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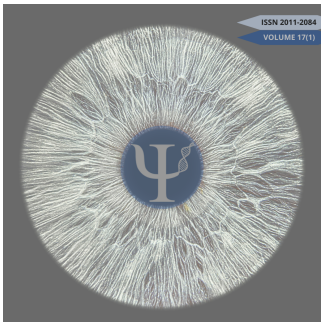

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Behavioral Changes after Traumatic Brain Injury: A Systematic Review and Meta-analysis on the Frontal Systems Behavior Scale

Cambios conductuales en pacientes con traumatismo craneoencefálico: una revisión sistemática y metaanálisis del Frontal Systems Behavior Scale

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Abstract.
Objective. To analyze the behavioral changes of patients with traumatic brain injury (TBI) based on their performance on the Frontal Systems Behavior Scale (FrSBe). **Method.** We performed a systematic review and meta-analysis of original articles that used the FrSBe scale in patients with TBI from the time of publication of the instrument (year 1999) to February 2022, using PubMed, Scopus, and EBSCO databases. **Results.** The search yielded a total of 4318 records, of which 28 met the selection criteria. The studies reported that patients with TBI showed impairments in some domains assessed by the FrSBe: apathy and executive dysfunction. **Conclusions.** The results are consistent with behavioral impairments frequently reported in TBI patients. Therefore, the FrSBe is presented as a useful and effective tool for the detection of behavioral changes in this population.

Resumen.
Objetivo. Caracterizar los cambios comportamentales de pacientes con traumatismo craneoencefálico (TCE) a partir del uso de la escala Frontal Systems Behavior Scale (FrSBe). **Método.** Se realizó una revisión sistemática y metaanálisis de artículos originales que hayan utilizado la escala FrSBe en pacientes con TCE, desde el momento de la publicación del instrumento (año 1999) hasta febrero de 2022, en las bases PubMed, Scopus y EBSCO. **Resultados.** La búsqueda arrojó un total de 4318 registros, de los cuales 28 cumplieron con los criterios de selección. Los estudios reportaron que los pacientes con TCE presentaron alteraciones en algunos de los dominios evaluados por la FrSBe: apatía y disfunción ejecutiva. **Conclusiones.** Los resultados son concordantes con las alteraciones comportamentales que presentan los pacientes con TCE, por ende, el FrSBe se presenta como una herramienta útil y eficaz en la detección de cambios comportamentales post TCE.

Keywords.
FrSBe, Neuropsychology, Behavior, Assessment.
Palabras Clave.
FrSBe, neuropsicología, conducta, evaluación.

1. Introduction

The Frontal Systems Behavior Scale (FrSBe; Grace & Malloy, 2001) is a brief and reliable scale designed to assess behavioral problems associated with frontal lobe lesions and compare behavior before and after a brain injury. The scale aims to identify three behavioral problems (apathy, disinhibition, and executive dysfunction) that may not be detectable in classical neuropsychological assessments. It does so via two versions: a self-rating form for patients and a family form for the patients' relatives. Of all the neurological pathologies in which FrSBe has been used, traumatic brain injury (TBI) is particularly relevant because it frequently compromises the frontal brain areas (Hogeveen et al., 2021; Levy & Dubois, 2006; Osborne-Crowley & McDonald, 2018), leading to behavioral changes (Lane-Brown & Tate, 2009; Smith et al., 2019; Weber et al., 2018).

Addressing the clinical characteristics of people with TBI is highly relevant to health systems in various regions of the world. A systematic review conducted by Peeters et al. (2015) concluded that in Europe, 262 cases per 100000 present TBI. Two of the most common causes are falls and car accidents. In 2006, the World Health Organization (WHO) warned that this pathology was considered the leading cause of death and disability in children and young adults worldwide (2006). In addition, in 2022, the Lancet Neurology Commission on TBI reported that TBI is the neurological pathology with the highest annual incidence and that around 50 million people are affected by this pathology (Maas et al., 2022). They indicate that there is a great need to address the behavioral problems characteristic of this population in long-term follow-ups, since behavioral changes can persist in people with TBI even up to 10 years post-injury (Maas et al., 2022). The most frequent behavioral disturbances in this population include changes in mood, such as apathy, difficulties in controlling behavior, which are presented as indicators of inhibition disturbances, or executive dysfunction (Azouvi et al., 2017).

Apathy was conceptualized by Marin (1991) as a neuropsychiatric syndrome characterized by lack of motivation, interest, energy, or emotion loss. Previous studies have shown that between 20% (Al-Adawi et al., 2004) and 69% (Lane-Brown & Tate, 2009) of patients with TBI present apathy, which usually appears as a result of prefrontal and basal ganglia dysfunction (Levy & Dubois, 2006). In addition, apathy frequently co-occurs with other usual disorders in patients with TBI, such as depression (Al-Adawi et al., 2004; Ciurli et al., 2011; Lane-Brown & Tate, 2009; Monsalve et al., 2012), fatigue (Lane-Brown & Tate, 2009), irritability, aggression/agitation, appetite disturbances, euphoria, anxiety, and, to a lesser extent, hallucinations (Ciurli et al., 2011; Monsalve et al., 2012).

On the other hand, disinhibition is defined as the inability to suppress an action or verbalization, which could be regarded as inappropriate for the context (Osborne-Crowley & McDonald, 2018). There is evidence indicating that this behavioral disturbance is present in 34-67% of patients during the first year after the injury, although it tends to persist over time (Pearce et al., 2016) and is associated with damage in the orbitofrontal cortex (Osborne-Crowley & McDonald, 2018). However, other studies (Floden et al., 2008; Hart et al., 2019; Rieger, 2002) have reported that patients with TBI do not present disinhibition compared to controls.

Lastly, executive functioning disorders are manifested at the behavioral level as difficulties in organizing, planning, executing tasks, conceptualizing, and exhibiting a capacity for mental flexibility (Polish et al., 2019). Several studies report that TBI patients present dysfunction in different executive aspects. A study conducted by Matheson (2010) found that TBI patients show impaired ability to change attentional focus, plan and organize tasks, organize materials, and monitor their performance. Likewise, it is reported that TBI patients with ten years of evolution have deficits in tasks that assess processing speed (Symbol Digit Modalities Test [SDMT] and Digit Symbol Coding) and executive functions (Hayling and SART), especially deficits in inhibitory control, which are associated with the presence of frontal brain lesions (Draper & Ponsford, 2008).

Even though there are plenty of neuropsychological tests that assess the performance of TBI patients, the FrSBe is certainly an extremely useful tool due to its simpleness and briefness that allows both patient and family member to characterize the behavioural changes of the former. In other words, the professional has a broad characterization of the patients' behavior after few minutes. Most importantly, it provides the possibility of analyzing and comparing the patients' behavior before and after the traumatic brain injury. Given that the FrSBe is a scale that allows the assessment of several altered domains in TBI patients, including apathy, disinhibition, and executive dysfunction, this paper aims to analyze patients' performance on this scale. We conducted a systematic review of the available literature and a meta-analysis study of the performance in each one of the subscales in order to estimate a measure of the overall effect of the impairment of each evaluated component.

2. Method

A systematic review and a meta-analytic study of the performance of TBI patients in the FrSBe scale was conducted. This paper was carried out following the PRISMA guidelines (Page et al., 2021).

2.1 Search Strategy

The following databases were used: PubMed, Scopus and EBSCO up to February 15, 2022. A combination of

Table 1

Characteristics of Included Studies for the Qualitative Synthesis and Meta-Analysis

Study (sorted by year)*	Study type	*n* (CG)	TBI					
			n (*n* stratification group)	% Female	Age: Mean (sd)	Education in years: Mean (sd)	TBI severity	Time since TBI: Mean (sd)
Reid-Arndt et al. (2007)*	TBI-o	–	76	28.9	35.1 (12.8)	–	–	35.4 (67.0) months
O'Keeffe et al. (2007)	CC	31	31	12.9	28.74 (8.52)	Range: 2 – >16	–	36.25 (22.37) months
Lane-Brown and Tate (2009)*	TBI-o	–	34	11.7	34.36 (9.39)	–	Sev	80.58 (71.64) months
Larson and Perlstein (2009)	TBI-o	–	16	25	30.88 (12.98)	13.63 (1.63)	Sev	10.69 (7.60) months
Aboulafia-Brakha et al. (2013)	TBI-o	–	10	20	47 (24-58)	Median 14 (range 12-16)	Mod/Sev	27.5 (range 16-166) months
Juengst et al. (2013)*	TBI-o	–	50	20	47.68 (15.6)	14.62 (2.7)	M/Mod/Sev	58.50 (range 14-150) months
Niemeier et al. (2013)	TBI-o	–	101	35.6	43.36 (19.19)	–	Mod/Sev	–
Barrett et al. (2013)*	CC	14	46 (gr1: 20, gr2: 26)	39.1	gr1: 21.7 (2.7); gr2: 22.9 (3.0)	–	M/Mod/Sev	> 5 years (mean gr 1 = 7; mean gr2 = 11.1)
Cantor et al. (2014)*	TBI-o	–	98 (gr1: 49, gr2: 49)	62.2	45.3 (14.0)	16.4 (2.6)	M/Mod/Se	12.6 (14.1) years
Juengst et al. (2014)*	CC	30	42 (gr1: 8, gr2: 34)	22.9	gr1: 33.54 (16.03); gr2: 34.31 (13.06)	–	–	gr1: 6 months; gr2: >12 months
Kim et al. (2014)*	CC	18	22	40.9	29.1 (11.5)	13.8 (2.1)	Mod/Sev	36.9 (68.0) months
Llorens et al. (2015)	TBI-o	–	42	35.7	41.71 (13.49)	–	Mod/Sev	227.95 (50.20) days
Lengenfelder et al. (2015)	CC	19	33	–	40.94 (11.08)	14.58 (2.26)	Mod/Sev	93.53 (66.49) months
Chiaravalloti et al. (2016)*	TBI-o	–	69 (gr1 35, gr2: 34)	–	gr1: 37.17 (11.24); gr2: 40.68 (11.28)	gr1: 13 (1.93); gr2: 14.25 (1.82)	Mod/Sev	gr1: 119.97 (128.91) months; gr2: 101.97 (70.78) months
Juengst et al. (2016)*	TBI-o	–	141 (gr1: 69, gr2: 72)	18.4	gr1: 32.3 (13.5); gr2: 46.3 (18.8)	–	Mod/Sev	gr1: 6 months; gr2: 7.2 (8.5) years
Myrga et al. (2016)	TBI-o	–	87 (gr1: 63; gr2: 24)	19.5	gr1: 34.16 (13,7); gr2: 37.38 (15.4)	Range 16-75	Mod/Sev	–
Juengst et al. (2017)*	TBI-o	–	88	20.4	37 (15.8)	13.1 (2.1)	Mod/Sev	> 6 months
Hart et al. (2017)*	TBI-o	–	90 (gr1: 30, gr2: 60)	18.8	gr1: 36.2 (13.3); gr2: 30.4 (10.2)	gr1: 13.4 (2.5); gr2: 13.4 (2.1)	Mod/Sev	gr1: median 72 months (range: 6 - 339); gr2: median 69 months (range: 6 - 298)
FitzGerald et al. (2017)*	TBI-o	–	11 (gr1: 5, gr2: 6)	27.2	gr2: 27.2 (5.6); gr1: 33.78 (13.33)	Range from gr1 and gr2: <12 to >16	Sev	gr1: 7.57 (4.91) months; gr2: 66.66 (87.02) months
Honan (2017)	CC	22	31	19.3	45.13 (15.56)	13.45 (2.73)	Mod/Sev	12.48 (10.49) years
Weber et al. (2018)*	TBI-o	–	42 (gr1: 15, gr2: 27)	–	gr 1: 36.3 (8.8); gr2 36.7 (12.8)	gr1: 14.4 (2.0): gr2: 14.3 (1.7)	M/Mod/Se	gr1: 128.8 (79.0) months; gr2: 95.1 (94.4) months
De Simoni et al. (2018)	CC	21	42	–	40.6 (11.7)	–	Mod/Sev	73.1 (86.9) months
Smith et al. (2019)*	TBI-o	–	65	20	49.91 (16.54)	14.63 (2.63)	M/Mod/Se	55.0 (range 14.0 -104.5) months
Jenkins et al. (2019)	CC	20	40	15	39.6 (11.7)	–	Mod/Sev	75.3 (88.5) months
Cavanagh et al. (2019)	CC	47	61 (gr1: 38; gr2: 23)	36	gr1: 26.74 (8.4); gr2: 36.22 (11.23)	gr1: 13.26 (2.05); gr2: 15.09 (2.57)	M/Mod	gr1: 10 (5) days; gr2: 2 (3) years
Rogers and McKinlay (2019)*	CC	43	126 (gr:61, gr2:65)	39.6	gr1: 22.3 (2.8); gr2: 23.3 (3.6)	–	M/Mod/Sev	gr1: 7.1 (4.0) years; gr2: 10.9 (4.9) years
Hart et al. (2019)*	CC	26	51	31.3	37.5 (16.3)	13.6 (2.5)	Mod/Sev	Range 2-3 months
Hogeveen et al. (2021)*	CC	33	70 (gr1: 44, gr2: 26)	–	gr1: 28.1 (9.61); gr2: 32.6 (12.0)	gr1: 13.7 (2.15); gr2: 15.8 (2.76)	M/Mod	gr1: 9.80 (3.38) days; gr2: 2021 (1515) days

Note. *Included in meta-analysis; CC = Case-control; TBI-o = TBI only; gr1= stratification group 1; gr2 = stratification group 2; M = mild; Mod = moderate; Sev = Severe.

Table 2

Scores and Versions of the FrSBe for each Study, and Cognitive, Functional, and Emotional Variables Studied

Study (sorted by year)*	FrSBe scores	FrSBE form	FrSBe version	Study variables
Reid-Arndt et al. (2007)*	TS/Ap/D/ED	S	A	FA
O'Keeffe et al. (2007)	TS/Ap/D/ED	S/F	A	–
Lane-Brown and Tate (2009)*	Ap	F	A	EA
Larson and Perlstein (2009)	TS/Ap/D/ED	S/F	A	–
Aboulafia-Brakha et al. (2013)	TS	S/F	B/A	–
Juengst et al. (2013)*	TS	S	A	FA
Niemeier et al. (2013)	TS/Ap/D/ED	S/F	A	–
Barrett et al. (2013)*	TS/Ap/D/ED	S/F	A	CA
Cantor et al. (2014)*	ED	S	A	–
Juengst et al. (2014)*	D	S	A	–
Kim et al. (2014)*	TS	S/F	A	–
Llorens et al. (2015)		S/F	B/A	–
Lengenfelder et al. (2015)	Ap/D/ED	S/F	B/A	CA
Chiaravalloti et al. (2016)*	TS/Ap/D/ED	F	A	–
Juengst et al. (2016)*	Ap/D/ED	S	A	–
Myrga et al. (2016)	TS	S/F	B/A	–
Juengst et al. (2017)*	Ap/D/ED	S/F	A	EA
Hart et al. (2017)*	TS	S	A	–
FitzGerald et al. (2017)*	TS	S/F	A	
Honan (2017)	D	S	A	–
Weber et al. (2018)*	TS/Ap/D/ED	S/F	A	–
De Simoni et al. (2018)	TS/Ap/D/ED	S/F	B/A	–
Smith et al. (2019)*	Ap/D/ED	S/F	A	EA/CA
Jenkins et al. (2019)	TS	S/F	B/A	–
Cavanagh et al. (2019)	TS	S	A	–
Rogers and McKinlay (2019)*	TS/Ap/D/ED	S	A	–
Hart et al. (2019)*	TS/Ap/D/ED	S/F	B/A	–
Hogeveen et al. (2021)*	Ap	S	A	–

Note. *Included in meta-analysis; TS = total score; Ap = apathy; D = disinhibition; ED = executive dysfunction; S = Self-Rating Form; F = Family Rating Form; B = Before injury; A = After injury; FA = Functional assessment; EA = Emotional assessment; CA = Cognitive assessment.

the following keywords was used: ("traumatic brain injury" OR "head injury" OR "acquired brain injury") AND ("frontal systems behavior scale" OR "FrSBe" OR (behav* AND ("dysfunction" OR "change" OR "abnormal")) OR "apathy" OR "disinhibition").

2.2 Eligibility Criteria

To be eligible for the study, all papers had to meet the following criteria: 1) original papers in English, Spanish, or Portuguese; 2) original papers published from the year 1999 onward; 3) papers which have administered the FrSBe to TBI patients in its original or adapted version and that report results of the patients' performance in at least one subscale; 4) studies that included TBI patients without any other neurological comorbidity.

On the other hand, the exclusion criteria were the following: 1) systematic reviews, meta-analytic studies, books, and conference presentations; 2) reported TBI patients results mixed up with other neurological pathologies; 3) single-case studies.

2.3 Study Selection

The results of the searches conducted were imported to a bibliographic reference manager (Mendeley desktop). Duplicate records were removed using the software's automatic detection tool and by manual detection. Then, for the selection of the papers, a two-step approach was used. First, the titles and abstracts were reviewed, and finally, the papers were fully analyzed following the eligibility criteria. The first step was carried out by two of the authors of this work (NC and PC), and the second step was carried out by two of the authors (NC and SL).

2.4 Data Extraction

2.4.1 Qualitative Data

The following data was extracted from each of the studies: type of study (single-group design of TBI patients or case-control design), type of control group (healthy or pathological) when applicable, number of participants evaluated, mean age of participants and standard deviation, gender, years of education, TBI severity, duration of TBI, cause of TBI, matching variables used between the evaluated groups for the case-control studies, version of the FrSBe administered and subscales used, and, finally, it was recorded whether the studies had analyzed the relationship between the performance of TBI patients on the FrSBe and scales, which assess mood, cognitive functions or functional alterations.

2.4.2 Quantitative Data

For the meta-analytic study, the outcomes analyzed were the performance T-scores of the after version of the FrSBe. Papers that reported any of the FrSBe scores in a standardized format (T-score calculated from the normative data) were included. Thus, all the scores analyzed were adjusted for age, gender, and years of education and were expressed in T-score. The mean and standard deviation of the score for the complete scale or the subscales were extracted from each study, depending on which score was presented in the paper. If the articles reported the scores stratified by any variable of interest, each subgroup was considered as a different one. For example, if a paper included separate reporting of results for two different samples of TBI patients (e.g. mild TBI and moderate TBI), they were included in the analysis separately, with their respective sample size, mean, and standard deviation.

2.5 Analysis of Data

2.5.1 Qualitative Synthesis

The studies were grouped according to whether they had reported associations between the TBI patients' performance in any of the subscales of the FrSBe and in scales that assess mood, cognitive functions, or functional alterations. The type of association described by the studies in each case and the relevant results in this regard were analyzed.

2.5.2 Meta-Analytic Aynthesis

Mean T-scores of the FrSBe scores reported for the after version only were analyzed. The four possible FrSBe scores were analyzed separately: the full scale score, and the scores for each subscale (apathy, disinhibition, and executive dysfunction). Overall means were calculated using the inverse variance method with a random effects model. The summary measures of the effects calculated were expressed in the same unit of measure (T-score). The heterogeneity and inconsistency among the studies were analyzed using the Cochran Q test and the I^2 statistic (values greater than 75% indicate high inconsistency; Higgins et al., 2003). In cases of high heterogeneity among studies, an analysis of influential data was performed using the leave-one-out cross-validation method, and a meta-regression was performed with the TBI time of evolution (in months) as an explanatory variable for the FrSBe scores. All the analyses were performed using version 4.2.1 of R (R Core Team, 2022) under the RStudio environment (RStudio Team, 2022), and the meta package version 6.0-0 (Balduzzi et al., 2019) was used. The data and script used for the meta-analysis can be found at https://osf.io/2p9xb/.

2.6 Risk of bias

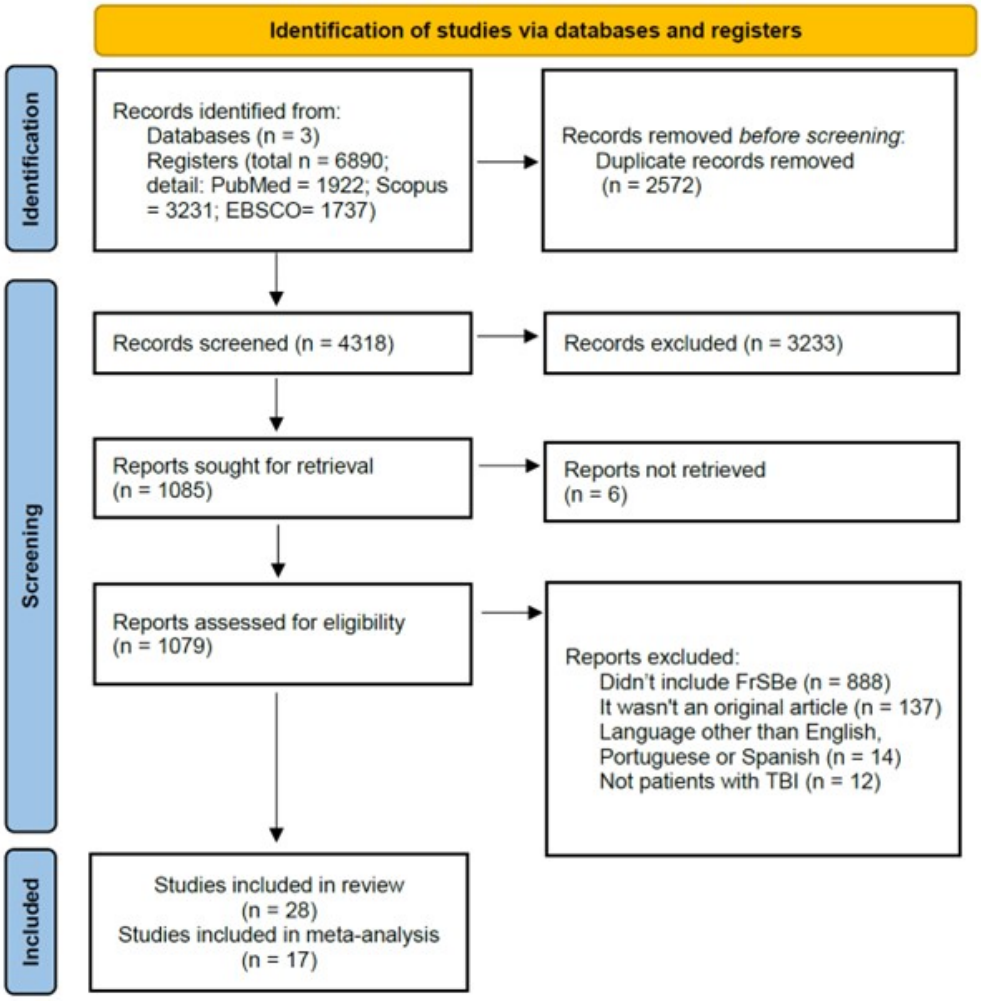
Publication bias for the studies included in the meta-analyses was analyzed by visualizing the funnel plot and, formally, by Egger's test (Egger et al., 1997).

3. Results

The search yielded a total of 4318 records, of which 28 met the eligibility criteria and 17 were included in the meta-analytic synthesis (Figure 1). Table 1 shows the characteristics of all the included studies and, in Table 2, the scores and versions of the FrSBe that each study

Figure 1

Flow Chart Depicting the Selection of Articles for the Qualitative Synthesis and Meta-Analysis



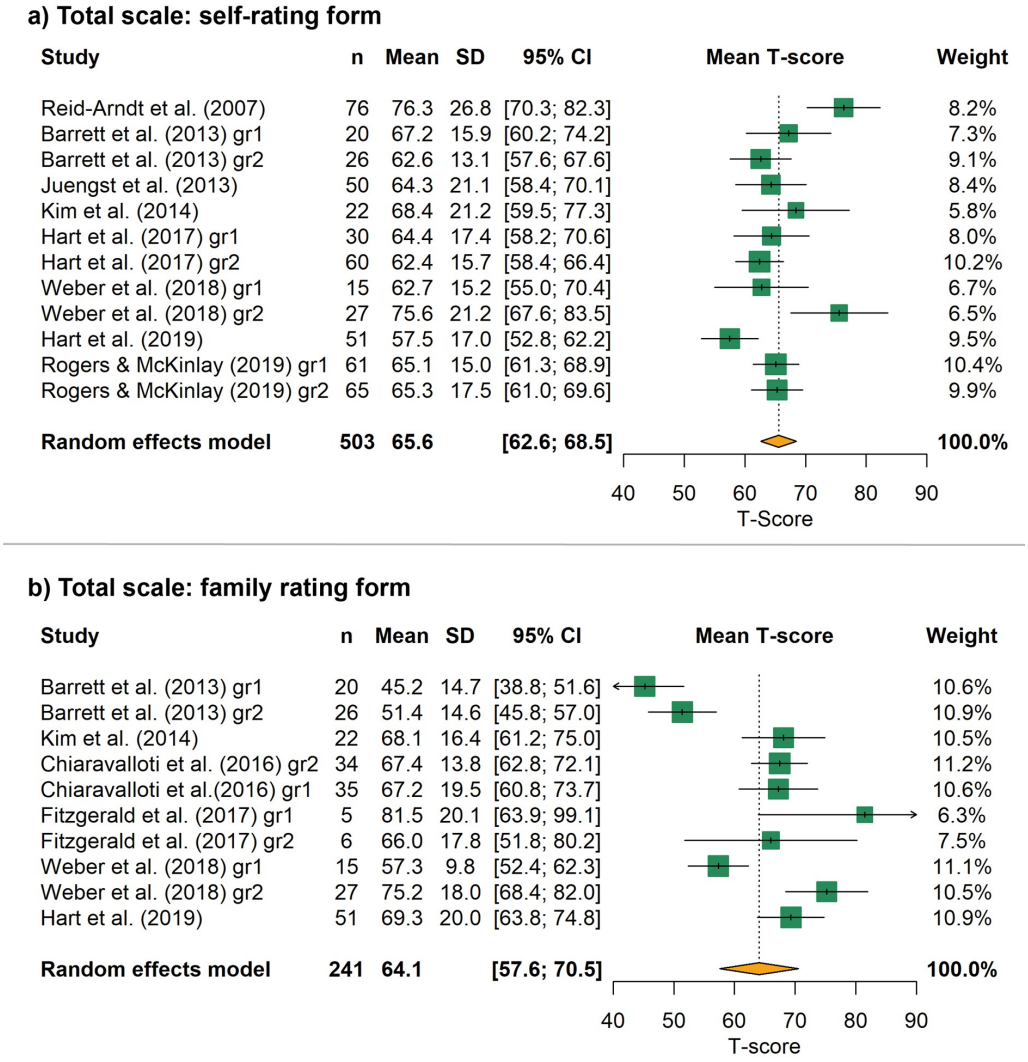
analyzed. Among the 28 articles analyzed for the qualitative synthesis, data from 1615 patients with TBI and 324 participants from the control group were considered. Most of the patients evaluated in the studies were adult men older than 18 years with moderate to severe TBI and with more than 9 years of formal education. The time since the occurrence of TBI varied considerably among studies, ranging from 2 months in the mildest cases to 13 years in the most severe cases. It is important to highlight that only one study (Honan, 2017) presented a greater range of evolution of TBI, since it included patients with 45 years of evolution of TBI, giving a range between 1 year and 45 years.

Regarding the case-control design studies that were included, 83% of the participants in the control group were healthy, while the rest presented orthopedic injuries. Considering all the case-control design studies, the participants were between 18 and 70 years of age and had more than 11 years of education.

Figure 2 shows the studies included for the meta-analytic synthesis of the full scale scores of the FrSBe, both the self-rating form (Figure 2a) and the family form (Figure 2b). Data from a total sample of 503 TBI participants were included for the self-rating form and data from 241 participants for the family rating form. Random-effects analysis estimated an overall mean full-scale T-score of 65.6 (95% CI: 62.6–68.5) for the self-rating form and 64.1 (95% CI: 57.6–70.5) for the family rating form. Moderate heterogeneity among studies was observed for the self-rating form (I^2 = 67.6% [95% CI: 40.7%–82.3%]; $Q = 33.94$, $df = 11$, $p < .001$). Analysis of influential data showed that by excluding the study by Reid-Arndt et al. (2007) inconsistency was reduced (I^2 = 47.7% [95% CI: .0%–73.8%]) and the overall mean estimate for the self-rating form of the full scale became 64.3 (95% CI: 62.1–66.6). On the other hand, a high heterogeneity was observed among the studies that reported scores for the family rating form (I^2 = 88.7%

Figure 2

Forest Plot of Mean Total Scale T-score on FrSBe Self-rating (a) and Family Rating Form (b)



Note. Studies presenting stratified results are considered separately and are referred to in the figure as gr1 and gr2 in each case. SD = standard deviation; CI = Confidence interval.

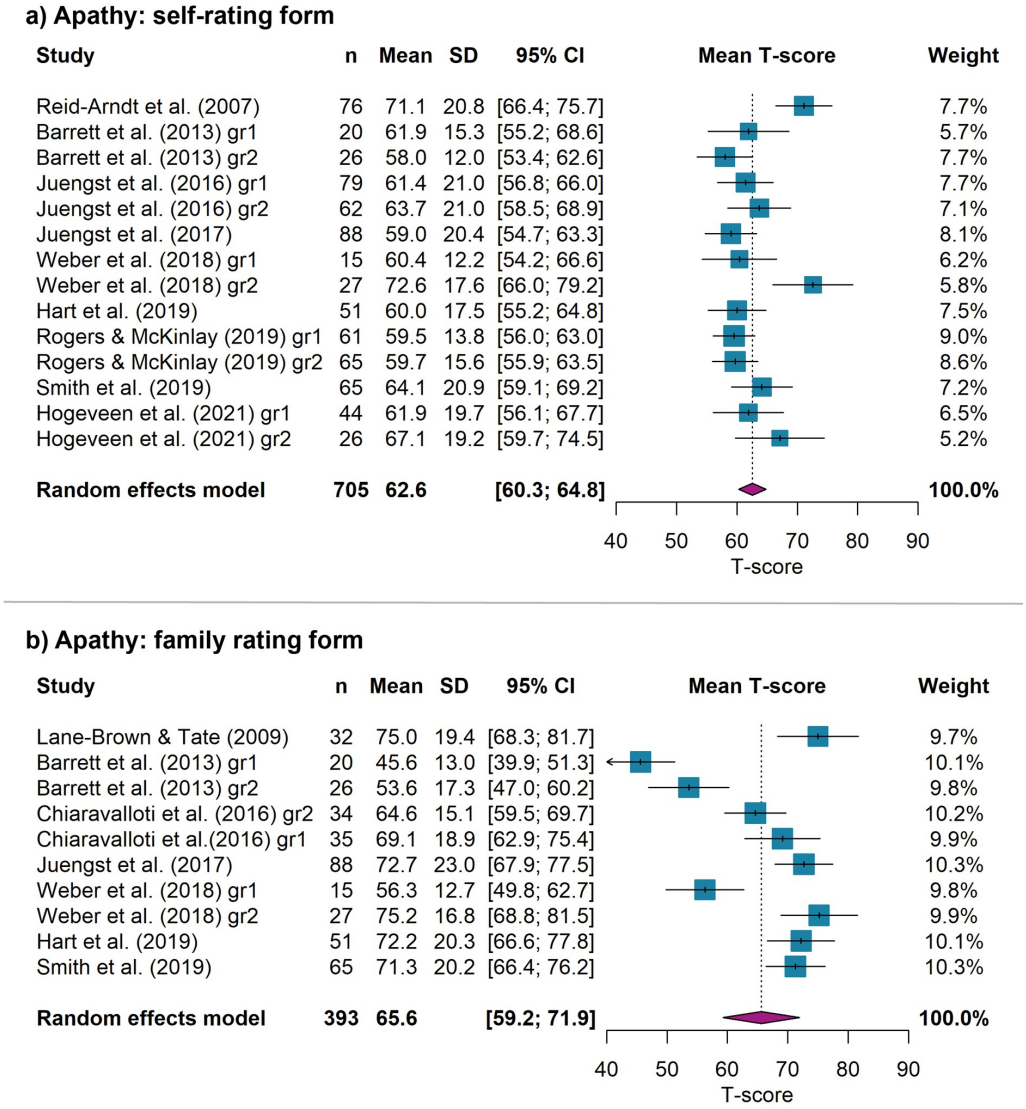
[95% CI: 81.4%–93.2%]; $Q = 79.95$, $df = 9$, $p < .001$). The cross-validation method did not reveal the existence of an influential group and no substantial changes were observed in the inconsistency among studies when removing each one of them from the analysis. Finally, the results of the meta-regression showed no effect of the TBI time of evolution on the scores of the full scale, neither for the self-rating form ($p = .956$) nor for the family rating form ($p = .222$).

3.1 FrSBe: Apathy Subscale Score (After Version)

Figure 3 shows the studies included for the meta-analytic synthesis of the apathy subscale scores of the self-rating form (Figure 3a) and family rating form (Figure 3b). For the self-rating form, data from a total sample of 705 participants with TBI were included and data from 393 participants for the family rating form. Random-effects analysis estimated an overall mean T-score for the self-rating form apathy subscale of 62.6 (95% CI: 60.3–64.8) and 65.6 (95% CI: 59.2–71.9) for the family rating form. Moderate heterogeneity among studies was observed for the self-rating form ($I^2 = 64.4\%$ [95% CI: 36.9%–79.9%]; $Q = 36.47$, $df = 13$, $p < .001$). Cross-validation showed that removing the study by Reid-Arndt et al. (2007) reduced inconsistency ($I^2 = 42.2\%$ [95% CI: .0%–69.9%]) and the overall mean T-score estimate for the self-rating form of the apathy scale became 61.6 (95% CI: 59.8–63.4). Conversely, high heterogeneity was observed among the studies that reported apathy subscale scores for the family rating form ($I^2 = 91.4\%$ [95% CI: 86.3%–94.6%]; $Q =$

Figure 3

Forest Plot of Mean Apathy T-score on FrSBe Self-rating (a) and Family Rating Form (b)



Note. Studies presenting stratified results are considered separately and are referred to in the figure as gr1 and gr2 in each case. SD = standard deviation; CI = Confidence interval.

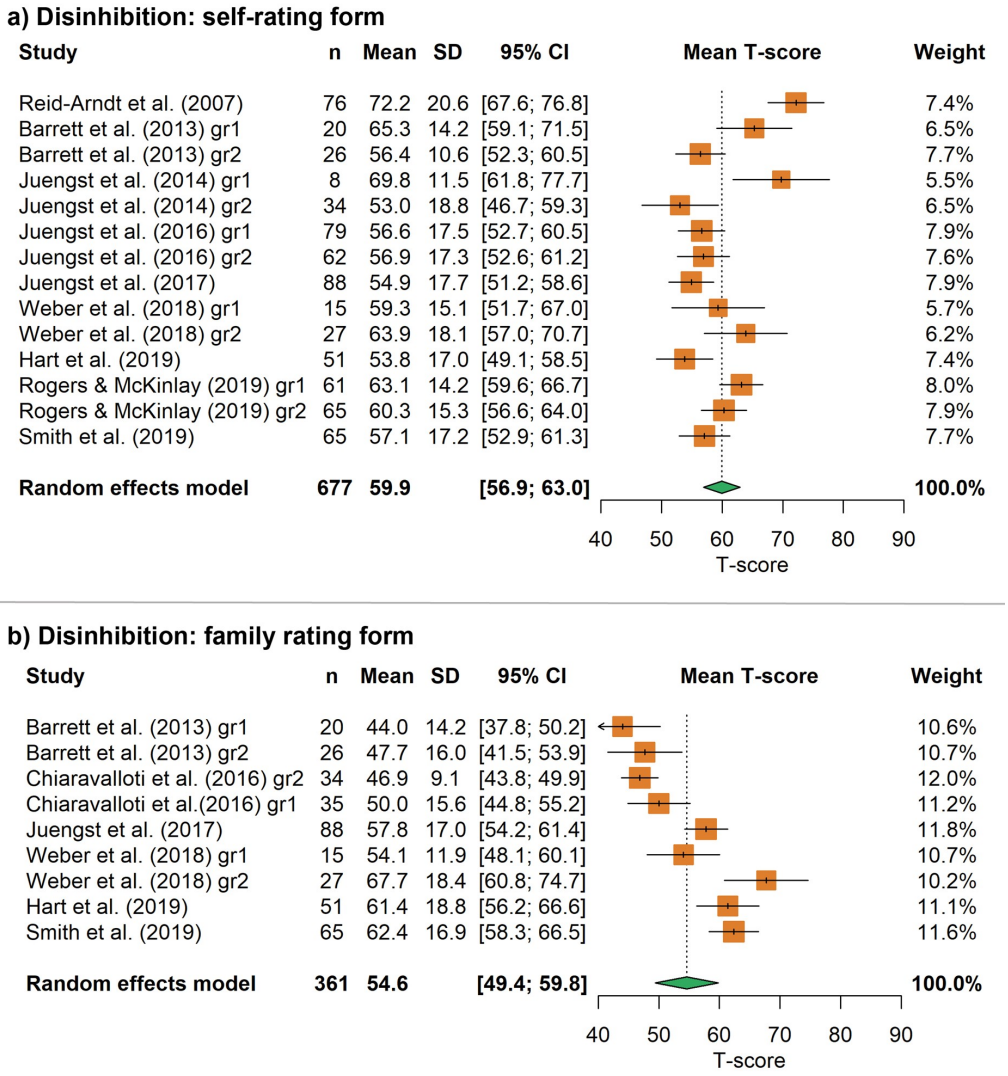
104.29,$df = 9$, $p < .001$). The cross-validation method did not reveal the existence of an influential group, and no substantial changes were observed in the inconsistency among studies when removing each one of them from the analysis. The results of the meta-regression showed no effect of the time of evolution on the scores of the apathy subscale, neither for the self-rating form ($p = .489$) nor for the family rating form ($p = .208$).

3.2 FrSBe: Disinhibition Subscale Score (After Version)

Figure 4 shows the studies included for the meta-analytic synthesis of the disinhibition subscale scores of the self-rating form (Figure 4a) and the family rating form (Figure 4b). Data from a total sample of 677 TBI participants were included for the self-rating form, and data from 361 participants were included for the family rating form. Random effects analysis estimated an overall mean T-score for the self-rating form disinhibition subscale of 59.9 (95% CI: 56.9–63.0) and 54.6 (95% CI: 49.4–59.8) for the family rating form. Evidence of high heterogeneity among studies was observed for the self-rating form (I2 = 80.6% [95% CI: 68.4%–88.1%]; $Q = 67.14$, $df = 13$, $p < .001$). Cross-validation showed that removing the study by Reid-Arndt et al. (2007) reduced inconsistency (I2 = 66.1% [95% CI: 39.1%–81.1%]), and the overall mean T-score estimate for the patient version of the disinhibition subscale became 58.8 (95% CI: 56.4–61.1). In addition, high heterogeneity was observed for the family

Figure 4

Forest Plot of Mean Disinhibition T-score on FrSBe Self-rating (a) and Family Rating Form (b)



Note. Studies presenting stratified results are considered separately and are referred to in the figure as gr1 and gr2 in each case. SD = standard deviation; CI = Confidence interval.

version of this subscale (I2 = 90.1% [95% CI: 83.4%–94.1%]; $Q = 80.7$, $df = 8$, $p < .001$), but no influential data that would substantially affect the inconsistency among studies was observed. The results of the meta-regression showed no effect of the time of evolution on the disinhibition subscale scores, neither for the patient version ($p = .859$) nor for the family version ($p = .147$).

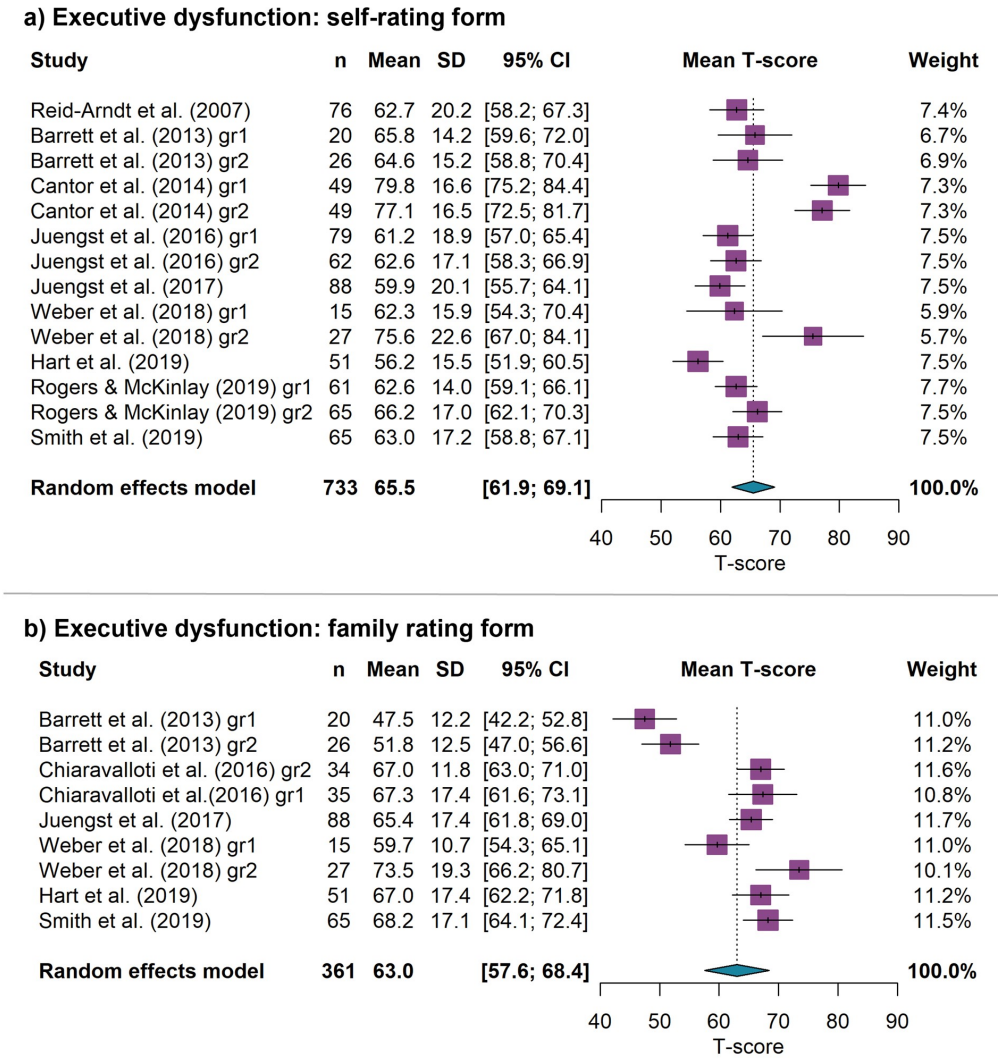
3.3 FrSBe: Executive Dysfunction Subscale Score (After Version)

Figure 5 shows the studies included for the meta-analytic synthesis of the scores of the executive dysfunction subscale of the self-rating (Figure 5a) and family form (Figure 5b). Data from a total sample of 733 TBI participants were included for the self-rating form, and data from 361 participants were included for the family rating form. Random-effects analysis estimated an overall mean T-score for the executive dysfunction subscale of 65.5 (95% CI: 61.9–69.1) for the self-ratign form and 63.0 (95% CI: 57.6–68.4) for the family rating form. Evidence of high heterogeneity among studies was observed for the self-rating form ($I^2 = 87.3\%$ [95% CI: 80.3%–91.8%]; $Q = 102.13$, $df = 13$,$p < .001$) and for the family rating form ($I^2 = 89.9\%$ [95% CI: 83.0%–94.0%]; $Q = 79.04$, $df = 8$, $p < .001$).

The cross-validation method did not reveal the existence of an influential group for the estimations of the executive dysfunction score, neither for the self-rating form nor for the family rating form, and no substantial changes were observed in the inconsistency among

Figure 5

Forest Plot of Mean Executive Dysfunction T-score on FrSBe Self-rating (a) and Family Rating Form (b)



Note. Studies presenting stratified results are considered separately and are referred to in the figure as gr1 and gr2 in each case. SD = standard deviation; CI = Confidence interval.

studies when removing each one of them from the analysis. An effect of TBI time of evolution was observed for the self-rating form scores (estimated $\beta = .092$ [95% CI: .039–.146], $z = 3.388$, $p < .001$, $R^2 = 56.2\%$) in which a longer time of evolution predicted a higher T-score on the subscale, which consists of a worse performance (Figure 6). No effect of time was observed on the family rating form of this subscale ($p = .427$).

3.4 Assessment of Risk of Bias of Meta-Analytic Estimates

Funnel plots were inspected for publication bias, and no evidence was found for any of the analyses. Therefore, the formal analysis of asymmetry using the Egger's test was not statistically significant in any case (Full scale self-rating form: $p = .146$; Full scale family rating form: $p = .544$; Apathy self-rating form: $p = .075$; Apathy family rating form: $p = .522$; Disinhibition self-rating form: $p = .374$; Disinhibition family rating form: $p = .634$; Executive dysfunction self-rating form: $p = .345$; Executive dysfunction family rating form: $p = .721$).

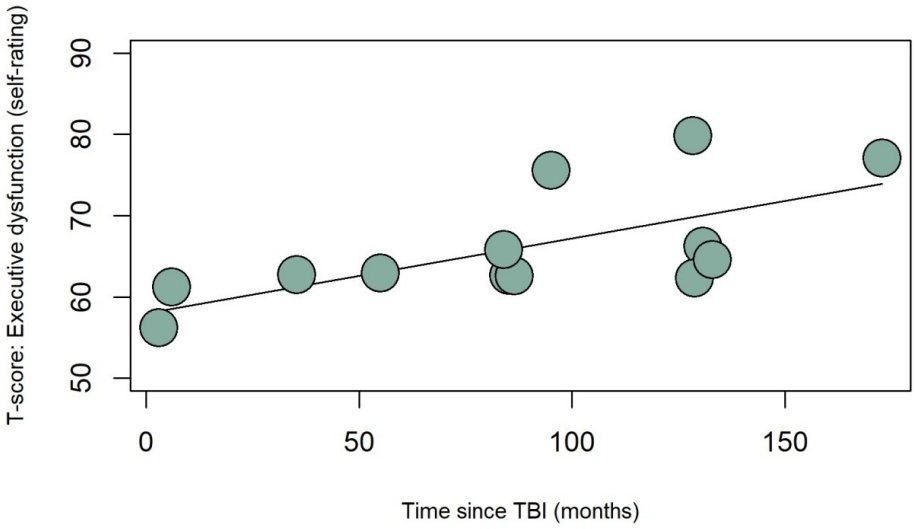
3.5 Results of the Qualitative Synthesis

3.5.1 FrSBe in TBI and Mood Assessments

Of the 28 papers included in the qualitative synthesis, only three presented performance associations between the FrSBe and scales that assess mood. Lane-Brown and Tate (2009) conducted a study with 34 TBI patients and used the apathy subscale of the FrSBe in conjunction with the Apathy Evaluation Scale (AES), the Depression, Anxiety and Stress Scale (DASS), and the Barrow Neurological Institute Fatigue Scale (BNIFS). The au-

Figure 6

Bubble Plot and Meta-regression Fit Line for Executive Dysfunction T-score (Self-rating Form) And Time since TBI in Months as Explanatory Variable



thors found a positive correlation between the FrSBe and the AES. Both scales had a 76% similarity in terms of detecting apathy. On the other hand, they examined the discriminant validity among all the scales and found no significant correlations between the FrSBe and the AES with the DASS and the BNIFS, indicating that both the AES and the FrSBe can dissociate between apathy, depression, and fatigue.

Moreover, Juengst et al. (2017) included 88 TBI patients in the study to whom The Patient-Health Questionnaire-9 (PHQ9) was administered to assess depression and FrSBe at 6 and 12 months of evolution. The results of the study showed that the depression the patients presented at 6 months after the injury was a significant predictor of depression at 12 months and elevated scores on the FrSBe at 12 months after the injury. However, although performance on the FrSBe at 6 months was a significant predictor of high scores at 12 months, it was not a predictor of the presence of depressive symptoms at 12 months.

Finally, Smith et al. (2019) conducted a study with 65 mild, moderate, and severe TBI patients to whom the FrSBe and the PRIME-MD that assesses depression were administered. The authors performed a linear regression model where they included the depression variable together with other variables (gender, severity, time of evolution, SADI score, premorbid IQ) and found that depression was not shown to be a predictor of FrSBe performance in disinhibition and executive dysfunction. These variables only explained .4% of performance variability on the FrSBe for the disinhibition subscale and 6.1% for the executive dysfunction subscale.

3.5.2 FrSBe in TBI and Cognitive Assessments

Although the vast majority of the papers used cognitive assessments that analyzed different domains such as attention, working memory, inhibitory control, among others, only 3 out of 28 papers analyzed correlations between these and the FrSBe. Smith et al. (2019) found positive correlations between the FrSBe domains and the California Verbal Learning Test (CVLT-II). The scores of the FrSBe apathy subscale were significantly correlated with the total number of intrusions obtained through the CVLT-II. Disinhibition scores on the FrSBe were associated with intrusions and repetitions of the CVLT-II and verbal fluency tasks and total intrusions. The FrSBe executive dysfunction subscale score also showed significant correlations with several CVLT-II indicators. The authors found that the cognitive variables explained 22% of the variability of performance in the FrSBe for the disinhibition subscale and 17.2% for the executive dysfunction subscale.

Furthermore, Barrett et al. (2013) conducted a case-control study with 20 mild TBI patients, 26 moderate and severe TBI patients, and 14 control participants with orthopedic injuries. They found associations between performance on the FrSBe for the executive dysfunction and disinhibition subscales with tests that assess working memory, attention, and executive functions, but only with the FrSBe self-rating form, and not with the familiar one. No significant correlations were found between performance on the FrSBe for the apathy subscale, either for the self-rating form or the family rating form. Conversely, the disinhibition subscale of the FrSBe self-rating form was significantly correlated with performance in tests evaluating working memory and attention.

Lastly, in a case-control study conducted by Lengenfelder et al. (2015), in which 33 patients with moderate and severe TBI and 19 healthy participants were included, it was found that the domains evaluated by the FrSBe are significantly related to care measures. The authors found that scores on the disinhibition subscale on both forms of the FrSBe were significantly correlated with performance on verbal fluency, whereas only scores on the family rating form on this subscale correlated with performance on the Failure to Maintain Set variable of the WCST. Although there were significant levels of apathy, this subscale had little association with scores on neuropsychological measures. This subscale was only correlated with Digit Span performance, as were the disinhibition and executive dysfunction subscales. No significant correlations were found between performance on the FrSBe subscales and the rest of the neuropsychological measures.

3.5.3 FrSBe in TBI and Functional Assessments

Only 2 of 28 papers presented associations between the FrSBe and scales that assess the social functioning of patients. Juengst et al. (2013) conducted a study with 50 patients with mild, moderate, and severe TBI. In this study, they used the full scale of the self-rating form of the FrSBe, the Mayo Portland Adaptability Inventory (MPAI) that assesses disability, the Fatigue Impact Scale (mFIS) and the PRIME-MD that assesses depression. They found that fatigue was the only strong predictor of disability variability. The authors concluded that although low performance on the FrSBe can lead to feelings of fatigue that significantly influence the level of disability presented by the patient, when fatigue is considered as a variable in itself, it is observed that this influences their level of disability to a greater extent than performance on the FrSBe.

Finally, Reid-Arndt et al. (2007) conducted a study with 76 TBI patients and found a positive correlation between performance on the self-rating form of the FrSBe and the Community Integration Questionnaire (CIQ). Therefore, the authors concluded that the greater the executive dysfunction, the greater the difficulties patients present in social integration.

4. Discussion

The objective of this systematic review and meta-analysis was to analyze the characteristics of behavioral changes in patients with TBI based on their performance on the FrSBe and to estimate a measure of the overall effect of the alteration of each behavioral component evaluated. In this study, 28 articles were included for the systematic review, and 17 articles for the meta-analysis. It was observed that not all the studies used all the scores proposed by the FrSBe, these being: full scale score, apathy score, disinhibition score, and executive dysfunction score. The selection criteria for the use of one score or another depended, naturally, on the objective of each study.

Regarding the quantitative results, an overall mean of the full scale T-score of 65.6 was obtained for the self-rating form and 64.1 for the family rating form. Considering the performance and severity classifications offered by the original authors of the scale (Grace & Malloy, 2001), a T-score of 65 or more is considered clinically significant and is an indicator of alterations in behavioral components related to the functioning of the frontal systems. On the other hand, T-scores between 60 and 64.9 are indicators of borderline abnormality, while those below 60 are classified within the non-pathological range (normal performance). Using this classification, it can be seen that the results of the present study estimate a clinically significant alteration in the performance of patients with TBI for the full scale of the self-rating form of the FrSBe and a borderline alteration for the scores obtained through family reports. This may be due to the lack of data on the family version, as opposed to the large amount of data on the patient version. However, various studies concluded that patients with TBI presented behavioral alterations, whether they are functional (Belmont et al., 2009; Benedictus et al., 2010; Sabaz et al., 2014), emotional (Delmonico et al., 2022), and/or cognitive (Benedictus et al., 2010; Spikman et al., 2012).

Similar scores were also observed for the executive dysfunction subscale, in which an overall mean T-score of 65.5 was obtained for the self-rating form and 63 for the family rating form. This is an indicator of a clinically significant alteration that manifests itself as difficulties to organize, plan, execute, and exhibit a capacity for mental flexibility, and a borderline alteration, respectively. These results are consistent with other studies in which alterations in executive functions were reported in patients with TBI assessed using other instruments such as WCST (Bivona et al., 2019), Hayling and SART (Draper & Ponsford, 2008), Behavior Rating Inventory of Executive Function (BRIEF-A; Matheson, 2010), California Verbal Learning Test (CVLT-II; Smith et al., 2019) and Digit Span (Lengenfelder et al., 2015). It should be noted that the time of evolution influenced the scores of the executive dysfunction subscale for the self-rating form, which indicates that the longer the time of evolution, the higher the T-score on the subscale, and therefore, the worse the performance. These results are consistent with other studies in which it was found that patients with TBI with more than 10 years of evolution continued to present low performance in cognitive tasks (Draper & Ponsford, 2008) and emotional alterations such as depression, anxiety, hostility, among others (Dan Hoofien et al., 2001). Furthermore, in a meta-analysis conducted by Li et al. (2017), TBI was identified as a risk factor for Alzheimer's disease. Another study by Huang et al. (2018) concluded that TBI is a potential risk factor for the development of dementia. Therefore, more studies should be carried out to assess the influence of the time of evolution at a cognitive, functional, and emotional level in patients with TBI.

In contrast, different results were found for the apathy scale, in which a lower T-score was estimated for the self-rating form than for the family rating form. In these cases, an overall mean T-score of 62.6 was obtained for the self-rating form, which is within the range of borderline disability, and 65.6 for the family version, which is within the clinical range. This means that patients exhibit a lack of interest, motivation, energy, or loss of emotion, followed by a lack of initiative or a decrease in goal-directed behaviors. Although the patient version is within the borderline range, this may be the result of a lack of self-awareness of the injury that TBI patients often present (Bivona et al., 2008; Larson & Perlstein, 2009; Trahan et al., 2006). In a study conducted by Lane-Brown and Tate (2009), it was found that more than half of TBI patients have apathy, according to the Apathy Evaluation Scale (AES). Likewise, in another study conducted by Ciurli et al. (2011), in which the Neuropsychiatric Inventory (NPI) scale was used, it was found that almost half of the patients had apathy.

Regarding the disinhibition subscale, scores indicating performance within normal ranges were obtained for both the mean summary of the self-rating form (estimated overall mean T-score at 59.9) and for the family rating form (estimated overall mean T-score of 54.6). This is an indicator that the patients do not present clinically significant disinhibition behaviors, such as impulsive behaviors, egocentric or childish speech, insults, among others. This result is consistent with a study carried out by Rieger (2002), in which the Stop Signal Task was used and no alterations were found regarding the ability to inhibit responses in patients with TBI. Likewise, in a study carried out by Floden et al. (2008), according to the Barratt Impulsiveness Scale, patients with TBI did not have impulsive behaviors. However, in other studies using the Neuropsychology Inventory (NPI) (Ciurli et al., 2011; Monsalve et al., 2012) and the Neuropsychiatric InventoryDisinhibition (NPID; Osborne-Crowley & McDonald, 2018), it was found that less than half of TBI patients manifested disinhibition. This inconsistency among the studies may be due to the result of a lack of consensus on its definition and, therefore, of scales that evaluate this construct (Arciniegas & Wortzel, 2014; Kocka & Gagnon, 2014). It is necessary to reach a consensus on its definition in order to have more consistent results in future studies.

Although the scores obtained in the subscales may not be within the clinical range, significant behavioral alterations may occur, which affect the patient's quality of life and, therefore, should be considered for possible treatment (Grace & Malloy, 2001). According to the results obtained in this qualitative synthesis, those patients with TBI who present clinically significant FrSBe scores may manifest behavioral alterations at an affective, cognitive, and/or functional level. According to studies carried out by Juengst et al. (2013, 2017) and Reid-Arndt et al. (2007), patients with TBI presented depression, disability, fatigue, stress, and difficulties in social integration, which are associated with poor performance on the FrSBe. These results are consistent with a study by Gorgoraptis et al. (2019) in which patients with TBI with cognitive impairment presented low scores in Health-related quality of life (HRQoL), an aspect that manifests as emotional and mental health problems, alterations in physical functioning, and difficulties at work, social activities and other daily activities. On the other hand, some studies established that 30% of patients with TBI have depression (Chui et al., 2021; Leong Bin Abdullah et al., 2018; Osborn et al., 2014). However, Osborn et al. (2014) stated that the percentage of patients with TBI varies depending on the scales used, since the authors did not obtain the same results when the self-rating form scales were used as when these were administered by a professional. Likewise, the authors (Osborn et al., 2014) concluded that this number could be also modified depending on which diagnostic manual is used, whether it is the DSM-III, the DSM-IV, or even the most recent, the DSM-V. Thus, it is important that standardized tools are used and that all the behavioral changes that patients with TBI present are evaluated, since these alterations at the cognitive, social, and emotional level clearly affect their quality of life.

On the other hand, we identified studies that show correlations between the FrSBe and cognitive assessment tools—Letter Fluency, CVLT (Smith et al., 2019); WCST, DKEFS, Digit Span (Lengenfelder et al., 2015)—, which indicate that patients with TBI may also present alterations that co-occur with behavioral changes such as alterations in attention, working memory and executive functions. Since the most common cause of TBI is a traffic accident (Peeters et al., 2015), patients are at greater risk of getting frontal lobe lesions and, as a consequence, greater impairments in executive functioning (Stuss, 2011). This is because the frontal lobe is related to executive functions, some of which are cognitive flexibility, inhibitory control, planning, among others (Cristofori et al., 2019).

All things considered, the studies included in this review show that the FrSBe was a practical and widely used scale for characterizing behavioral alterations in patients with TBI. Additionally, unlike other tools, it has the advantage of analyzing several behavioral changes using a single scale and obtaining information about the patient's behavior before and after the injury through the patient's and a family member's perspective.

5. Limitations

The studies included in the meta-analytic study presented great heterogeneity. Although no particular studies have been found to greatly influence the level of heterogeneity, this one may be due to the level of severity

presented by the patients. Very few studies presented patients with mild severity, and those that did grouped them with patients with moderate TBI. Likewise, the majority also presented the results of patients with moderate and severe severity as a single group. Therefore, due to the scarcity of patients with mild severity and the lack of groups stratified by severity, a stratified analysis could not be performed to evaluate whether severity was indeed an influential variable in the performance of the FrSBe or not. Future studies should include more homogeneous groups in order to evaluate severity as a potentially influential variable in the TBI behavioral changes and, at the same time, to further assess the performance of TBI patients in the FrSBe.

6. Conclusion

The FrSBe is considered a useful tool in detecting behavioral changes, specifically, apathy, disinhibition, and executive dysfunction. Even though there are plenty of other tools that assess such behavioral alterations, the FrSBe is not only brief and accessible, but also it includes the perspective of the patients' family and allows the characterization of the patients' behaviors both before and after the injury. Nevertheless, patients with TBI tend to manifest other behavioral changes, which definitely impact their quality of life. Therefore, it is of paramount importance the use of other scales, which assess the cognitive, emotional, and social aspects of these patients. On the other hand, it should be considered the time of evolution for future studies, since it impacts on the patients' perfomance on the FrSBe scale. Even though associations between severity and performance on the FrSBe were not analyzed, it is fundamental to carry out new studies to assess its influence, which will eventually lead to new scales.

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