Posttraumatic Amnesia and Personality Changes after Severe Traumatic Brain Injury: Preliminary Findings

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Personality changes are one of the most prevalent neuropsychiatric impairments following severe traumatic brain injury (TBI) and are related to significant functional impairment, caregiver burden, direct and indirect costs [1]. According to the Diagnostic and Statistical Manual of Mental Disorders IV – Text Revision (DSM-IV-TR), personality changes are characterized “by a marked change in personality style and traits from a previous level of functioning. Patients must show evidence of a causative organic factor antedating the onset of the personality changes” [2]. The new edition of the Manual, the DSM-5, reconceptualizes it as a “neurocognitive disorder due to traumatic brain injury” with a behavioral disturbance [3], in agreement with Tate’s view, for whom behavioral changes following TBI would be deeply associated with cognitive impairment [4].

Ninety years ago, W. Ritchie Russel published a study [5] in which the duration of loss of full consciousness was associated with functional outcome in TBI patients. This interval, posteriorly renamed “posttraumatic amnesia (PTA),” is estimated based on the first clearly remembered event after the accident. This measurement provides the base for the retrospective PTA evaluation, which is a validated methodology [6] conducted by asking the patients which and when was their first declarative memory of facts or events that they can recall after the TBI. Four weeks of PTA duration was found by Brown et al. for predicting global outcome [7].

Although prognostic models have been successfully developed to predict the mortality and outcome determined by the Glasgow Coma Scale (GCS) in TBI patients, the identification of predictors

for personality changes after the severe TBI remains a scientific challenge [8].

For this prospective case–control study, independent associations were investigated among social, demographic and hospitalization variables (Table 1) and the presence of personality changes according to DSM-IV-TR [2] criteria at 18 months after severe TBI in a representative sample ($n = 41$) from 60 consecutive eligible surviving patients. Patients were attended between June 2008 and May 2012 at the Hospital Governador Celso Ramos, a reference center for the approximately 1 million inhabitants of the Florianópolis metropolitan area. The inclusion criteria were as follows: (1) severe TBI as defined by GCS score 8 or lower at admission, (2) 16 years of age or older at the time of injury, and (3) resident of Florianópolis metropolitan area. Exclusion criteria were patients admitted for gunshot injuries.

Psychiatry disorders were assessed 18 months after severe TBI with full administration of Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) by two board-certified psychiatrists (APD and MLS) blinded for all the hospitalization variables. As the retrospective evaluation of psychiatric disorders could be influenced by recall bias, only the presence/absence of past major depressive disorder, past alcohol abuse or dependence, and past substance abuse or dependence were included in the analysis. Major depressive disorder, anxiety disorder, alcohol abuse or dependence, and substance abuse or dependence disorder at the moment of evaluation were also assessed, given that the symptoms associated with these conditions could mistake the per-

Table 1 Social, demographic, psychiatric and clinical variables associated with personality changes 18 months after severe traumatic brain injury

Variables	All patients N = 41 (%)	Personality changes		Unadjusted OR (CI 95%)	P-value	Adjusted OR (CI 95%)	P-value
		No n = 29 (67%)	Yes n = 14 (33%)				
Gender							
Female	6 (14.6)	5 (18.5)	1 (7.1)	1.0			
Male	35 (85.4)	22 (81.5)	13 (92.9)	2.95 (0.31–28.14)	0.35	–	–
Mean age in years ($\pm$ SD)	31 ($\pm$ 12)	29.8 ($\pm$ 11.9)	33.9 (12.7)	–	0.31		
Marital status							
Married	17 (41.5)	10 (37)	7 (50)	1.0			
Unmarried	24 (58.5)	17 (63)	7 (50)	0.59 (0.16–2.17)	0.43	–	–
Psychiatric variables							
Major depressive disorder before TBI ^a							
No	35 (85.4)	22 (84.6)	13 (92.9)	1.0			
Yes	5 (12.2)	4 (15.4)	1 (7.1)	0.42 (0.04–4.20)	0.46	–	–
Major depressive disorder at evaluation							
No	30 (73.2)	21 (77.8)	9 (64.3)	1.0			
Yes	11 (26.8)	6 (22.2)	5 (35.7)	1.9 (0.47–8.05)	0.36	–	–
^b Anxiety disorder at evaluation							
No	33 (80.5)	23 (85.2)	10 (71.4)	1.0			
Yes	8 (19.5)	4 (14.8)	4 (28.6)	2.3 (0.48–11.1)	0.30	–	–
Alcohol abuse or dependence at evaluation							
No	35 (85.4)	23 (85.2)	12 (85.7)	1.0			
Yes	6 (14.6)	4 (14.8)	2 (14.3)	0.96 (0.15–6.0)	0.96	–	–
Alcohol abuse or dependence before TBI							
No	25 (61)	16 (59.3)	9 (64.3)	1.0			
Yes	16 (39)	11 (40.7)	5 (35.7)	0.81 (0.21–3.07)	0.75	–	–
^c Substance abuse or dependence at evaluation							
No	37 (90.2)	24 (88.9)	13 (92.9)	1.0			
Yes	4 (9.8)	3 (11.1)	1 (7.1)	0.61 (0.06–6.53)	0.69	–	–
Substance abuse or dependence before TBI							
No	30 (73.2)	20 (74.1)	10 (71.4)	1.0			
Yes	11 (26.8)	7 (25.9)	4 (28.6)	1.14 (0.27–4.84)	0.86	–	–
Clinical and laboratorial variables							
Posttraumatic amnesia at evaluation							
Less than one month	20 (48.8)	18 (66.7)	2 (14.3)	1.0		1.0	
More than one month	21 (51.2)	9 (33.3)	12 (85.7)	12 (2.2–65.5)	0.004	9.26 (1.56–54.92)	0.001
^d Glasgow Coma Scale							
7 or 8	15 (36.6)	11 (40.7)	4 (28.6)	1.0			
5 or 6	11 (26.8)	6 (22.2)	5 (35.7)	2.29 (0.44–11.92)	0.32	–	–
3 or 4	15 (36.6)	10 (37.1)	5 (35.7)	1.37 (0.29–6.60)	0.69	–	–
^d Pupils							
Isocorics	29 (70.7)	19 (70.4)	10 (71.4)	1.0			
Anisocorics	12 (29.3)	8 (29.6)	4 (28.6)	0.95 (0.23–3.94)	0.94	–	–
^d Marshall CT classification ^a							
Type I, II, or III injury	19 (47.5)	12 (46.2)	7 (50)	1.0			
Type IV, V, VI, or VII injury	21 (52.5)	14 (53.8)	7 (50)	0.86 (0.23–3.15)	0.82	–	–
^d SAH ^a							
No	15 (37.5)	10 (38.5)	5 (35.7)	1.0			
Yes	25 (62.5)	16 (61.5)	9 (64.3)	1.12 (0.29–4.33)	0.86	–	–

(continued)

Table 1 (Continued)

Variables	All patients N = 41 (%)	Personality changes		Unadjusted OR (CI 95%)	P-value	Adjusted OR (CI 95%)	P-value
		No n = 29 (67%)	Yes n = 14 (33%)				
^d Associated thorax/abdominal trauma ^a							
No	10 (25)	7 (26.9)	3 (21.4)	1.0			
Yes	30 (75)	19 (73.1)	11 (78.6)	1.35 (0.29–6.32)	0.70	–	–
^d SBP Mean (mmHg) (±SD)	126.8 (±22.5)	125.4 (±20.3)	129.4 (±26.7)	NA	0.60	–	–
^d DBP Mean (mmHg) (±SD)	72.1 (±16.6)	71 (±14.5)	74.3 (±20.6)	NA	0.56	–	–
Time of ITU ^a							
Less than 7 days	12 (30)	11 (42.3)	1 (7.1)	1.0	0.04	1.0	0.23
More than 7 days	28 (70)	15 (57.7)	13 (92.9)	9.53 (1.08–84.14)		4.26 (0.40–45.60)	
^{d,e} Na ⁺ (mEq/L) Median (IQ) ^a	139 (138 / 141)	139.5 (137.7 / 141)	139 (138 / 141.2)	NA	0.83	–	–
^d Hematocrit (%) Mean (±SD)	32.9 (±7.5)	31.9 (±7.2)	34.8 (±8)	NA	0.26	–	–
^d Hemoglobin (g/dL) Mean (±SD)	11.4 (±2.5)	11 (±2.3)	12 (±2.9)	NA	0.25	–	–
^d Leukocytes ^f > 11.000/μL	29 (74.4)	19 (76)	10 (71.4)	1.0			
<11.000/μL	10 (25.6)	6 (24)	4 (28.6)	1.27 (0.29–5.56)	0.75	–	–

Hosmer–Lemeshow goodness of fit test: *P*-value = 0.37. Accuracy of the model: 80% (CI 65.24–89.5%); sensitivity: 85.71% (CI 60.06–95.99%); specificity: 76.92% (CI 57.95–88.97%). Positive predictive value: 66.67% (CI 43.75–83.72%); negative predictive value: 90.91% (72.18–97.47%). ^aOne missing. ^bPanic disorder, generalized anxiety disorder, and posttraumatic anxiety disorder were all grouped as a dichotomous variable “Anxiety disorder.” ^cAbuse or dependence of cannabinoid, cocaine and derivate, amphetamine, opioid or benzodiazepine were all grouped as a dichotomous variable “Substance abuse or dependence.” ^dAt admission. ^eSignificance level analyzed by Mann–Whitney *U*-test because the distributions violated assumptions for parametric testing. ^fTwo missing.

sonality changes diagnosis. Personality changes diagnosis was determined using criteria of the DSM-IV-TR and was assessed mainly using information gained from relatives/significant others during the interview.

Since functional deficits after TBI are associated with the severity of the trauma [8] and the degree of secondary lesions [9], hospitalization variables directly or indirectly associated with systemic insults were also analyzed.

PTA was evaluated retrospectively at the moment of psychiatric evaluation, a validated assessment [6] which was conducted by asking the patients the following question: “which and when was your first memory that you can recall after the TBI?” With the assistance of relatives/significant others and the examiner, the period of time between TBI and the moment at which the autobiographic episodic memory became relatively continuous [5,10] was dichotomized in “more than or less than one month” due to the association of this interval with global outcome [7] (Figure 1).

The study protocol was approved by the Human Research Ethics Committee of the Universidade Federal de Santa Catarina (UFSC) and conducted to conform the provisions of the Declaration of Helsinki. Written informed consent was obtained from relatives and patients. Magnitude of the association among the independent variables and occurrence of personality changes was measured by the crude and adjusted odds ratio (OR) and the respective 95% confidence interval (CI) determined by binary unconditional logistic regression. Statistical analysis was conducted using SPSS 17.0 (Chicago, IL, USA) and Open Epi 3.01 (Atlanta, GA, USA).

Figure 1 Sampling course for psychiatric evaluation of adults consecutively admitted to an intensive care unit (ICU) due to severe nonmissile traumatic brain injury (TBI) an average of 18 months following trauma.

Table 1 shows the multiple logistic regression analysis models. The Hosmer–Lemeshow test of goodness of fit had a probability value of 0.37, indicating the model’s estimates fit the data at an acceptable level. Among the variables investigated, only prolonged PTA remained highly (OR 9.26, CI 95% 1.56–54.92) and

independently associated with the diagnosis of personality changes ($P = 0.001$).

Our findings demonstrated PTA duration determined by a simple, fast and low-cost evaluation in patients with severe TBI was independently associated with the occurrence of personality changes 18 months after the injury. The observed association remains strong even after controlling for confounders variables commonly associated with TBI prognosis.

The negative predictive value of 90.91% suggests that patients who recover the autobiographic memory earlier after the injury have low chance of long-term development of personality changes due the severe TBI. If confirmed in other populations and larger sample sizes, the present findings may be useful for the patient's family, health and insurance systems in planning long-term patient care.

The sample size and the absence of an analysis of association between the outcome and brain lesion topography provided from neuroimaging findings are some of the limitations of this study.

The present study design did not allow for concluding if the mechanisms involved with the transitory or permanent disruption

of the autobiographic memory processing integrity are the same factors related to personality changes development after severe TBI. Understanding the common mechanisms linking personality changes to PTA-related cognitive domains may help understand one of the most devastating and prevalent neuropsychiatric consequences of TBI.

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Conflict of Interest

The authors declare no conflict of interest.

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