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REVIEW

The Effects of Moderate-to-Severe Traumatic Brain Injury on Episodic Memory: a Meta-Analysis

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Abstract

Memory impairment following Traumatic Brain Injury (TBI) is among its most pronounced effects. The present meta-analysis focused only on studies of episodic memory ($n = 73$) conducted with adult patients with moderate-to-severe TBI. The results indicate that verbal Memory, and more specifically Verbal Recall, is most sensitive to the effects of moderate-to-severe TBI. Furthermore, verbal more than visual memory and recall more than recognition are sensitive to the effects of TBI. These effects are more pronounced in delayed than in immediate testing. Several moderating factors were found: age at testing - the younger the age, the greater the effect size of verbal recall. A greater effect size of delayed story recall was related to an older age of testing and longer time since the injury. The higher the educational level, the smaller is the effect size of visual recall. The clinical implications are discussed.

Keywords TBI · Episodic memory · Meta-analysis · Time delay · Word list · Story recall

Traumatic brain injury (TBI) has become a significant health problem in modern industrialized countries. The Centers for Disease Control and Prevention (CDCP), based on data gathered in 2013, reported that 2.8 million people in the US alone suffered from TBI (Taylor, Bell, Breiding, & Xu, 2017). TBI is associated with high mortality rates and multiple functional deficits, including occupational, social, mental, and physical health problems (Andelic et al., 2010).

The effects of TBI on memory can be long lasting and affect a wide range of everyday functioning such as school performance and employment (Brooks, McKinlay, Symington, Beattie, & Campsie, 1987; Ewing-Cobbs, Fletcher, Levin, Iovino, & Miner, 1998). Episodic memory deficits after TBI interfere with the recall of tasks, meetings, various commitments, new learning, and vocational rehabilitation (Russell, Arenth, Scanlon, Kessler, & Ricker, 2011). Thus, it is not surprising that these are among the most frequent complaints made by patients who sustained TBI (Rabinowitz & Levin, 2014), and as a result episodic memory deficits are the most studied cognitive domain following TBI (Goldstein & Levin, 1995). Memory impairments are also predictive of recovery after TBI as reported by Allanson, Pestell, Ginac, Yeo, and Weinborn (2017). Therefore, characterization of memory impairment following TBI has significant clinical and diagnostic implications (for review, see Vakil, 2005).

TBI also affects a wide range of cognitive processes such as executive functions (EF), processing speed, and attention (Azouvi, Vallat-Azouvi, & Belmont, x`). Some studies attribute the pervasive memory deficits to a more basic impairment in EF and working memory (WM). According to Azouvi et al. (2016), these EF and WM impairments are considered a "core impairment" following severe TBI. EF (subserved by the pre-frontal cortex) contribute to episodic memory in several ways: they are involved in the use of encoding strategies, effortful retrieval, source monitoring, temporal order memory, and the labelling of memory with temporal and contextual information (Dickers & Eichenbaum, 2010; see also Moscovitch's, 1994 "working with memory" model).

These neurocognitive deficits are assumed to stem from characteristic brain lesions. Neuroimaging studies following

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TBI have primarily reported frontal lobe as well as temporal lobe lesions (Avants et al., 2008; Bigler, 2013). The frontal lobe is associated with EF and WM (Azouvi, Arnould, Dromer, & Vallat-Azouvi, 2017). The frontal lobes are also involved in some aspects of memory that are dependent on EF (see Moscovitch, 1994). The temporal lobe, especially its medial part, is a major component of the brain's episodic memory system (Dickers & Eichenbaum, 2010). Lesions to the white matter, expressed as a diffuse axonal injury, are also common following TBI; these lesions interfere with the widespread connectivity among frontal and temporal lobes and subcortical structures (Caeyenberghs, Verhelst, Clemente, & Wilson, 2017; Hayes, Bigler, & Verfaellie, 2016; Wolf & Koch, 2016). Finally, edema and ischemia complicate further the functional outcome of TBI. Long-term follow-up studies after TBI victims have found brain atrophy, apoptosis, inflammations, microgliosis, loss of myelin, and cerebral blood flow changes (Bramlett & Dietrich, 2015).

The wealth of research on TBI's effect on memory has been reviewed in several papers and book chapters (Azouvi et al., 2017; Canty, Shum, Levin, & Chan, 2014; Goldstein & Levin, 1995; Vakil, 2005, 2013). It is clear from reading this literature that memory functions are significantly impaired following moderate-to-severe TBI. However, there is clearly a need for a comprehensive and quantitative meta-analysis in order to measure the extent of episodic memory impairment following TBI. In addition, a meta-analysis will enable the quantitative comparison of the various dimensions of episodic memory, detect whether a typical pattern of memory deficit exists, measure the heterogeneity and discrepancies among studies, and analyze the moderating effects of certain putative variables. Various studies used a wide range of procedures and did not always control for patients' age at testing, time elapsed since injury, and other possibly relevant variables, such as educational level. We believe that this analysis may assist clinicians and investigators to draw more clear and accurate conclusions regarding the effects of TBI on various aspects of episodic memory. The clinician, in particular, might benefit from such an analysis regarding the choice of the optimal and most sensitive memory measures and their interpretation.

Several meta-analyses were conducted on the effects of TBI on memory functioning. Some of these included participants with mild TBI while others combined different memory measures with no reference to memory modality, retrieval type, or the effects of delay on memory performance. Belanger, Curtiss, Demery, Lebowitz, and Vanderploeg (2005) studied the effects of mild TBI on measures of memory acquisition and delayed recall, but made no reference to memory modality. Their results indicated that acute effects (less than three months after the injury) were more evident in delayed memory; however, the sample type moderated the long-term effects of TBI – clinic patients and patients who were involved in litigation had more pronounced memory deficits as compared to other TBI participants who exhibited no difference from the healthy controls. A similar meta-analysis focused on concussion following mild head injury caused by sport injury. The main findings were that memory acquisition and delayed recall measures (verbal and visual combined) were deficient in the first 24 h post-injury and persisted over seven to ten days. These effects were more evident if healthy participants served as a control group; when TBI participants were compared to their pre-injury functioning, the effects were smaller (except delayed memory) (Belanger & Vanderploeg, 2005). The same authors found that multiple self-reported concussions in athletes were associated with deficits in EF and delayed verbal and visual memory measures (Belanger, Spiegel, & Vanderploeg, 2010). Padgett, Summers, and Skilbeck (2016) used global measures of verbal, visual and WM in an effort to study the contribution of the APOE gene to TBI effects. They compared mild to severe TBI groups characterized by the presence or absence of this gene. Their conclusion was that this gene had no effect on memory measures. In the meta-analysis reported by Allanson et al. (2017), verbal recall measures were associated with functional outcome in mild to severe TBI; no distinction was made between unorganized material (word list) and organized, meaningful material (story recall). The effects of moderate-to-severe TBI on working and short-term memory were analysed by Dunning, Westgate, Adlam, and R. (2016). Related to our study, participants with TBI had significantly more deficits in short-term verbal memory, with time since injury serving as a moderator variable. More severe deficits were associated with longer periods since the injury, suggesting that these memory deficits worsen with time. Ruttan, Martin, Liu, Colella, and Green (2008) conducted a meta-analysis comparing the effects of moderate-to-severe TBI on timed and untimed tests. Their study included memory data, but they combined these measures with other cognitive domains such as EF and visuospatial measures. These authors reported that significant cognitive deficits persisted for many years after the injury. Königs, de Kieviet, and Oosterlann (2012) and Königs, Engenhorst, & Oosterlaan, 2016 analysed the effects of injury severity, age and time since the injury on global measures of intelligence in participants with mild, moderate and severe TBI. There was no reference to specific memory measures, which were confounded within these measures. In addition, some of the studies did not have a healthy control group. Schultz and Tate (2013) performed a meta-analysis of four follow-up studies of cognitive recovery after moderate-to-severe TBI using a combined verbal-visual memory index. They found a gradual recovery of memory functions, with great variability among the measures and long-lasting effects of TBI on these measures. Finally, Wong Gonzalez (2015) performed a meta-analysis of prospective memory in moderate-to-severe TBI participants reporting a significant deficit after TBI. After reviewing these meta-analyses, to the

best of our knowledge, the present study is the first to analyse the effects of moderate-to-severe TBI on episodic memory breaking down the effects according to memory modality, retrieval condition, stimulus complexity, and the effects of testing delay.

The Present Study

This meta-analysis review focuses only on studies conducted on patients with moderate-to-severe TBI for the same reasons that we have focused on this population in our previous review (Vakil, 2005): first, because the diagnosis of these patients is usually clearer than in mild TBI, and there are fewer issues of differential diagnosis. Secondly, memory impairment in this group occurs frequently and is expected to be more pronounced than in milder injuries. In these mild injuries, it is not always clear whether a memory deficit exists at all. These considerations rule out studies with patients suffering from heterogeneous severity of TBI (e.g., Numan, Sweet, & Ranganath, 2000), or studies in which the inclusion and exclusion criteria were not sufficiently clear to indicate whether patients with mild TBI were included.

Memory research and related theoretical literature produced over the last three decades, have clearly demonstrated that memory consists of several sub-systems that interact with each other. These memory systems are subserved by different brain regions, which create a neuronal network, enabling interaction between these different components (for review, see Squire & Wixted, 2011). The present study focuses on the most studied aspect of memory in TBI, which is episodic memory: the memory of events that are context dependent (i.e., time and place) (Moscovitch, Cabeza, Winocur, & Nadel, 2016; Tulving, 2002).

The aim of the present meta-analysis review is to focus on four dimensions frequently used in memory assessment (e.g., Lezak, Howeison, Bigler, & Tranel, 2012; Vakil, 2012): specifically, testing time (immediate memory vs. delayed memory), retrieval condition (recall vs. recognition), modality (auditory vs. visuospatial), and stimulus complexity (discrete, unorganized stimuli vs. organized, structured stimuli). Time is an important dimension in determining memory impairment in general and amnesia in particular. For example, according to Parkin (1997), while immediate and remote memories are preserved in amnesia, formation of new long-term memories is impaired. Griffith et al. (2003) have shown that the size of the left hippocampus is associated with the delayed, but not with the immediate, measures of three verbal memory tests (i.e., Logical Memory and Verbal Paired Associated tests from WMS III and Verbal Selective Reminding Test). The importance of looking into the role of the retrieval condition stems from studies demonstrating that memory impairment will be pronounced in patients with frontal lobe damage under recall more than under recognition conditions (Janowsky, Shimamura, Kritchevsky, & Squire, 1989). Sensory modality is highly relevant to memory testing because of the differential effect of damage to the left or right cerebral hemisphere on verbal and non-verbal material, respectively (Pillon et al., 1999). In order to analyze the effects of the stimulus complexity on recall, we have distinguished between the recall of supra-span word lists and stories. Although these two types of verbal memory tests were originally treated as reflecting similar memory processes (Delis, Cullum, Butters, Cairns, & Prifitera, 1988), more recent studies have shown that they tap different aspects of verbal memory. Unlike stories that consist of an organized, logical structure, the recall of a very long word list is more dependent on EF and top-down processes (Mansbach, Mace, & Clark, 2014; Tremont, Halpert, Javorsky, & Stern, 2000; Zahodne et al., 2011).

Methods

The study was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA); Moher, Liberati, Tetzlaff, & Altman, 2009).

Search Methodology and Study Selection

The present meta-analysis includes studies reviewed by Vakil (2005) and studies published after this review. Vakil's criteria included only studies that were in English and focused mainly on adults with moderate-to-severe TBI.

The characterization of severity of TBI is based primarily on three measures: Glasgow Coma Scale (GCS), Loss of consciousness, and Post Traumatic Amnesia (PTA). In moderate TBI, GCS is 9–12, length of coma is between 20 min and 36 h, and PTA is 1–7 days. In severe TBI, GCS is 3–8, length of coma is more than 36 h, and PTA is more than 7 days (Williamson, Scott, & Adams, 1996). Levin, Goldstein, High, and Williams (1988) would consider severity of injury as moderate even when GCS is greater than 12, when it is accompanied by at least one of the following deficits: a neurological deficit, brain imaging or surgical findings indicating a brain lesion or cerebral edema, or a depressed skull fracture with an indication of a dural laceration (for a similar definition of 'severe TBI' see Frankowski, Annegers, & Whitman, 1985).

It is important to note that some previous studies such as that of Dikmen, Machamer, Winn, and Temkin (1995) have used more refined criteria for looking at moderate-to-severe levels of severity of injury. Unfortunately, the information regarding the severity of injury provided in the studies reviewed here was not sufficiently detailed to enable us to divide the samples of the patients into distinct subgroups based on severity level.

The additional studies were retrieved from PsychINFO and Medline databases and other meta-analyses (Belanger et al., 2005; Wong Gonzalez 2015; Ruttan et al., 2008). We also searched for additional articles in the reference sections of the retrieved studies and in academic sites of investigators that are active in the study of TBI, in order to reach the maximal possible number of studies. Some authors were contacted and a reprint request was sent to them, where the studies were not accessible.

The computerized search, terminated on May 31, 2019, was limited to studies published in English and performed on adult human participants. The key words used were: "traumatic," "brain," "Injury," "damage," "head," "memory," and "learning."

Inclusion Criteria

The final analysis included several studies cited in Vakil (2005) and additional studies that satisfied the following criteria: traumatic head injury as the sole cause of hospitalization (e.g., motor vehicle accident, falls, and sports injury); moderate-to-severe TBI levels as assessed by the Glasgow Coma Score or determined by the authors using other methods. Studies were excluded if severity of TBI was unavailable; adults or older adolescents (16 years of age and older); samples used were larger than a case study; comparisons were conducted with a control group without any brain damage; a memory measure was used (either a standardized test, e.g., Wechsler Memory Scale, or a clinically or experimentally validated memory test constructed by the authors, that yielded a clear memory measure); and adequate statistical data to allow comparison (*t*-test, ANOVA, MANCOVA, or at least the availability of means and standard deviations). For the purpose of arriving at a global effect size in studies that presented more than one measure of the same memory task or repeated testing of the same task, an average effect size was calculated. This was done in order not to violate the independence assumption of meta-analysis (Rosenthal, 1995). Averaging effect sizes might bias the results. Therefore, we searched for possible outliers. Effect sizes with standardized residuals that fell outside the 95% confidence interval on either side of the pooled effect size were identified and considered as outliers. In addition, we analysed all possible combinations of memory dimensions in order to reach the maximal number of independent effect sizes, as described below.

Data Extraction

The following variables were obtained from each study: age of the participants, size of the groups, gender distribution, educational level, detailed memory measures, descriptive and inferential statistics, and time elapsed since TBI. The age at which TBI took place was calculated by subtracting the age at testing from the time that elapsed since the injury took place.

Classification of Memory Tasks for Inclusion in the Meta-Analysis

We classified the memory tasks according to sensory modality and task characteristics:

visuospatial tasks included studies that presented visuospatial stimuli (e.g., pictures, faces, drawings), regardless of the type of response required from the participant (e.g., verbal response, pointing, or drawing). Auditory tasks included studies that presented stimuli aurally (e.g., words, sentences, stories). In these studies, the stimuli were consistently verbal and participants were always required to respond verbally, so we will now consider these measures as Verbal Memory measures. Recall tasks included studies that presented stimuli and tested immediate or delayed memory without presenting any retrieval cues to the participant. These studies mostly included stories (e.g., Logical Memory from the Wechsler Memory Scale (WMS)) supra-span tasks, either verbal (e.g., the California Auditory Verbal Learning Test (CVLT) or the Rey Auditory Verbal Learning Test (AVLT)) or visuospatial (e.g., Corsi Blocks from the WMS). All studies that tested memory immediately after the learning phase were classified as immediate memory studies. Studies that did not administer the memory test immediately after the learning phase, regardless of the time delay, were classified as delayed memory studies. Delay intervals ranged between 10 and 60 min, and most studies used 20–30 min delay intervals. Recognition tasks included studies that presented various stimuli and tested immediate or delayed memory by presenting retrieval cues to the participant (using a multiple choice or a yes/no paradigm, e.g., trial 9 of the AVLT). In addition, we defined working memory tasks as tasks that presented stimuli and asked the participant to perform a complex mental operation on the stimuli presented (e.g., Digits Backwards, *n*-back tasks). These data were not included in the present analysis. Figure 1 presents the flowchart of the search and selection process of the studies included in the meta-analysis. Table 1 presents the various details of the studies included in the meta-analysis.

Data Analysis

The effect sizes (Hedge's *g*) were calculated using the means, standard deviations and sample sizes or, when unavailable, using values of *t* or *F*, and the sample sizes. Heterogeneity was analyzed using the τ^2 measure of between-study variance and Cochrane's *Q* statistics. The meta-analyses and other analyses were conducted using Version 3 of the Comprehensive Meta-Analysis program (Borenstein, Hedges, Higgins, & Rothstein, 2005) and the SPSS program version 20. A random

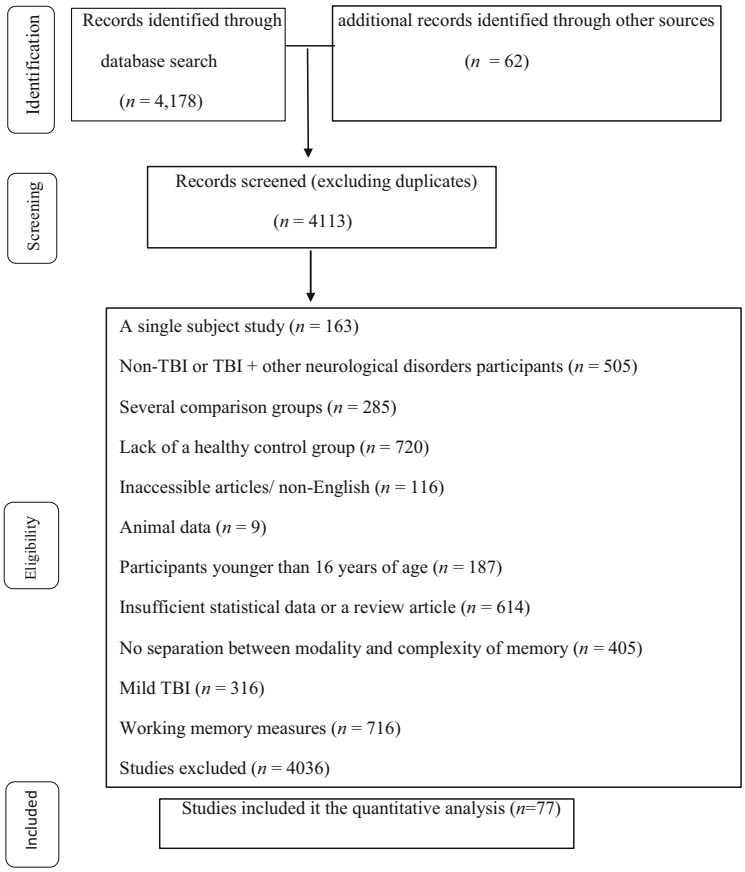

Fig. 1 PRISMA Flowchart showing the search procedure and selection process of the studies included in the meta-analysis

effects model was chosen for all analyses due to the heterogeneity of the studies included.

Results

The present meta-analysis analyzes the data extracted from seventy-seven studies. We adopted a multi-step approach to the analysis of the data. In the first step, we searched for outliers. Then we analyse the global memory measures. Following that, we present the effect sizes of the different memory dimensions, their combinations and their comparison. In the final analysis, we will examine the effects of possible moderators.

The first step of the analysis was to detect any outliers. Effect sizes with standardized residuals that fell outside the 95% confidence interval on either side of the pooled effect size were considered as outliers. Twelve such effect sizes were detected. Removing these outliers slightly changed some of the effect sizes, but substantially reduced the heterogeneity measures. Therefore, these effect sizes were excluded from the analysis. The final analysis is executed on seventy-three studies.

In Table 2 we present the effect sizes and measures of heterogeneity of the main memory dimensions.

The comparison of TBI participants to non-TBI participants clearly shows that all memory measures are considerably impaired after TBI. However, significant heterogeneity exists in the data. Figure 2 presents the forest plot of the effect sizes.

In order to further explore the origins of the heterogeneity and attain a finer differentiation of the impact of TBI, we analyzed the effect sizes of the various combinations of the main memory dimensions. Table 3 presents the measures of effect size and heterogeneity of the combinations of all memory dimensions. Figures 3 and 4 present the forest plot of the effect sizes. We compared the various effect sizes according to the memory dimensions analyzed in the present study. Regarding modality, the effect size of Verbal Memory was significantly higher than Visuospatial Memory, (Q_b (1) = 3.76 $p < .05$). This modality effect also exists in Immediate and Delayed testing: Immediate Verbal Memory was higher than Immediate Visuospatial Memory, ($Q_b(1) = 4.6$, $p < .03$); Delayed Verbal Memory was higher than Delayed Visuospatial Memory, (Q_b (1) = 6.15 $p < .01$); and Delayed Verbal Recall was higher than Delayed Visuospatial Recall, (Q_b (1) = 3.67 $p < .05$). No significant differences were found between Verbal and Visuospatial Recognition and its related measures. Regarding Type of Retrieval, Recall Memory (whether verbal or visuospatial) was higher than Recognition Memory, ($Q_b(1) = 5.58, p < .02$); Verbal Recall was marginally higher than Verbal Recognition, (Q_b (1) =

Table 1 The studies that were used in the meta-analysis

Study	*n* TBI	*n* Non-TBI	Age at Testing (years)	Age at Injury (years)	Time Since Injury (years)	Education (years)	% males	Weight In the meta-analysis (%)	Effect Size
Anderson et al., (2011)	15	15	33.9	33.8	.10	12.5	66.67	1.26	0.65
Ariza et al. (2006)	20	20	25.7	25.0	.67	11	80.0	1.53	.98
Arnould, Rochat, Azouvi, & van der Linden (2018)	38	36	34.2	30.5	3.7	13.4	84	1.64	.63
Arnould, Rochat, Dromer, Azouvi, &Van der Linden (2018b)	34	36	34.3	29.7	4.6	13.7	82	1.61	.65
Bennett-Levy (1984)	39	32	22.5	19.5	3.00	NA	82.0	2.01	.54
Brooker et al. (1984)	14	14	49.3	NA	NA	NA	100	1.26	1.14
Brooks (1974)	82	34	31.7	31.5	.25	15.6	89.0	2.07	.77
Brooks (1976)	34	34	31.2	NA	NA	NA	97.0	2.18	.91
Carlesimo et al. (1998)	20	20	25.1	23.7	1.38	10.9	80.0	1.45	1.46
Carlesimo et al. (2004)	24	24	29	27.9	1.05	10.6	70.8	1.76	.26
Carlozzi et al. (2013)	65	100	37.7	31.6	6.10	NA	70.8	2.44	.52
Coste et al. (2015)	15	15	29.4	26.3	3.15	12.8	73.3	1.29	1.35
DeLuca, Schultheis, Madigan, Christodoulou, & Averill (2000)	28	21	NA	NA	2.50	NA	NA	1.76	.54
De Simoni et al. (2018)	42	21	40.6	34.5	6.09	NA	88	1.46	1.00
Dockree et al. (2004)	10	10	35.8	29.3	6.50	NA	80.0	1.01	1.24
Draper et al. (2008)	60	43	41.9	31.4	10.6	12.1	55.0	2.18	.65
Dywan, Segalowitz, Henderson, & Jacoby (1993)	13	24	27.1	NA	NA	12	84.6	1.49	.27
Goldstein, Levin, Boake, & Lohrey (1990)	16	14	26.9	23.3	3.60	12.8	100	1.26	1.39
Goverover, Chiaravalloti, & DeLuca (2010)	10	15	42.5	34.3	8.20	NA	50.0	1.19	1.03
Goverover et al. (2015)	10	10	45.5	36.9	8.60	13.8	80.0	.92	1.61
Hart (1994)	6	50	31.8	30.4	1.38	12.5	66.7	1.19	.49
Hill-Jarrett, Gravano, Sozda, & Perlstein (2015)	12	12	28.7	23.3	5.36	14.6	58.3	1.26	.45
Honan et al. (2015)	28	28	44.9	32.9	12.0	12.7	71.4	1.86	.30
Kennedy et al. (2003)	16	16	32.9	29.2	3.70	13.8	37.5	1.40	.83
Kinsella et al. (1996)	24	24	32.5	NA	NA	NA	75.0	1.71	.65
Knight, Harnett, & Titov (2005)	35	20	39.0	30.3	8.75	12.4	100	1.76	.86
Larson, Kaufman, & Perlstein (2009)	21	21	30.8	30.3	.87	13.4	66.7	1.66	.48
Levin et al. (1988)	15	14	26	22.7	3.30	12.0	46.7	1.19	1.66
Marini et al. (2011)	14	14	35.4	30.1	5.30	10.9	100	1.12	1.83
Marini, Zettin, & Galetto (2014)	10	20	36.6	34.9	1.72	11.0	100	1.33	.36
Mathias et al. (2004)	25	25	NA	NA	.58	NA	100	1.71	.86
Maujean, Shum, McQueen (2003)	14	14	32.9	NA	NA	NA	NA	1.29	.92
McDonald, Bornhofen, & Hunt (2009)	22	32	NA	NA	10.8	14.2	72.7	1.81	.61
McDonald, Hunt, Henry, Dimoska, & Bornhofer (2010)	29	32	43.9	33.8	10.1	13.9	79.3	1.91	.38
McDowall et al. (1996)	20	20	34.5	NA	NA	NA	60.0	1.57	.81
Milders (1998)	12	15	31.4	29.2	2.2	NA	91.7	1.29	.80
Mioni et al. (2017)	18	24	43.5	38.5	5	12.4	61	1.30	.86
Nissley et al. (2002)	19	19	35.2	24.7	10.5	14.3	84.2	1.45	1.18
Novack, Kofoed, & Crosson (1995)	35	35	29.0	28.9	.15	NA	100	1.86	.97
Palacios et al., (2013)	26	22	27.4	23.3	4.20	13.7	61.5	1.62	.47
Paniak, Shore, & Rourke (1989)	21	21	26.0	25.9	.07	12.0	57.1	1.57	1.06
Pavawalla et al., (2006)	17	10	34.1	23.2	10.9	13.8	88.2	1.15	1.21

Table 1 (continued)

Study	*n* TBI	*n* Non-TBI	Age at Testing (years)	Age at Injury (years)	Time Since Injury (years)	Education (years)	% males	Weight In the meta-analysis (%)	Effect Size
Potvin, Rouleau, Audy, Charbonneau, & Ois Gigue're (2011)	30	15	32.3	29.4	2.85	11.5	60.0	1.53	1.18
Ries et al. (2006)	20	20	28.8	25.5	3.30	13.2	100	1.14	1.57
Rigon et al. (2018)	29	20	49.9	NA	NA	14.2	59	1.41	.53
Robertson et al. (2015)	90	90	37.2	37.1	.05	13.5	68.9	1.96	1.20
Roberston et al. (2017)	30	30	30.4	30.3	.1	12.6	67	1.47	1.17
Schmitter-Edgecombe (1996)	27	27	32.6	NA	NA	13.9	51.8	1.42	1.10
Schmitter-Edgecombe et al. (2000)	24	24	NA	NA	NA	14.1	75.0	1.76	.79
Schmitter-Edgecombe et al. (2001)	18	18	32.5	NA	NA	13.6	83.3	1.49	.77
Schmitter-Edgecombe et al. (2003)	30	30	34.0	26.9	7.15	14.5	80.0	1.86	.93
Schmitter-Edgecombe et al. (2005)	20	20	31.4	26.2	5.20	12.8	65.0	1.57	.98
Schmitter-Edgecombe et al. (2006)	18	18	30.6	23	7.60	12.8	72.2	1.45	1.08
Schmitter-Edgecombe et al. (2007)	21	21	33.1	26.2	6.9	13.1	71.4	1.57	1.08
Schmitter-Edgecombe et al. (2015)	40	40	31.4	31.3	.11	12.7	75.0	2.07	.34
Schmitter-Edgecombe & Kibby (1998)	20	20	33.1	NA	NA	14.5	60	1.53	.67
Schmitter-Edgecombe, Marks et al. (2004)	24	24	35.6	25.1	10.5	14.0	83.3	1.66	.72
Schmitter-Edgecombe & Rogers (1997)	10	10	28.4	NA	NA	13.9	90	1.02	1.54
Schmitter-Edgecombe & Rueda (2008)	27	27	32.8	32.0	.81	12.6	67.0	1.81	.89
Schmitter-Edgecombe & Wright (2003)	30	30	34.0	23.0	11	14.0	80.0	1.91	.25
Schmitter-Edgecombe & Wright (2004)	24	24	34.3	NA	NA	14.1	83.3	1.66	1.14
Strong et al. (2008)	53	53	34.7	NA	NA	13.0	69.8	2.18	1.09
Takayanagi et al. (2013)	10	47	43.7	37.7	6	14.8	80.0	1.45	1.06
Turkstra et al. (2018)	58	66	42.3	NA	NA	15	NA	1.86	.83
Vakil, Biederman, Liran, Groswasser, & Aberbuch (1994)	14	15	30.0	29.7	.33	12.0	57.1	1.26	1.34
Vakil, Golan, Grunbaum, Groswasser, & Aberbuch (1996)	15	19	29.5	29.0	.46	12.4	80.0	1.26	1.79
Vakil, Langelben-Cohen, Frenkel, Groswasser, & Aberbuch (1996)	13	13	23.3	22.9	.43	11.6	76.9	1.06	1.79
Vakil et al., (1997)	24	24	28.3	25.1	3.20	12.3	79.2	1.62	1.36
Vakil, Sherf, Hoffman, & Stern (1998)	27	27	30.2	29.5	.7	11.6	62.9	1.66	1.58
Watt, Shores, Baguley, Dorsch, & Fearnside (2006)	23	23	26.2	26.1	.07	10	100	1.66	.90
Wearne, Osborne-Crowley, Rosenberg, Dethier, & McDonald (2019)	25	28	45.8	32.76	13	13.16	80	1.39	1.20
Wright, Schmitter-Edgecombe, & Woo (2010)	56	62	34.4	26.2	8.20	14.2	69.6	2.28	.87
Zec et al. (2001)	32	27	34.4	24.4	10.0	12.7	75.0	1.86	.88

NA- not available

3.2, $p < .07$); but Delayed Verbal Recall was significantly higher than Delayed Verbal Recognition, (Q_b (1) = 5.26, $p < .02$). Delayed Recall (whether verbal or visuospatial) was higher than Immediate Recall, (Q_b (1) = 5.83, $p < .02$); Delayed Recall (whether verbal or visuospatial) was higher than Delayed Recognition, (Q_b (1) = 8.29, $p < .005$); Delayed Verbal Recall was higher than Immediate Verbal Recall, (Q_b (1) = 5.71 $p < .02$). This variation is related to the significant difference between Delayed (g = 1.00) and Immediate Word-List Recall (g = .87), Q_b (1) = 4.06 $p < .04$. No significant difference exists between the effect sizes of word-list and story memory and their combinations with type of retrieval and testing time.

When analyzing the Visuospatial Memory measures, no significant differences were found regarding type of retrieval (recall vs. recognition) and time of testing (immediate vs. delayed). TBI participants were consistently impaired and inferior to non-TBI individuals in these aspects of visuospatial memory. Non-significant differences were also found when

Table 2 The effect sizes and heterogeneity measures of the main memory dimensions

Memory Measure	*k*	No. of effects averaged	n TBI	n non-TBI	*g*	se	*Z*	95% CI	95% PI	τ^2	Q
Global Memory	73	151	1962	1949	.88	.04	20.56**	.79, .96	.47, 1.28	.04	105.6**
Verbal Memory	59	87	1503	1442	.92	.05	17.52**	.81, 1.02	.41, 1.43	.06	99.6**
Visuospatial Memory	34	47	893	929	.76	.07	11.46*	.62, .89	.26, 1.26	.06	56.9**
Recall Memory	60	106	1555	1524	.91	.05	19.90**	.82, 1.01	.52, 1.31	.04	85.4**
Recognition Memory	22	25	564	572	.74	.08	9.41**	.57, .90	.29, 1.19	.04	30.9**
Immediate Testing	54	16	1408	1385	.84	.05	16.80**	.74, .94	.43, 1.26	.04	78.8**
Delayed Testing	53	63	1289	1248	.90	.05	17.04**	.80, 1.01	.42, 1.38	.05	86.8**
Word-List memory	47	49	1169	1173	.91	.06	11.12**	.80, 1.02	.45, 1.37	.05	72.3**
Story Memory	21	27	548	451	.94	.09	10.59**	.75, 1.12	.34, 1.54	.07	35.9**

k = number of effect sizes; *g* = Hedge's effect size; se = standard error; *z* = standard score; CI = confidence interval; PI = prediction interval; τ^2 = between-study variance, Q = Cochran's measure of heterogeneity

*$p < .05$. ** $p < .01$

comparing the groups on combinations of the above-mentioned variables.

We concluded the analysis by performing a weighted meta-regression analysis using several moderator variables: age at injury, age at memory testing, time elapsed since the injury, percent of males in the TBI group, and the educational level of the TBI participants at memory testing.

The meta-regression analysis yielded the following statistically significant results: Age at Testing was negatively related to several memory measures, indicating that older participants tended to have smaller effect sizes: Verbal Recognition, B = −.06, SE = .03, 95% CI = −.12 to .00, β = −.54, z = −2.14; and Delayed Verbal Recognition, B = −.07, SE = .03, 95% CI = −.14 to .00, β = −.58, z = −2.06. Age at testing was positively related to Delayed Story Recall, B = .03, SE = .01, 95% CI = .00 to .07, β = .57, z = 2.41, indicating that older participants tended to have a larger effect size. Time elapsed since the injury was related to Delayed Story Recall, B = .06, SE = .03, 95% CI = .01 to .12, β = .54, z = 2.2. Percent of males was not related to any of the memory measures. Level of education was related to Visual Recall (B = −.11, SE = .05, 95% CI = −.22 to .00, β = −.41, z = −2.01, the higher the educational level, the smaller the effect size.

Discussion

The present meta-analysis enabled us to compare the extent of impairment of various aspects of memory among individuals suffering from moderate-to-severe TBI. The data reported here indicate that moderate-to-severe TBI significantly impairs several aspects of memory compared to controls.

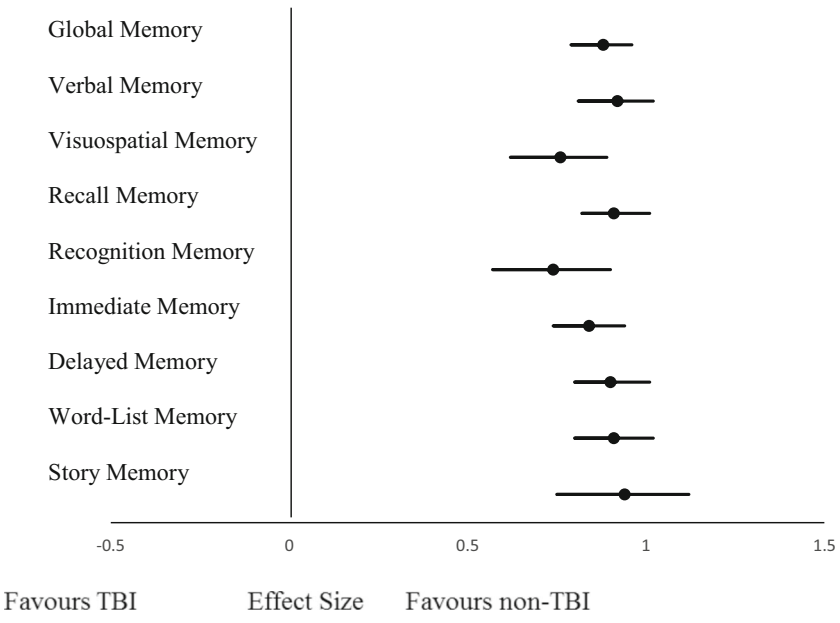

Fig. 2 Forest plot of the main memory dimensions

Table 3 The effect sizes and heterogeneity measures of the different combinations of the main memory dimensions#

Memory Measure	*k*	No. of effects averaged	n TBI	n non-TBI	*g*	Se	Z	95% CI	95% PI	τ^2	Q
Verbal Recall	51	78	1413	1349	.94	.05	17.29**	.83, 1.05	.46, 1.42	.05	81.2**
Visuo-spatial Recall	24	33	639	637	.86	.08	11.3**	.70, 1.02	.37, 1.34	.05	36.5*
Verbal Recognition	13	4	282	256	.80	.13	6.25**	.52, 1.07	.05, 1.54	.10	24.2*
Visuo-spatial Recognition	14	12	424	407	.66	.09	7.13**	.46, .86	.19, 1.13	.04	19.3*
Immediate Recall	49	36	1474	1438	.84	.05	16.10**	.74, .95	.43, 1.25	.04	71.4**
Delayed Recall	45	38	1085	1076	.97	.04	17.38**	.83, 1.07	.47, 1.43	.05	63.9**
Immediate Recognition	8	5	253	230	.81	.14	5.64**	.47, 1.15	.06 1.57	.08	14.8*
Delayed Recognition	15	16	394	416	.72	.10	7.55**	.52, .93	.22, 1.22	.05	21.4**
Immediate Verbal Memory	45	16	1371	1308	.89	.06	14.00**	.76, 1.02	.32, 1.45	.08	82.0**
Immediate Visuospatial Memory	23	8	647	623	.72	.08	9.55**	.56, .87	.25, 1.18	.05	32.9**
Delayed Verbal Memory	45	19	1123	1095	.98	.06	15.9**	.86, 1.11	.45, 1.51	.07	76.3**
Delayed Visuospatial Memory	26	19	507	525	.77	.07	11.43**	.63, .91	.43, 1.11	.02	31.1**
Immediate Word-List Memory	33	4	809	827	0.87	.07	10.40**	.73, 1.02	.38, 1.37	.05	51.9**
Delayed Word-List Memory	37	3	925	921	.96	.07	14.40**	.84, 1.11	.44, 1.52	.07	63.2**
Immediate Story Memory	18	0	514	407	.91	.10	8.67**	.69, 1.13	.17, 1.65	.11	38.0**
Delayed Story Memory	15	2	298	292	1.03	.10	9.85**	.81, 1.25	.48, 1.58	.05	21.4
Word-List Recall	36	47	989	992	0.96	.06	15.76**	.84, 1.09	.55, 1.37	.04	50.6*
Word-List Recognition	10	4	240	235	.84	.15	5.81**	.52, 1.17	.01, 1.67	.12	22.0**
Story Recall	21	24	545	451	.97	.09	10.99**	.78, 1.15	.38, 1.55	.07	35.4*
Immediate Verbal Recall	42	14	1298	1232	.88	.06	13.80**	.75, 1.01	.34, 1.43	.07	74.1**
Delayed Verbal Recall	37	12	9911	981	1.02	.07	15.05**	.88, 1.16	.49, 1.55	.06	62.0**
Delayed Verbal Recognition	10	2	212	186	.78	.14	5.45**	.46, 1.11	.01, 1.56	.1	18.1*
Immediate Visuo-Spatial Recall	16	4	482	486	.75	.09	8.07**	.56, .95	.23, 1.28	.05	26.6*
Immediate Visuo-Spatial Recognition	5	2	224	200	.74	.14	4.31**	.43, 1.03	.01, 1.55	.08	5.6
Delayed Visuo-Spatial Recall	18	9	373	385	.84	.09	9.40**	.67, 1.01	.41, 1.27	.03	22.8
Delayed Visuo-Spatial Recognition	10	8	250	298	.65	.11	5.82**	.40, .91	.12, 1.19	.04	13.7
Immediate Word-List Recall	31	2	928	835	.87	.07	12.45**	.73, 1.01	.41, .33	.05	45.80*
Delayed Word-List Recall	28	0	825	837	1.00	.07	13.40**	.85, 1.15	.49, 1.51	.06	45.1*
Delayed Word-List Recognition	9	2	146	141	.84	.15	5.48**	.49, 1.19	.04, 1.64	.10	15.9*
Immediate Story Recall	18	0	504	437	.91	.10	8.67**	.69, 1.13	.17, 1.65	.11	38.0**
Delayed Story Recall	15		298	292	1.06	.10	10.24**	.84, 1.29	.52, 1.61	.05	21.2

k = number of effect sizes; *g* = Hedge's effect size; se = standard error; z = standard score; CI = confidence interval; PI = prediction interval; τ^2 = between-study variance; Q = Cochran's measure of heterogeneity. # Not enough data exists for Immediate Verbal Recognition and Immediate and Delayed Story Recognition.

*$p < .05$. ** $p < .01$

However, Verbal Memory, and more specifically Verbal Recall, show the largest effect size. This is also the most frequent measure reported in the studies analyzed. As can be seen in Tables 1 and 2, verbal recall, whether measured by a word list or a story, and especially when tested after a time delay, is highly sensitive to the effects of moderate-to-severe TBI. These results are consistent with the conclusions of previous reviews (Canty et al., 2014; Goldstein & Levin, 1995; Vakil, 2005, 2013). One clear diagnostic recommendation can be derived from the present meta-analysis: recall memory and specifically, verbal recall measures, should be used routinely in memory testing of TBI individuals due to their higher sensitivity to TBI effects on memory processes. These measures are also more dependent on EF that are especially vulnerable to TBI. No significant differences were found among the various recognition measures, both visuospatial and verbal, since all are impaired to the same extent following TBI. Also, the various measures of visual memory are not significantly different from one another. Immediate, as compared to delayed testing, shows a smaller effect size in the recall of a word-list, but the delay of testing has no effect on story memory or visual stimuli. No significant differences were found between the memory of word-lists and stories, indicating the lack of effect of material complexity or organization on memory performance of TBI individuals. It is therefore evident from our data that modality (verbal > visual) and memory type (recall >

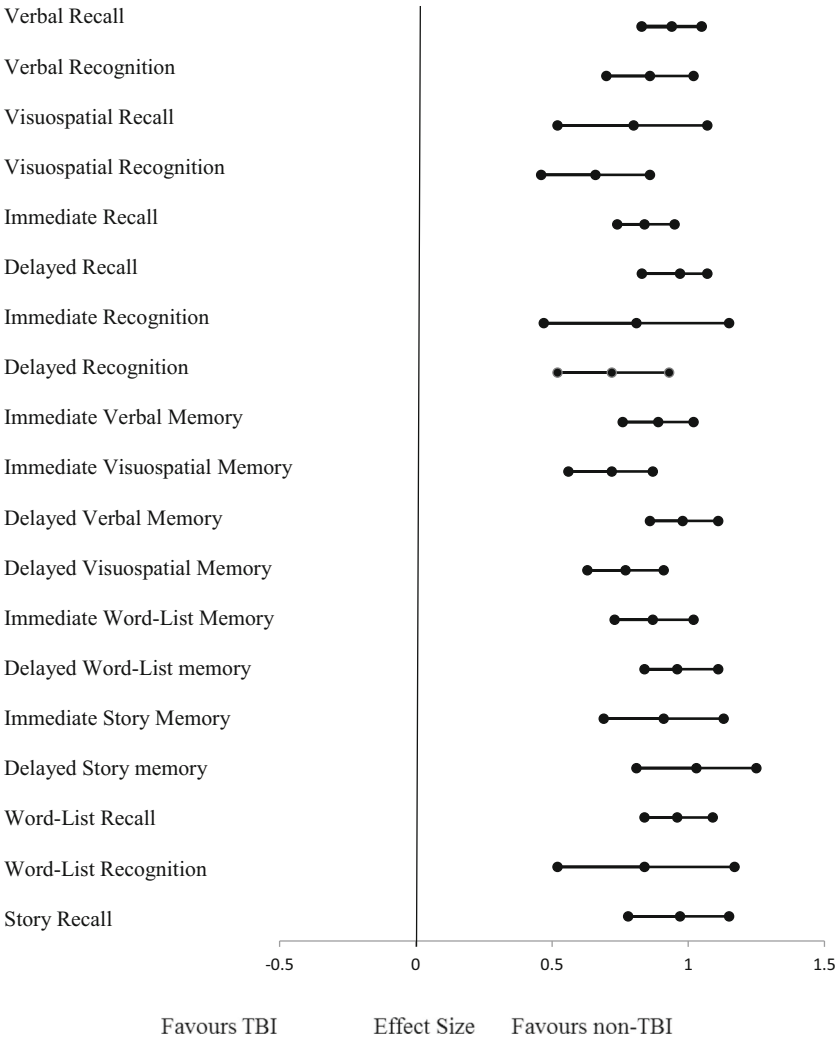

Fig. 3 Forest plot of the combinations of the main memory dimensions

recognition) are the more salient factors that are affected by moderate-to-severe TBI. Time of testing (delayed > immediate) affects verbal stimuli and more specifically word-list tests. Stimulus complexity/organization (word list = story) are similarly impaired following moderate-severe TBI.

Recall memory is associated with strategic and effortful processes, all of which are considered components of EF. These EFs develop with age, mature slowly, and are dependent on the pre-frontal lobes and its connections with the mid-temporal and parietal lobes (Ofen, Chai, Schuil, Whitfield-Gabrieli, & Gabrieli, 2012). Verbal recall also demands more semantic organization, a process that is also dependent on intact frontal lobe functioning (MacPherson, Turner, Bozzali, Cipolotti, & Shallice, 2016). Slow maturation (up to early adulthood), in addition to size and location, make the frontal lobes more susceptible to the effects of traumatic brain damage (Phillips, Parry, Mandalis, & Lah, 2017). With regard to recognition memory, when a retrieval cue is presented and matches the stored memory, recognition can take place with less effortful, strategic retrieval (Bastin, Van der Linden, Lekeu, Andrés, & Salmon, 2006), so that less involvement of the frontal lobes is required. This could explain the greater effect size of recall vs. recognition in individuals with TBI. However, recognition memory assessment is based almost exclusively on correct answers ('hits'); false-positive recognitions ('false alarms') are usually not reported (Davidson, Troyer, & Moscovitch, 2006). Since frontal lesions are associated with more intrusions and memory monitoring deficits (Davidson et al., 2006), the present finding of recall > recognition effect size may not tell the whole story about recognition deficits following TBI. It is recommended that clinicians and researchers also report false-positives. This may allow a better understanding of the effects of TBI on memory.

The poorer performance of individuals that sustained TBI on verbal memory tests, as compared to visuospatial tests, might be related to the neuropathology of TBI as described previously. Avants et al. (2008) and Bigler (2013) reported that following TBI there are characteristic frontal and temporal lobe lesions in addition to DAI. Posterior brain areas are usually more spared.

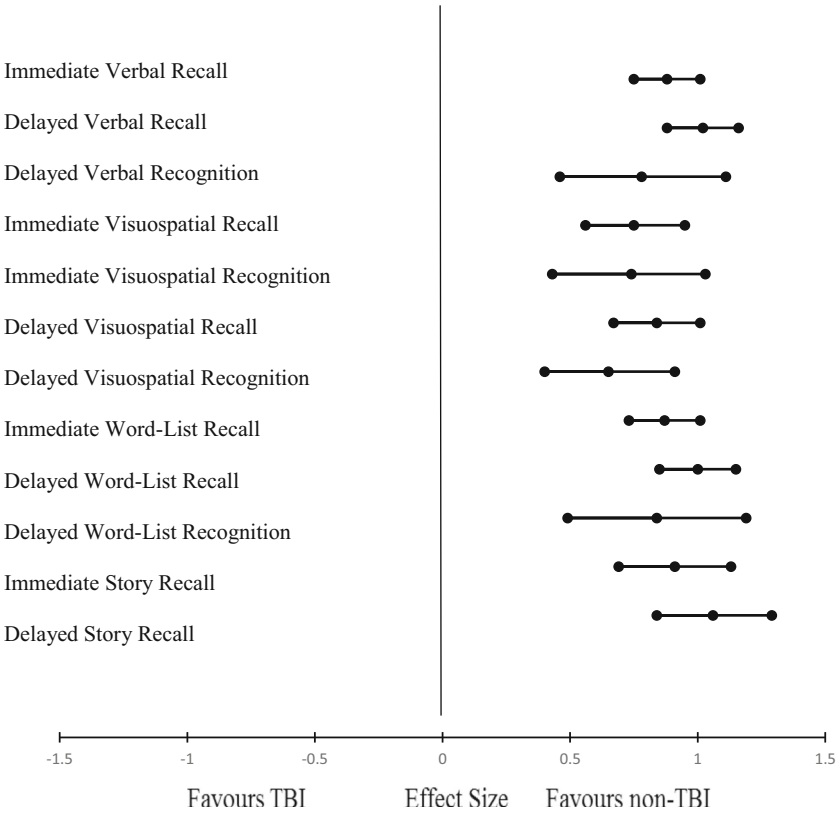

Fig. 4 Forest plot of the combinations of all memory dimensions

Delayed verbal recall measures had larger effect sizes than immediate recall measures following moderate-to-severe TBI. This data is compatible with previous reports. Several studies reported a dissociation between immediate and delayed verbal memory following TBI. Till, Colella, Verwegen, and Green (2008) performed a 5-year follow-up of moderate-to-severe TBI. They found a decrease in delayed verbal recall on the AVLT as compared to total learning score (averaged across five trials). The authors raised the possibility that deterioration of verbal retrieval ability takes place with time. In addition, they noted the great variability in their participants' performance. Several investigators reported a steep forgetting rates of verbal material (Logical Memory from the WMS) following TBI (Haut, Petros, & Frank, 1990; Vakil, Arbell, Gozlan, Hoofien, & Blachstein, 1992). Patients with TBI were found to be impaired on all indices of the WMS-R. However, impairment of delayed memory was more pronounced (Reid & Kelly, 1993). A similar dissociation was reported by Schmitter-Edgecombe, Marks, Wright, and Ventura (2004). They found that only delayed verbal memory on the CVLT was impaired following TBI. However, other reports by the same group (e.g., Schmitter-Edgecombe & Rueda, 2008) found both memory measures of the CVLT or AVLT to be impaired when TBI participants were compared to healthy controls. We mentioned the meta-analysis performed by Belanger, Spiegel, and Vanderploeg (2010) who reported on delayed verbal and visual memory deficits in concussed athletes. Recently, Marini, Zettin, Bencich, Bosco, and Galetto (2017) found that only individuals with severe TBI were inferior to healthy controls on both immediate and delayed verbal memory, while participants with moderate TBI were not different from the control group. Therefore, it seems that a great variability exists regarding TBI effects on immediate vs. delayed verbal memory. Possible reasons might include time elapsed since injury, organizational quality of the stimuli (word-list vs. story, the categorical structure of the word list), and pre-morbid variables, among others. The inconsistent results regarding TBI effects on delayed and immediate memory highlight the importance of the present meta-analysis in elucidating this research subject.

Another finding of the present study is the lack of difference between organized verbal memory (e.g., story) and unorganized verbal material (e.g., word-list), both showing a large effect size. Previous studies demonstrated that recall of word list is more associated with EF than story recall. The reason for that is probably the fact that stories are more structured than word lists and have a logical flow to them. Thus, stories are less dependent than word lists on effortful memory strategies associated with frontal lobe functioning (Mansbach et al., 2014; Tremont et al., 2000; Zahodne et al., 2011). The data regarding TBI effects on story and word-list are mixed. Some studies found inferior performance in both measures by participants with TBI, as compared to healthy controls (Pavawalla & Schmitter-Edgecombe, 2006; Schmitter-

Edgecombe & Anderson, 2007), while others reported a dissociation. Consistent with the results of the present analysis, Larson et al. (2009) found a difference only in delayed word-list recall but not in immediate story memory. Schmitter-Edgecombe et al. (2004) reported a difference in story and delayed word-list memory, but not in immediate word-list recall. Story memory (Logical Memory sub-test of the WMS-R) predicted return to work after moderate-severe TBI, one year after the injury, whereas unorganized verbal material (AVLT) showed only a trend towards statistical significance (Green et al., 2008). These discrepancies among the various reports might be attributed to the proportion of moderate-to-severe TBI participants, the use of the total score of word-list (trials 1–5 of the AVLT or CVLT), and the nature of the test itself: the CVLT words belong to different semantic categories, enabling some of the less-injured participants to use semantic clustering to aid recall.

In the present meta-analysis, testing age was found to be positively associated with the effect sizes of delayed story recall. This memory measure is also positively related to the time elapsed since the injury. These findings suggest that there is a deterioration with time in the ability for effortful retrieval of verbal organized and complex stimuli following moderate-severe TBI. It should be noted that the association between testing age and time since injury could simply be a result of confounding between these two variables. It is reasonable to assume that when older individuals are tested, more time has elapsed since injury. Further research is required in order to test the contribution of each of these measures independently. As mentioned previously, recall memory is more dependent on the pre-frontal cortex, a brain region that matures up to early adulthood and is more vulnerable to TBI.

Our findings are compatible with other studies reporting that older age is associated with more severe effects of TBI. With age, it is claimed, there is less compensatory ability of the brain, more comorbidities, and an overall cognitive decline (Schönberger, Ponsford, Reutens, Beare, & O'Sullivan, 2009). However, none of these studies specifically tested episodic memory. The meta-analysis on WM, mentioned previously, showed that more severe deficits in verbal short-term memory were associated with longer periods of time since the injury (Dunning et al., 2016). It is noteworthy that the latter study included pre-adolescent participants. Other studies did not present any data relating to memory functioning at all, but instead used composite measures of recovery. Therefore, it is difficult to compare these studies with the present meta-analysis. Using recovery scales, it was found that younger individuals with moderate-to-severe TBI show better recovery rates, and that younger age at injury was associated with less disability (Forslund et al., 2017; Marquez de la Plata et al., 2008). Studying severe TBI individuals, Dahm and Ponsford (2015) found that younger age at TBI was associated with better recovery one year later in speed of processing, and older age was associated with less employment after TBI. Baum, Entezami, Shah, and Medhkour (2016) reported that older age (combined with injury severity) was associated with poorer prognosis following TBI.

Testing age was negatively related to the effect sizes of verbal recognition and more specifically delayed verbal recognition. This indicates that older, less than younger, participants with TBI are impaired in these measures. Although this result was not predicted, a possible explanation could be that this result reflects a difference between younger and older participants in response bias rather than sensitivity. That is because in most studies, only hit rate is reported but not false alarm rate. A more liberal response bias by the elderly group would yield a higher hit rate as well as a higher false alarm rate which does not necessarily reflect better recognition. Further research is needed in order to clarify this point, by using purer measures of recognition such as d' (that is not confounded with response bias) rather than hit rate.

The percent of males was not related to any of the memory measures. It has long been documented in the literature that female participants perform better than males in episodic verbal memory, an effect that also persists at older ages (Graves et al., 2017), and even after resection of the left temporal lobe (Berenbaum, Baxter, Seidenberg, & Hermann, 1997). The lack of the gender effect in our study might be attributed to the devastating effect of moderate-severe TBI on memory processes, blurring the difference between male and female TBI victims.

Finally, the higher participants' educational level at testing, the smaller the effect sizes of visuospatial recall. A similar finding was reported by De Wit et al. (2017), who found that obese participants with higher education showed better visual memory, compared to participants with less education. Fastenau, Denburg, and Hufford (1999) also found a beneficial effect of education on the recall of the Rey-Osterrieth Complex Figure Test. Visual Recall memory is associated with posterior brain regions that are less affected by TBI as noted previously.

Education might cause changes in the brain, reinforce neuronal networks, recruit alternative pathways and networks, and lead to better functional reorganization (Barulli & Stern, 2013). Ponsford, Draper, and Schönberger (2008) reported that more years of education were associated with better recovery after TBI. A prospective study of 769 moderate-to-severe TBI patients also found that level of education predicted better recovery (Schneider et al., 2014). Recently, Fortune, Walsh and Richards (2016) followed a group composed of TBI and stroke patients. Controlling for type of injury, severity, and time since injury at 18 months post-injury, higher education was associated with better recovery (albeit not with community integration).

We did not find any moderating effect of education on the verbal memory measures. This contradicts the findings by

Leary et al. (2018), who found in participants with TBI (mild-to-severe), one to five years post-injury, that estimated pre-morbid IQ and education were associated with higher performance on the CVLT. The difference may be attributed to the inclusion of mild TBI in that study. The lack of protective effects of education on verbal memory was also found in other studies. A follow-up 5 years after TBI revealed that up to one year, age moderated the effects of TBI on memory, with younger participants showing more preserved memory functions. However, after the first year, age, gender, and education were no longer related to AVLT performance, and a great variability in recovery was noted (Chu et al., 2007). Rabinowitz, Hart, Whyte, and Kim (2018) found that education was not related to recovery after moderate-severe TBI, followed up to 12 months. The involvement of education in the recovery from TBI is not straightforward; pre-morbid educational attainment might serve as a cognitive reserve. However, TBI might hinder survivors from attaining further education or limit their academic abilities. Willmott, Ponsford, and Downing (2014) found that following moderate-to-severe TBI, many survivors complain about fatigue and cognitive difficulties, and some leave schools or transfer to part-time studies. Of those who were enrolled in school, only 56% returned to their studies. Therefore, it is important to separate the premorbid educational level of TBI individuals from post-injury educational attainment in order to elucidate more clearly the contribution of education to TBI recovery. The present findings may be related to the neuropathology of TBI, as mentioned previously, and highlight the chronic effects of moderate-severe TBI on verbal memory and learning.

This study has several limitations that need to be addressed in future research. As mentioned above, there are a limited number of studies on the effect of moderate-to-severe TBI on visuospatial memory and on recognition. Also, data on recognition memory relies only on hits and ignores important information regarding false alarms. Therefore, the contribution of response bias is not taken into account. Thus, more studies of these aspects of memory are required to enable eventually a more comprehensive meta-analysis on the effects of TBI on memory. The patient groups reported in most of the studies analyzed are quite heterogeneous; in most studies, moderate and severe TBI patients were mixed. Furthermore, the information provided in these studies about the severity of injury was not sufficiently detailed to enable us to divide the samples of the patients into more homogeneous subgroups. In some cases, time since injury was reported as a range. Thus, more homogeneous patient samples would enable the analysis of the contribution of each one of the above mentioned variables to memory performance following TBI.

In summary, the present study is the first one to use meta-analysis to quantify the effects of moderate-to-severe TBI on episodic memory focusing on four dimensions frequently used in memory assessment: memory modality, retrieval condition, stimulus complexity and the effects of testing delay. The data, systematically analysed and reviewed here, yielded important empirical and clinical information. The findings of the present analysis are consistent with and confirm the conclusions of Vakil (2005): "The profile of the memory deficit in patients with TBI resembles that of patients with frontal injury rather than that of patients with amnesia." (p. 1011). The current quantitative analysis (as opposed to the qualitative analysis in Vakil's review) also showed that memory processes dependent on EF (e.g., recall > recognition) are more vulnerable to moderate-to severe TBI. This is in accordance with the nature of TBI, which affects primarily the frontal lobes (Avants et al., 2008; Bigler, 2013). In addition, the clinical implications of these findings are that they guide the clinician to the most vulnerable aspect of memory following TBI, in terms of assessment and remediation. One implication might be that following TBI, it would be efficient to focus on remediation of executive functions, as well as directly on memory processes, to ameliorate memory functioning.

Another interesting finding that emerged from the literature review of the studies of memory following moderate-to-severe TBI is that studies are not evenly distributed among the various aspects of memory. As reported in the Method section, many more studies have used recall as compared to recognition tests, and more verbal than visuospatial tests. Immediate and delayed memory tests were used with similar frequency. These findings indicate the need for more research in these generally overlooked aspects of memory in patients with TBI, specifically, more frequent use of recognition tests and visuospatial stimuli. Vakil (2005) suggested that the reason for the higher rates of auditory-verbal studies of memory, as compared with visuospatial studies, is their relevance to education and academic performance.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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Studies Included in the Meta-Analysis Are Indicated by an Asterisk

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