjects post-stroke suggested that language impairment or aphasia was predicted by lesions of the left inferior frontal area, left insula, thalamus, temporal pole, and dorsal or ventral white matter paths (Flowers et al., 2017; Kümmerer et al., 2013; Magnusdottir et al., 2013). However, following TBI, few studies suggested that linguistic dysfunctions are strongly associated with fronto-temporal lesions (Chabok et al., 2012; Rigon et al., 2016). Consequently, communicative-linguistic skills can be disrupted post-TBI; nevertheless, there is a lack of available information on the association between the severity of warinduced TBI and long-term language difficulties.

Furthermore, studies have provided promising information on the effectiveness of communicative-linguistic rehabilitation following TBI, as it enhances functional communication and improves coping strategies in patients (Gilmore et al., 2019; Gindri et al., 2014). Therefore, considering linguistic assessments within the acute phase following TBI is important, so that, sustained difficulties at this level can highly disrupt daily life functioning, impact survivor's quality of life, and influence their possibility to re-integrate into work later on (Bales et al., 2009; Cattelani et al., 2002; Hooson et al., 2013). The current study aims to promote the knowledge and understanding of medical professionals toward communicative-linguistic impairments post-TBI. The

main goal of this study is to evaluate the relationship between brain CT findings performed on admission and long-term acquired language difficulties in Lebanese patients with war-induced traumatic brain injury.

Materials and methods

Study design and participants

This is a retrospective observational study conducted in Lebanon during the period extending from December 2018 until June 2019. Inclusion criteria were: (a) Lebanese participants aged above 18 years, (b) diagnosed with TBI due to war or explosions, (c) having a brain CT scan on initial hospital admission confirming the TBI and (d) at least one-year post-TBI. Subjects with other neurological or neurodegenerative diseases were excluded. Participants were recruited during the chronic phase of TBI from centers concerned with the neurological rehabilitation of war-injured subjects across the different Lebanese districts. According to the archives of the centers, 62 individuals met the inclusion criteria, however, 13 refused to participate. Thus, the study included a convenient sample size of 49 males with warinduced TBI.

Procedure

Participants and/or caregivers were contacted face to face, during the chronic phase of TBI, to explain the objectives and procedure of the study. After taking their approval to participate in the study, the informed consent was signed. Data collection was initiated by the administration of a socio-demographic questionnaire; the questionnaire covered the general personal information and the medical history of the participant. Subsequently, each of the participants underwent a speech-language pathology assessment using the Arabic Diagnostic Aphasia Battery (A-DAB-1) during the chronic phase of TBI (at least 1-year post-injury). As for the severity of brain injury, it was determined based on the CT scan findings during acute hospitalization; so that, the CT scans were extracted from the medical records of the participants. A neurosurgeon and a specialist in neuroimaging, who were blinded to the study and the participants, identified the location(s) of brain injury and the involved hemisphere(s). They also calculated the Helsinki CT score for each participant.

Ethical considerations

The study was reviewed and approved by the scientific committee of the Neuroscience Research Center, Faculty of Medical Sciences at the Lebanese University. The study protocol was conducted with respect to the ethical guidelines proposed in the Declaration of Helsinki for medical research (Williams, 2008).

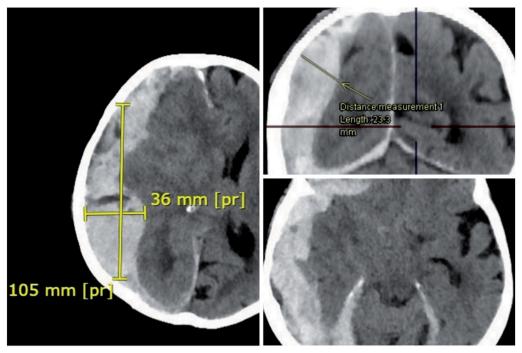


Figure 1. The Helsinki CT score calculations; Mass lesion as SDH = 2 points, Mass lesion size > 25 cc = 2 points, absence of IVH = 0, Basal cisterns are compressed = 1 point, Sum = 5.

Assessment measures

The Helsinki computed tomography scoring system

The Helsinki CT score is identified as a trauma scoring system, established by Raj in 2014, to quantify the severity of brain damage (Raj et al., 2014). It is recognized by its improved capacity to predict outcomes following TBI (Thelin et al., 2017). Furthermore, the Helsinki CT score is calculated by scoring four main variables including the mass lesion type and size, presence of intraventricular hemorrhage, and status of suprasellar cisterns (Table 1) (Raj et al., 2014); the total score ranges between -3 and 14, with increasing scores indicating worse outcomes (Raj et al., 2014). Figure 1 presents the appropriate calculation of the Helsinki CT score. As reported, the Helsinki CT score exhibited good psychometric characteristics with an accuracy of 74.5% for mortality, a specificity of 74.6%, and a sensitivity of 74.1%, all at a cutoff value of 4.5 (Yao et al., 2017). As for predicting unfavorable outcomes, the accuracy is 71.5%, the specificity is 81.2%, and the sensitivity is 56.8% (Yao et al., 2017). Upon using it within this study, permission was granted from the initial author.

The Arabic diagnostic aphasia battery (A-DAB-1)

A-DAB-1 is an assessment battery used to diagnose and assess the severity of aphasia, with an administration time of 15 to 20 minutes (Al-Thalaya et al., 2018). It is an Arabic scale developed in 2017 based on the framework of the Western Aphasia Battery (Risser & Spreen, 1985); and it is validated among the Lebanese aphasic population (Al-Thalaya et al., 2018). This assessment battery is subdivided into six subtests targeting the content and fluency of descriptive speech, auditory comprehension, complex auditory commands, repetition, and confrontational naming (AlThalaya et al., 2018). Each subtest is graded on a basis of 10 points, which are summed up to constitute the total scoring system, to be divided by the number of subtests and multiplied by 10 (Al-Thalaya et al., 2018). Thus, the total score of the A-DAB-1 ranges from 0-100, with higher score corresponding to better linguistic performance. The total score obtained represents the severity of language impairment in terms of the following categories: very severe (0-25), severe (26-50), moderate (51-75), and mild (76-89). As for its psychometric properties, the A-DAB-1 exhibits good content validity ratio (>0.75), high internal consistency ($\alpha = 0.961$) and excellent test-retest reliability (Intraclass correlation coefficient = 0.988. p-value < 0.001). Furthermore, at a cutoff value of 90, the A-DAB-1 showed a sensitivity and a specificity of 1 (Al-Thalaya et al., 2018). Approval and permission were granted from the corresponding author.

Statistical analysis

The statistical software SPSS (Statistical Package for Social Sciences) version 22.0 was used to analyze the data. Continuous variables were presented in terms of means and standard deviations, whereas categorical variables were presented in terms of percentages. The normality of data was evaluated using Shapiro-Wilk test. Independent samples test and one-way ANOVA test were implemented to compare means of two and three categories, respectively. For estimating the correlation between the Helsinki CT score and the language skills of subjects, a Spearman correlation was used. A simple linear regression was conducted between the A-DAB-1 total score (dependent variable) and the Helsinki CT score (independent variable), defined by the equation y = a + b*x. All statistical tests were two-tailed and a p-value < 0.05 was considered statistically significant.

Table 2. Socio-demographic characteristics of participants.

	Frequency (n)	Percentage (%)		
Gender				
Male	49	100		
Geographic region				
Beirut	2	4.1		
Mount Lebanon	23	46.9		
South	16	32.7		
Bekaa	8	16.3		
Marital status				
Single	18	36.7		
Married	31	63.3		
Educational level				
1 to 12 years	32	65.3		
>12 years	17	34.7		
	Mean ± SD ^a			
Age	31.90 ± 10.24			

^aStandard deviation.

Results

Sample characteristics

An overall sample of 49 males, having war-induced TBI, were enrolled in this study. Their ages ranged between 20 and 59 years, with a mean of 31.9 ± 10.24 years. For the geographic distribution, the majority were from Mount Lebanon (46.9%). Most of the sample were married (63.3%). Regarding the educational level, 65.3% received 1 to 12 years of education, while 34.7% had more than 12 years of education. Normality testing showed that data were normally distributed. For analytical purposes, the sample was split into two groups based on the time since injury. So that, group 1 included subjects living with TBI for 1-2 years, and group 2 presented subjects living with TBI for 3-4 years. No significant differences were found in terms of age and educational level. Therefore, the results were reported for the whole sample (Table 2).

Performance on language testing

The outcome scores of the participants, divided based on times since injury, are presented in Table 3. As mentioned before, the assessment measures included the Helsinki CT score and the A-DAB-1 with its six subtests. For the Helsinki CT score, groups 1 and 2 showed a significant difference in the severity of brain injury. Taking into account that the cutoff value of the Helsinki CT score is 4.5 (Yao et al., 2017), group 1 scored an average of 2.53 ± 2.29 presenting mild brain injury, whereas group 2 depicted a moderate one (4.75 ± 2.02) , with p-value = 0.001. The evaluation of language skills, using the A-DAB-1, revealed a mean score of 75.78 ± 30.87 and 73.49 ± 28.82 among groups 1 and 2 respectively, indicating mild-to-moderate language impairment. Across all the subtests, the participants of both groups showed low scores, while the lowest scores were demonstrated within the verbal fluency subtest. The mean scores were compared, showing no significant differences among both groups on all the subtests (p-value > 0.05). Thus, years since injury and injury severity did not affect performance on language testing. Therefore, the remaining analysis was carried out as a whole cohort (one group n = 49).

Table 3. Outcome scores of participants (n = 49).

	Group 1 (1–2 years) n = 17	Group 2 (3–4 years) n=32	
	Mean	p Value	
Helsinki CT score	2.53 ± 2.29	4.75 ± 2.02	0.001*
A-DAB-1 ^b total score	75.78 ± 30.87	73.49 ± 28.82	0.59
Content of descriptive speech	7.65 ± 3.78	7.59 ± 3.30	0.95
Verbal fluency	4.71 ± 3.01	4.34 ± 2.67	0.66
Auditory comprehension	8.29 ± 2.93	8.16 ± 2.85	0.87
Complex auditory commands	8.29 ± 2.95	8.19 ± 2.92	0.55
Repetition	8.18 ± 3.20	7.81 ± 3.19	0.46
Naming	8.35 ± 3.57	8.00 ± 3.55	0.74

Independent samples test; *p-value < 0.05 is significant. ^aStandard deviation; ^bThe Arabic Diagnostic Aphasia Battery.

To perform lobal function analysis, the outcome scores of participants were compared based on the location of brain injury including the specific lobe(s) or region(s), using one-way ANOVA test. The sites of injury across participants were as follows: frontal (n=3), parietal (n=3), temporal (n=4), occipital (n=3), cerebellum (n=2), temporo-parietal (n=4), fronto-parietal (n=9), frontotemporal (n=3), parieto-occipital (n=4), fronto-temporoparietal (n = 10), fronto-parieto-occipital (n = 3), basal ganglia (n = 1). However, no significant difference was found among the different brain regions in terms of language functioning (results shown in Supplementary File 1). Another attempt included studying the differences in severity of language impairment depending on the side of brain injury (right, left, and bilateral injuries). The targeted results are displayed in Table 4. For the Helsinki CT score, there is a significant difference between the severity levels of brain injury among the 3 groups representing the sides of injuries. On average subjects with right-side injury scored 2.86 ± 2.11 on the Helsinki CT score, subjects with left-side injury scored 4.12 ± 2.23, and subjects with bilateral injuries scored 5.33 ± 2.45 (p-value = 0.04). Moreover, performance on language tasks varied across the three groups. So that, subjects with right-side injury exhibited good language skills with an average of 92.08 ± 6.53 on the A-DAB-1 total score, while subjects with left-side injury and bilateral injuries presented moderate language impairment with averages of 66.08 ± 31.73 and 70.28 ± 33.57 , respectively (p-value < 0.021). It is important to note that subjects with left-side injury and bilateral injuries had scores fluctuating between 0 and above on the different subtests of A-DAB-1. Furthermore, subjects with left side injury displayed low scores in most of the tasks ranging from comprehension to expression (p-value < 0.05).

Correlation analysis

To assess the correlation between the Helsinki CT score and the language skills of subjects, a Spearman correlation was measured. As shown in Table 5, statistically significant results were obtained between the Helsinki CT score and the total score of the A-DAB-1 with r = -0.544, p-value < 0.0001, thus, demonstrating a negative linear association.

Table 4. Outcome score of participants based on side of lesion.

		Right side	e injury		Left sid	le injury		Bilatera	linjuries		
Test/subtest	(n = 14)			(n = 26)		(n = 9)					
	Min	Max	Mean ± SD ^a	Min	Max	Mean ± SD ^a	Min	Max	Mean ± SD ^a	p Value	
Helsinki CT score	0	6	2.86 ± 2.11	-1	8	4.12 ± 2.23	0	8	5.33 ± 2.45	between groups right-left side right-bilateral left-bilateral	0.040* 0.013* 0.024* 0.166
A-DAB-1 ^b total score	76.67	96.67	92.08 ± 6.53	0	98.33	66.08 ± 31.73	0	93.33	70.28 ± 33.57	between groups right-left side right-bilateral left-bilateral	0.021* 0.006* 0.023* 0.056
Content of descriptive speech	8	10	9.57 ± 0.85	0	10	6.69 ± 3.69	0	10	7.22 ± 4.18	between groups right-left side right-bilateral left-bilateral	0.034* 0.011* 0.026* 0.158
Verbal fluency	3	8	6.57 ± 1.74	0	9	3.54 ± 2.79	0	7	3.89 ± 2.42	between groups right-left side right-bilateral left-bilateral	0.002* 0.001* 0.014* 0.531
Auditory comprehension	9	10	9.71 ± 0.47	0	10	7.54 ± 3.24	0	10	7.78 ± 3.15	between groups right-left side right-bilateral left-bilateral	0.039* 0.021* 0.042* 0.823
Complex auditory commands	8	10	9.71 ± 0.73	0	10	7.65 ± 3.21	0	10	7.56 ± 3.47	between groups right-left side right-bilateral left-bilateral	0.043* 0.031* 0.036* 0.652
Repetition	9	10	9.75 ± 0.43	0	10	7.08 ± 3.54	0	10	7.61 ± 3.71	between groups right-left side right-bilateral left-bilateral	0.036* 0.011* 0.023* 0.107
Naming	9	10	9.93 ± 0.27	0	10	7.15 ± 4.04	0	10	8.11 ± 3.82	between groups right-left side right-bilateral left-bilateral	0.046* 0.017* 0.028* 0.468

One-way ANOVA test, multiple comparisons; *p-value < 0.05 is significant.

Table 5. Correlation between Helsinki CT score and A-DAB-1 (n = 49).

	A-DAB-1 ^a Total	Subtest 1 ^b	Subtest 2 ^c	Subtest 3 ^d	Subtest 4 ^e	Subtest 5 ^f	Subtest 6 ^g
CT score ^h	r = -0.544 $p < 0.0001*$	r = -0.542 p < 0.0001*	r = -0.534 p < 0.0001*	r = -0.566 p < 0.0001*	r = -0.590 p < 0.0001*	r = -0.442 p = 0.001*	r = -0.511 p < 0.0001*

Spearman Correlation; *p-value < 0.05 is significant.

Also, this correlation was significant between the Helsinki CT score and the six subtests of the A-DAB-1 (r ranging between -0.442 and -0.590, p-value < 0.01).

For the regression analysis, a simple linear model was conducted between the A-DAB-1 total score and the Helsinki CT score. The findings indicated a prominent relationship between the Helsinki CT score calculated from CT scans done on initial hospital admission and the A-DAB-1 total score in subjects with TBI up to 4 years post-injury (pvalue < 0.0001). So that, as the Helsinki CT score increases reflecting a more severe brain injury, the A-DAB-1 decreases indicating deficits in language skills (Figure 2). The coefficient of determination is 0.327, which signifies that the Helsinki CT score explains 32.7% of the total variance of the A-DAB-1 score. Therefore, it is suggested that brain CT findings on admission provide highly important information that aids the prediction of long-term language impairment up to 4 years.

Discussion

In the present study, the aim was to assess the relationship between brain CT findings on admission and long-term language impairment in subjects with TBI. This was targeted by evaluating the correlation between the severity of brain injury and language abilities, along with studying the differences in receptive and expressive skills depending on the location of the injury. Obtained results provided initial evidence that the outcome for subjects living with TBI, in terms of language skills up to 4 years are related to CT findings on admission.

To discuss the outcome measures of the subjects, the sample was split into 2 groups according to the date of injury. Groups 1 and 2 included participants living with TBI for 1-2 years and 3-4 years respectively. On average, group 1 had a score of 2.53 ± 2.29 on the Helsinki CT score, while, group 2 had a mean score of 4.75 ± 2.02 . Thus, both groups presented different levels of severity of brain injury, with

^aStandard deviation; ^bBedside Version of Arabic Diagnostic Aphasia Battery.

^aThe Arabic Diagnostic Aphasia Battery; ^bContent of descriptive speech; ^cVerbal fluency; ^dAuditory comprehension; ^eComplex auditory commands; ^fRepetition; ⁹Naming; ^hHelsinki CT score.

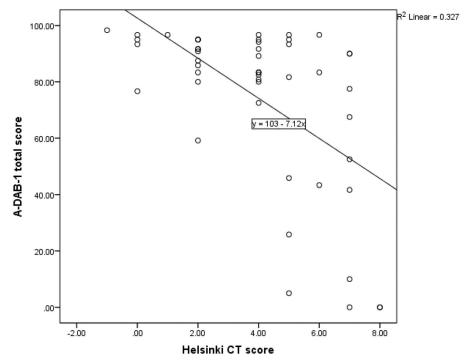


Figure 2. A scatter plot depicting the linear regression line and equation for the association between the A-DAB-1 total score and the Helsinki CT score. R-squared linear = coefficient of determination.

group 2 demonstrating a higher severity (p-value = 0.001). Subjects of both groups showed impaired performance on the different language subtests. However, this poor performance was most apparent within the verbal fluency task. Groups 1 and 2 scored 4.71 ± 3.01 and 4.34 ± 2.67 , respectively, on the subtest of verbal fluency signifying impairment at this level. Such findings are parallel with those of studies supporting regression in verbal fluency skills following TBI (Bittner & Crowe, 2007; Chabok et al., 2012; Zaninotto et al., 2014). Verbal fluency tasks are sensitive to evaluating the individual's ability to access lexical stocks and retrieve information from semantic memory (Zaninotto et al., 2014). It is believed that due to impairment in the lexical-semantic encoding system, patients with TBI show poor performance on verbal fluency tasks (Chabok et al., 2012). Verbal fluency in its essence has been shown to be related to language skills primarily as well as to cognitive/executive function skills, all of which are affected by TBI (Whiteside et al., 2016). Impaired executive function mediates deficiencies in different cognitive skills including mental flexibility, self-generation behaviors, attention, and verbal fluency (Henry & Crawford, 2004). Moreover, in the present study, no significant difference was found in verbal fluency scores among groups 1 and 2 reproducing the findings of a previous study stating that verbal fluency tasks were associated neither with the time since injury nor with the severity of injury (Jurado et al., 2000).

Moreover, variations in language abilities among subjects with TBI based on the site or specific lobal region of injury were assessed. While some studies supported the classical model of language processing indicating that language comprehension is likely located in the posterior temporal lobe and language production is located in the left frontal region

(Benson et al., 1985; Broca, 1861; Geschwind, 1971; Kandel et al., 2000; Lichtheim, 1885; Wernicke, 1974), the present study could not prove such correlations. This might be related to the small number of participants having similar lobal injuries. Furthermore, a previous prospective study was done in Brazil on subjects with aphasia post-stroke reported the absence of direct association between specific topographic lesions and language abilities, even though their participants presented focal brain lesions (Devido-Santos et al., 2012). Similarly, different studies verified this conclusion, pinpointing no relationship between lesion sites and aphasia (Mansur et al., 2002; Radanovic et al., 2003). Taking into account the dual-stream model of the neural basis of language processing, this model highlights the involvement of different cortical regions rather than the classical Broca's and Wernicke's areas, as well as white matter tracts (Binder et al., 1997; Chang et al., 2015; Hickok & Poeppel, 2004). Thus, language deficits cannot be easily localized to specific brain regions. Furthermore, as documented in the literature, TBIs caused by wars and explosions are known for their invasive nature, inducing "complex shock waves" in the brain and consequently leading to multiple head assaults (Ling & Ecklund, 2011). Thus, knowing that recruited subjects within the present study had war-induced TBIs, can elucidate the findings demonstrating no association between the performance on receptive and expressive language tasks and specific topographic lesions due to the complexity of injury pattern.

On the other hand, the results of this study showed that the linguistic abilities of subjects with TBI varied when compared based on side of injury or brain damage. Subjects with right hemisphere injury showed by average good linguistic skills $(92.08 \pm 6.53$, the cutoff score is 90) characterized by approximately intact receptive and expressive abilities, however, they showed impairment on verbal fluency tasks. To discuss, the contribution of the right hemisphere to language processing is still under research, so that, some studies conveyed that right hemisphere damage restricts language processes (Joanette et al., 2008; Lehman Blake, 2003), while others did not report such deficits following unilateral right hemisphere damage (Klepousniotou & Baum, 2005; Tompkins et al., 2008). Also, this can be influenced by the fact that left hemisphere damage results in aphasic symptoms, while right hemisphere damage rarely does. But this does not assure that subjects with right hemisphere damage do not exhibit language deficits, however, such deficits are not detected in simple conversational contexts, as the involvement of the right hemisphere in language processing is accompanied by complex linguistic stimuli (Johns et al., 2008). For subjects with left hemisphere or bilateral damage, total scores on language testing were reduced when compared to subjects with right hemisphere damage; however, the latter exhibited milder levels of brain injury as computed by the Helsinki CT score. Subjects with bilateral hemisphere injury showed the highest severity of brain injury among all $(5.33 \pm 2.45, p$ -value < 0.05), but better language performance than subjects with left hemisphere damage. Subsequently, subjects with left hemisphere or bilateral damage demonstrated a statistically significant impaired performance on the different language tests (p-value < 0.05 for all subtests). But also, it is important to highlight that the number of participants having left side injury (n = 26) is greater than those having bilateral injuries (n=9). Replicating previous studies, the existing study revealed that following TBI, and specifically those of left side damage, subjects demonstrated reduced performance on verbal fluency, auditory comprehension, repetition, and naming tasks (Gauthier et al., 2018; Rigon et al., 2016). The mentioned disruptions were proven to be significantly related to underlying deficits of reasoning and long-term verbal and visual memories following brain injury (Vukovic et al., 2008). Moreover, as observed, performance on verbal fluency tests was mostly reduced for the different groups. Relying on a recent functional magnetic resonance study, this finding can be explicated by the evidence that verbal fluency tasks activate bilateral brain regions comprising the fronto-temporal lobes (McAlonan et al., 2005).

Furthermore, the results indicated a significant correlation between performance on language testing and CT findings up to 4 years post-TBI, suggesting an inversely proportional pattern characterized by decreased scoring on the A-DAB-1 test with the increase in Helsinki CT score. Thus, as the severity of injury increases, language deficits increase, too. Such results replicate the findings of an Iranian study conducted in 2012 supporting such correlation and emphasizing specifically fronto-temporal lesions as strong predictors of acquired language impairment (Chabok et al., 2012). Very few papers were published discussing long-term linguistic outcomes following TBI. However, an Australian study assessed the influence of brain injury on long-term recovery and stated that subjects who developed language

disturbances following TBI showed sustained difficulties after one-year postinjury (Elbourn et al., 2019). Moreover, another study aimed to describe the conversational abilities of severely injured TBI participants and demonstrated that 69.3% of their sample experienced persistent disturbances in expressive skills after 2 years (Snow et al., 1998). Having this background, it is believed that the present study provided strong evidence to support the correlation between brain CT findings and language disruptions in a group of Lebanese TBI subjects. In addition to that, the findings of this study highlighted the different linguistic outcomes of diverse severities as consequences of TBI. Accordingly, it is highly recommended to assess language abilities post-TBI, so that, adequate interventions and adaptations can be implemented as early as possible.

To the best of our knowledge, this is the first study conducted in Lebanon, implementing a CT scoring system and quantifying brain imaging findings among the TBI population to investigate the association with language deficits. So that, language impairments and their association with CT findings have been poorly studied in the literature. In addition, in Lebanon, few researchers were interested in evaluating the outcomes of TBI due to war and explosions (Fares et al., 2014; Haddad et al., 2008; Summaka et al., 2020; Taha et al., 1991). Nevertheless, no studies have targeted language skills post-TBI in Lebanon and Arab countries, especially in the field of neuroimaging, which explains the motivation to conduct this study. Furthermore, this study has a potentially wide application, given the widespread availability of CT scans.

Despite the mentioned strength points, this study exhibited some limitations. First, all the recruited subjects were men; the sample reflects the country's circumstances, where Lebanon is involved in a regional war conflict and only men are allowed to defend any assault. Second, the sample recruited was a convenient one, as in Lebanon a gap is still present in the field of TBI in terms of epidemiology. In addition to that, most of the hospitals and medical centers do not preserve medical records of patients and lack a TBI registry, thus, making it hard to extract the medical history of patients. Altogether, such reasons constituted obstacles in the way of implementing random recruitment methods and restricted the representativeness of Therefore, this study can be viewed as a pilot study defining the framework of possible consequent studies. Finally, for the above-mentioned obstacles, along with the limited number of specialized centers providing rehabilitation services for subjects with TBI, a multi-centered approach couldn't be covered. Regardless of these limitations, the current study highlighted valuable information about acquired language disabilities following TBI and emphasized the prominence of implementing a CT scoring system during the acute phase of TBI as a tool to predict long-term linguistic outcomes, and hence, facilitating the initiation of early rehabilitation plans. Such findings must be generalized to the different Arabic societies to prompt launching subsequent studies enrolling larger numbers of participants comprising both genders.

Conclusion

In conclusion, this study has demonstrated that subjects with TBI showed increased language impairment defined by the severity of the injury. The results are aimed to raise awareness regarding linguistic disabilities following TBI, as they can negatively influence communicative attempts in patients manifested by their difficulties in expressing basic needs, understanding well their medical condition and making decisions regarding their therapy choices. In addition to that, such findings will guide healthcare professionals in predicting prognostic linguistic outcomes post-TBI, and thus, encourages referring patients to suitable speech-language pathology assessments.

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References

- Al-Thalaya, Z., Nilipour, R., Sadat Ghoreyshi, Z., Pourshahbaz, A., Nassar, Z., & Younes, M. (2018). Reliability and validity of bedside version of Arabic Diagnostic Aphasia Battery (A-DAB-1) for Lebanese individuals. Aphasiology, 32(3), 323-339. https://doi.org/10. 1080/02687038.2017.1338661
- Bales, J. W., Wagner, A. K., Kline, A. E., & Dixon, C. E. (2009). Persistent cognitive dysfunction after traumatic brain injury: A dopamine hypothesis. Neuroscience and Biobehavioral Reviews, 33(7), 981-1003. https://doi.org/10.1016/j.neubiorev.2009.03.011
- Benson, D. F. (1985). Aphasia and related disorders: a clinical approach. In M. M. Mesulam (Ed.), Principles of behavioral neurology (pp. 193-238).
- Binder, J. R., Frost, J. A., Hammeke, T. A., Cox, R. W., Rao, S. M., & Prieto, T. (1997). Human brain language areas identified by functional magnetic resonance imaging. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 17(1), 353-362. https://doi.org/10.1523/JNEUROSCI.17-01-00353.1997
- Bittner, R. M., & Crowe, S. F. (2007). The relationship between working memory, processing speed, verbal comprehension and FAS performance following traumatic brain injury. Brain Injury, 21(7), 709-719. https://doi.org/10.1080/02699050701468917
- Broca, P. (1861). Remarques sur le siège de la faculté du langage articulé, suivies d'une observation d'aphémie (perte de la parole). Bulletin et Memoires de la Societe Anatomique de Paris, 6, 330-357.
- Byom, L., & Turkstra, L. S. (2017). Cognitive task demands and discourse performance after traumatic brain injury. International

- Journal of Language & Communication Disorders, 52(4), 501-513. https://doi.org/10.1111/1460-6984.12289
- Cattelani, R., Tanzi, F., Lombardi, F., & Mazzucchi, A. (2002). Competitive re-employment after severe traumatic brain injury: Clinical, cognitive and behavioural predictive variables. Brain Injury, 16(1), 51-64. https://doi.org/10.1080/02699050110088821
- Chabok, S. Y., Kapourchali, S. R., Leili, E. K., Saberi, A., & Mohtasham-Amiri, Z. (2012). Effective factors on linguistic disorder during acute phase following traumatic brain injury in adults. Neuropsychologia, 50(7), 1444-1450. https://doi.org/10.1016/j.neuropsychologia.2012.02.029
- Chang, E. F., Raygor, K. P., & Berger, M. S. (2015). Contemporary model of language organization: an overview for neurosurgeons. Journal of Neurosurgery, 122(2), 250-261. https://doi.org/10.3171/ 2014.10.Jns132647
- Devido-Santos, M., Gagliardi, R. J., & Mac-Kay, A. P. (2012). Language disorders and brain lesion topography in aphasics after stroke. Arquivos de Neuro-Psiquiatria, 70(2), 129-133. https://doi.org/10. 1590/s0004-282x2012000200011
- Elbourn, E., Kenny, B., Power, E., Honan, C., McDonald, S., Tate, R., Holland, A., MacWhinney, B., & Togher, L. (2019). Discourse recovery after severe traumatic brain injury: exploring the first year. Brain Injury, 33(2), 143-159. https://doi.org/10.1080/02699052.2018.
- Elbourn, E., Togher, L., Kenny, B., & Power, E. (2017). Strengthening the quality of longitudinal research into cognitive-communication recovery after traumatic brain injury: A systematic review. International Journal of Speech-Language Pathology, 19(1), 1-16. https://doi.org/10.1080/17549507.2016.1193896
- Eshel, I., Bowles, A. O., & Ray, M. R. (2019). Rehabilitation of cognitive dysfunction following traumatic brain injury. Physical Medicine and Rehabilitation Clinics of North America, 30(1), 189-206. https:// doi.org/10.1016/j.pmr.2018.08.005
- Fares, Y., Fares, J., & Gebeily, S. (2014). Head and facial injuries due to cluster munitions. Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 35(6), 905-910. https://doi.org/10.1007/s10072-013-1623-2
- Flowers, H. L., AlHarbi, M. A., Mikulis, D., Silver, F. L., Rochon, E., Streiner, D., & Martino, R. (2017). MRI-based neuroanatomical predictors of dysphagia, dysarthria, and aphasia in patients with first acute ischemic stroke. Cerebrovascular Diseases Extra, 7(1), 21-34. https://doi.org/10.1159/000457810
- Gauthier, S., LeBlanc, J., Seresova, A., Laberge-Poirier, A., A Correa, J., Alturki, A. Y., Marcoux, J., Maleki, M., Feyz, M., & de Guise, E. (2018). Acute prediction of outcome and cognitive-communication impairments following traumatic brain injury: The influence of age, education and site of lesion. Journal of Communication Disorders, 73, 77-90. https://doi.org/10.1016/j.jcomdis.2018.04.003
- Geschwind, N. (1971). Current concepts: aphasia. The New England Journal of Medicine, 284(12), 654-656. https://doi.org/10.1056/ nejm197103252841206
- Gilmore, N., Ross, K., & Kiran, S. (2019). The intensive cognitive-communication rehabilitation program for young adults with acquired brain injury. American Journal of Speech-Language Pathology, 28(1S), 341-358. https://doi.org/10.1044/2018_AJSLP-17-0153
- Gindri, G., Pagliarin, K. C., Casarin, F. S., Branco, L. D., Ferré, P., Joanette, Y., & Fonseca, R. P. (2014). Rehabilitation of discourse impairments after acquired brain injury. Dementia and Neuropsychologia, 8(1), 58-65. https://doi.org/10.1590/S1980-57642014DN81000009
- Haddad, M. C., Khoury, N. J., & Hourani, M. H. (2008). Radiology of terror injuries: The American University of Beirut Medical Center experience. Clinical Imaging, 32(2), 83-87. https://doi.org/10.1016/j. clinimag.2007.09.007
- Hammond, F. M., Hart, T., Bushnik, T., Corrigan, J. D., & Sasser, H. (2004). Change and predictors of change in communication, cognition, and social function between 1 and 5 years after traumatic brain injury. The Journal of Head Trauma Rehabilitation, 19(4), 314-328. https://doi.org/10.1097/00001199-200407000-00006

- Henry, J. D., & Crawford, J. R. (2004). A meta-analytic review of verbal performance following focal cortical Neuropsychology, 18(2), 284-295. https://doi.org/10.1037/0894-4105. 18.2.284
- Hickok, G., & Poeppel, D. (2004). Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition, 92(1-2), 67-99. https://doi.org/10.1016/j.cognition. 2003.10.011
- Hooson, J. M., Coetzer, R., Stew, G., & Moore, A. (2013). Patients' experience of return to work rehabilitation following traumatic brain injury: a phenomenological study. Neuropsychological Rehabilitation, 23(1), 19-44. https://doi.org/10.1080/09602011.2012.713314
- Joanette, Y., Ansaldo, A. I., Kahlaoui, K., Côté, H., Abusamra, V., Ferreres, A., & Roch-Lecours, A. (2008). The impact of lesions in the right hemisphere on linguistic skills: theoretical and clinical perspectives. Revista de Neurologia, 46(8), 481-488.
- Johns, C. L., Tooley, K. M., & Traxler, M. J. (2008). Discourse impairments following right hemisphere brain damage: A critical review. Language and Linguistics Compass, 2(6), 1038-1062. https://doi.org/ 10.1111/j.1749-818X.2008.00094.x
- Jurado, M. A., Mataro, M., Verger, K., Bartumeus, F., & Junque, C. (2000). Phonemic and semantic fluencies in traumatic brain injury patients with focal frontal lesions. Brain Injury, 14(9), 789-795. https://doi.org/10.1080/026990500421903
- Kandel, E. R., Schwartz, J. H., Jessell, T. M., Siegelbaum, S., Hudspeth, A. J., & Mack, S. (2000). Principles of neural science. (Vol. 4): McGraw-Hill.
- Klepousniotou, E., & Baum, S. R. (2005). Processing homonymy and polysemy: effects of sentential context and time-course following unilateral brain damage. Brain and Language, 95(3), 365-382. https://doi.org/10.1016/j.bandl.2005.03.001
- Kümmerer, D., Hartwigsen, G., Kellmeyer, P., Glauche, V., Mader, I., Klöppel, S., Suchan, J., Karnath, H.-O., Weiller, C., & Saur, D. (2013). Damage to ventral and dorsal language pathways in acute aphasia. Brain: A Journal of Neurology, 136(Pt 2), 619-629. https:// doi.org/10.1093/brain/aws354
- LeBlanc, J., de Guise, E., Champoux, M.-C., Couturier, C., Lamoureux, J., Marcoux, J., Maleki, M., & Feyz, M. (2014). Early conversational discourse abilities following traumatic brain injury: An acute predictive study. Brain Injury, 28(7), 951-958. https://doi.org/10.3109/ 02699052.2014.888760
- Leblanc, J., De Guise, E., Feyz, M., & Lamoureux, J. (2006). Early prediction of language impairment following traumatic brain injury. Brain Injury, 20(13-14), 1391-1401. https://doi.org/10.1080/ 02699050601081927
- Lehman Blake, M. (2003). Affective language and humor appreciation after right hemisphere brain damage. Seminars in Speech and Language, 24(2), 107-119. https://doi.org/10.1055/s-2003-38902
- Lichtheim, L. (1885). On aphasia. Brain, 7, 433-484.
- Ling, G. S., & Ecklund, J. M. (2011). Traumatic brain injury in modern war. Current Opinion in Anaesthesiology, 24(2), 124-130. https://doi. org/10.1097/ACO.0b013e32834458da
- Magnusdottir, S., Fillmore, P., den Ouden, D. B., Hjaltason, H., Rorden, C., Kjartansson, O., Bonilha, L., & Fridriksson, J. (2013). Damage to left anterior temporal cortex predicts impairment of complex syntactic processing: A lesion-symptom mapping study. Human Brain Mapping, 34(10), 2715-2723. https://doi.org/10.1002/ hbm.22096
- Mansur, L. L., Radanovic, M., Rüegg, D., Mendonça, L. I. Z. d., & Scaff, M. (2002). Descriptive study of 192 adults with speech and language disturbances. Sao Paulo Medical Journal = Revista Paulista de Medicina, 120(6), 170-174. https://doi.org/10.1590/s1516-31802002000600003
- Marsh, N. V., Ludbrook, M. R., & Gaffaney, L. C. (2016). Cognitive functioning following traumatic brain injury: A five-year follow-up. NeuroRehabilitation, 38(1), 71-78. https://doi.org/10.3233/nre-151297
- McAlonan, G., McGuire, P., Frcpsych Chua, S., Cheung, C., McAlonan, G., & McGuire, P. (2005). Bilateral brain activation in Chinese Speech functional magnetic resonance imaging evaluation of

- bilateral brain activation in Chinese speech. Hong Kong Journal of Psychiatry, 15(3), 77-81.
- McLafferty, F. S., Barmparas, G., Ortega, A., Roberts, P., Ko, A., Harada, M., Nuño, M., Black, K. L., & Ley, E. J. (2016). Predictors of improved functional outcome following inpatient rehabilitation for patients with traumatic brain injury. NeuroRehabilitation, 39(3), 423-430. https://doi.org/10.3233/NRE-161373
- Menon, D. K., Schwab, K., Wright, D. W., & Maas, A. I.; Demographics and Clinical Assessment Working Group of the International and Interagency Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health. (2010). Position statement: definition of traumatic brain injury. Archives of Physical Medicine and Rehabilitation, 91(11), 1637-1640. https://doi.org/10.1016/j.apmr.2010.05.017
- Pervez, M., Kitagawa, R. S., & Chang, T. R. (2018). Definition of traumatic brain injury, neurosurgery, trauma orthopedics, neuroimaging, psychology, and psychiatry in mild traumatic brain injury. Neuroimaging Clinics of North America, 28(1), 1-13. https://doi.org/ 10.1016/j.nic.2017.09.010
- Ponsford, J. L., Downing, M. G., Olver, J., Ponsford, M., Acher, R., Carty, M., & Spitz, G. (2014). Longitudinal follow-up of patients with traumatic brain injury: outcome at two, five, and ten years post-injury. Journal of Neurotrauma, 31(1), 64-77. https://doi.org/ 10.1089/neu.2013.2997
- Radanovic, M., Azambuja, M., Mansur, L., Porto, C., & Scaff, M. (2003). Thalamus and language: interface with attention, memory and executive functions. Arquivos de Neuro-Psiquiatria, 61(1), 34-42. https://doi.org/10.1590/S0004-282X2003000100006
- Raj, R., Siironen, J., Skrifvars, M. B., Hernesniemi, J., & Kivisaari, R. (2014). Predicting outcome in traumatic brain injury: development of a novel computerized tomography classification system (Helsinki computerized tomography score). Neurosurgery, 75(6), 632-646. discussion 646-637. https://doi.org/10.1227/NEU.000000000000533
- Rigon, A., Voss, M. W., Turkstra, L. S., Mutlu, B., & Duff, M. C. (2016). Frontal and temporal structural connectivity is associated with social communication impairment following traumatic brain injury. Journal of the International Neuropsychological Society, 22(7), 705-716. https://doi.org/10.1017/S1355617716000539
- Risser, A. H., & Spreen, O. (1985). The western aphasia battery. Journal of Clinical and Experimental Neuropsychology, 7(4), 463-470. https://doi.org/10.1080/01688638508401277
- Rosenbaum, A. M., Gordon, W. A., Joannou, A., & Berman, B. A. (2018). Functional outcomes following post-acute rehabilitation for moderate-to-severe traumatic brain injury. Brain Injury, 32(7), 907–914. https://doi.org/10.1080/02699052.2018.1469040
- Rousseaux, M., Verigneaux, C., & Kozlowski, O. (2010). An analysis of communication in conversation after severe traumatic brain injury. European Journal of Neurology, 17(7), 922-929. https://doi.org/10. 1111/j.1468-1331.2009.02945.x
- Sainson, C., Barat, M., & Aguert, M. (2014). Communication disorders and executive function impairment after severe traumatic brain injury: an exploratory study using the GALI (a grid for linguistic analysis of free conversational interchange). Annals of Physical and Rehabilitation Medicine, 57(9-10), 664-683. https://doi.org/10.1016/j. rehab.2014.08.011
- Snow, P., Douglas, J., & Ponsford, J. (1998). Conversational discourse abilities following severe traumatic brain injury: a follow-up study. Brain Injury, 911-935. https://doi.org/10.1080/ 12(11), 026990598121981
- Stenberg, M., Koskinen, L. D., Jonasson, P., Levi, R., & Stalnacke, B. M. (2017). Computed tomography and clinical outcome in patients with severe traumatic brain injury. Brain Injury, 31(3), 351–358. https://doi.org/10.1080/02699052.2016.1261303
- Summaka, M., Zein, H., Elias, E., Naim, I., Fares, Y., & Nasser, Z. (2020). Prediction of quality of life by Helsinki computed tomography scoring system in patients with traumatic brain injury. Brain Injury, 34(9), 1229-1236. https://doi.org/10.1080/02699052.2020. 1799435
- Taha, J. M., Haddad, F. S., & Brown, J. A. (1991). Intracranial infection after missile injuries to the brain: report of 30 cases from the



- Lebanese conflict. Neurosurgery, 29(6), 864-868. https://doi.org/10. 1097/00006123-199112000-00010
- Thelin, E. P., Nelson, D. W., Vehviläinen, J., Nyström, H., Kivisaari, R., Siironen, J., Svensson, M., Skrifvars, M. B., Bellander, B.-M., & Raj, R. (2017). Evaluation of novel computerized tomography scoring systems in human traumatic brain injury: An observational, multicenter study. PLoS Medicine, 14(8), e1002368. https://doi.org/10. 1371/journal.pmed.1002368
- Tompkins, C. A., Fassbinder, W., Scharp, V. L., & Meigh, K. M. (2008). Activation and maintenance of peripheral semantic features of unambiguous words after right hemisphere brain damage in Aphasiology, 22(2), 119-138. https://doi.org/10.1080/ 02687030601040861
- Tsyben, A., Guilfoyle, M., Timofeev, I., Anwar, F., Allanson, J., Outtrim, J., Menon, D., Hutchinson, P., & Helmy, A. (2018). Spectrum of outcomes following traumatic brain injury-relationship between functional impairment and health-related quality of life. Acta Neurochirurgica, 160(1), 107-115. https://doi.org/10.1007/ s00701-017-3334-6
- Vukovic, M., Vuksanovic, J., & Vukovic, I. (2008). Comparison of the recovery patterns of language and cognitive functions in patients with post-traumatic language processing deficits and in patients

- with aphasia following a stroke. Journal of Communication Disorders, 41(6), 531-552. https://doi.org/10.1016/j.jcomdis.2008.04. 001
- Wernicke, C. (1974). Der aphasische symptomenkomplex. In Der aphasische Symptomencomplex (pp. 1-70). Springer. https://doi.org/10. 1007/978-3-642-65950-8_1
- Whiteside, D. M., Kealey, T., Semla, M., Luu, H., Rice, L., Basso, M. R., & Roper, B. (2016). Verbal fluency: language or executive function measure? Applied Neuropsychology. Adult, 23(1), 29-34. https://doi.org/10.1080/23279095.2015.1004574
- Williams, J. R. (2008). The Declaration of Helsinki and public health. Bulletin of the World Health Organization, 86(8), 650-652. https:// doi.org/10.2471/blt.08.050955
- Yao, S., Song, J., Li, S., Cao, C., Fang, L., Wang, C., & Xu, G. (2017). Helsinki computed tomography scoring system can independently predict long-term outcome in traumatic brain injury. World Neurosurgery, 101, 528-533. https://doi.org/10.1016/j.wneu.2017.02.072
- Zaninotto, A. L., de Paula Guirado, V. M., Baldivia, B., Núñes, M. D., Amorim, R. L. O., Teixeira, M. J., & Paiva, W. S. (2014). Improvement of verbal fluency in patients with diffuse brain injury over time. Neuropsychiatric Disease and Treatment, 10, 1155-1160. https://doi.org/10.2147/NDT.S62728