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Review

The effectiveness of memory remediation strategies after traumatic brain injury: Systematic review and meta-analysis

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A B S T R A C T

Background: Traumatic brain injury (TBI) is a steadily rising health concern associated with significant risk of emotional, behavioral and cognitive impairments. Cognitive memory impairment is one of the most concerning outcomes after TBI, affecting a wide range of everyday activities, social interactions and employment. Several comparative and comprehensive reviews on the effects of cognitive interventions in individuals with TBI have been conducted but usually with a qualitative rather than quantitative approach. Thus, evidence synthesis of the effects of TBI interventions on memory difficulties is limited.
Objective: In this meta-analysis, we examined the memory-remediating effects of internal and external interventions, injury severity and the interaction of both factors for patients with TBI.
Methods: Data were extracted from studies published between 1980 and 2020 that used objective memory measures (computerized or pencil-and-paper), and multiple meta-analyses were conducted to compare effectiveness across these interventions. Publication bias was assessed, as was quality of evidence using the Cochrane Risk of Bias tool for randomized controlled studies. Our final meta-analysis included 16 studies of 17 interventions classified into 3 categories: internal, external and mixed.
Results: Mixed interventions demonstrated the highest average effect size for memory difficulties (Morris $d = 0.79$). An evaluation of injury severity yielded 2 categories: mild-moderate and moderate-severe. Analyses demonstrated a homogenous medium effect size of improvement across injury severity, with moderate-severe injury with the largest average effect size (Morris $d = 0.65$). Further evaluation of injury severity interaction with intervention type revealed a mediating effect for both factors, demonstrating the largest effect size for mixed interventions with moderate-severe injury (Morris $d = 0.81$).
Conclusion: This study highlights the effectiveness of memory remediation interventions on memory impairment after TBI. A wide range of interventions are more effective because they address individual variability for severity and memory deficits. The study further supports and expands existing intervention standards and guidelines.

1. Introduction

Remediation of memory after traumatic brain injury (TBI) has become increasingly significant in rehabilitation [1–4]. One factor contributing to the effectiveness of treatment with the strongest prognostic value is the severity of injury [5–7].

TBI patients present a wide range of memory impairments, including working, prospective, semantic and episodic memory [8,9]. Another factor contributing to the effectiveness of treatment is the intervention type. Most reviews of cognitive remediation address memory problems with a range of approaches [3,8,10–17]. However, they fail to address efficiency statistically, thus reducing their ability to infer and compare efficiencies of various intervention approaches.

Most interventions reviewed can be organized around 2 categories: “internal” versus “external” [9,18,19]. “Internal” approaches attempt at training mental, restorative strategies by manipulations, using less impaired cognitive resources such as categorization or dual coding [20]. “External” approaches focus on using compensatory tools or aids such as keeping a diary or shelf labeling [21].

When examining efficacy of intervention studies, cross-study comparisons become difficult because of the heterogeneous population, the diversity of interventions, and the types of outcome measures used. Severity of injury and appropriate objective neuropsychological outcome measures need to be adequately controlled to avoid confounding spontaneous recovery or practice effects with treatment efficacy [12,22,23].

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Several systematic reviews have discussed the effects of memory rehabilitation interventions on individuals after TBI [5,24]. However, interpreting these reports is complicated by the inclusion of trials using non-randomized designs and non-TBI samples. Predominately, the lack of objective measures is also problematic, as evidence suggests that self-reports by people with cognitive deficits may not reflect their actual functioning [25].

Additionally, studies in this field are often small and underpowered. The current study addresses these limitations by merging all studies into extensive analyses with greater statistical value. It also endeavors to lower variability across the field by limiting methodology to studies using objective memory measures. While recognizing the importance of other outcomes (e.g., emotional symptoms) as treatment targets for patients with TBI, analyses of such measures are beyond the scope of the current study.

The present systematic review and meta-analysis aimed to address the following questions:

- Does injury severity moderate efficiency of memory remediation interventions?
- Is intervention type (''internal'' vs ''external'') a predictor of the intervention's efficacy?
- How do these 2 variables interact?

Is efficacy of intervention type a function of severity of injury or memory domain? To address these questions, multiple meta-analyses were performed. First, we hypothesized that memory remediation interventions will be effective after TBI, beyond intervention type and injury severity. Second, based on literature reviews in the field [14,26], we do not have a specific hypothesis regarding the effectiveness of internal versus external interventions nor regarding injury severity. However, an interaction is expected between these 2 factors; individuals with greater TBI severity will benefit more from external interventions, and less severely affected individuals will benefit more from internal interventions [33]. Our strategy to address these questions was to classify memory interventions into 3 categories (external, internal and mixed external and internal) and injury severity into 2 severity levels (mild-moderate and moderate-severe).

2. Materials and methods

2.1. Literature search and selection criteria

This study design is appropriate for summarizing and synthesizing research evidence to inform policy and practice [27]. The development of this study protocol was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol (PRISMA-P), [28,29] guidelines.

This study consists of 3 stages: literature identification, literature screening, and literature selection based on the specified eligibility criteria, yielding a set of studies included in the meta-analysis. The initial stage encompassed a wide literature search for papers published from January 1980 until January 2020. We used the PsycNET and Google Scholar search engines to search for the terms *rehabilitation or intervention AND TBI* within the abstract. To better control publication bias, we searched Google Scholar for additional articles that may have been missed in the initial search. We also included the additional *memory* and *memory remediation* search terms. Literature was also sourced from previously published literature reviews including the previously mentioned literature reviews [3,18–21,23–25,30,31]. All articles in English were searched. Following initial extraction, interventions were divided into internal, external and mixed (internal and external). Memory domains were divided into 5 categories: working memory, long-term visual, long-term verbal, immediate visual, immediate verbal and prospective memory.

2.2. Inclusion criteria

The study intervention needed to be tested on participants with a medical TBI diagnosis, including information about severity [32,33]. It had to examine the effect of one of the 3 interventions on memory domains (i.e., measured by objective validated neuropsychological tests) and include data or statistical information that could be used to generate an effect size (Morris *d* value). The study needed to contain a control group/comparison group including patients with TBI. To this end, we included both randomized and non-randomized control trials because the number of papers with randomized control trials was limited, given potential ethical concerns in randomly denying treatment. Additionally, the study needed to contain pre- and post-intervention measures.

2.3. Exclusion criteria

We did not include studies evaluating the effect of interventions on emotional, physiological or neurological functions. From the initial broad search terms, 749 studies in English were retrieved. Duplicates and studies in foreign languages were removed ($n = 21$) before narrowing down to the 3 categories of interventions studied (451 removed). The broadness of the search terms allowed us to ensure that all relevant studies were identified, even if they did not necessarily include cognitive assessment or memory as a keyword or within the abstract (303 removed). Finally, 41 publications that reviewed the neuropsychological effects of interventions were identified and reviewed. Most of the eliminated studies did not have a TBI control group or did not use neuropsychological measures, relying instead on self or observer reports of behavior and symptomology. Other reasons for exclusion included inability to access relevant data or calculated effect sizes. In total, 17 studies fulfilled all inclusion and exclusion criteria (from unique publications). Ten studies used randomized control trials, and 7 did not. Four studies used blinded assessment, and 13 did not mention the assessment method. One study [34] had 2 intervention groups and an additional control group, so the data from the control group were included twice (with just half the stated sample size). From each study, we calculated and included all significant and non-significant results. Eight studies were included from previous meta-analyses and the rest were from additional searches. Asterisks in the reference section are used to identify studies included in the meta-analyses, and Fig. 1 provides an overview of the search process.

2.4. Quality assessment

Two reviewers (BL and EV) assessed the quality of data in included studies. We used the US National Institutes of Health (NIH) quality assessment tools [35]. The NIH tool was preferred because it is comprehensive and thus enables an exhaustive quality assessment of included studies.

2.5. Data coding

Statistical data including means (SD) and number of participants were extracted from each study for pre- and post-intervention results in both groups. The results of each memory test were classified according to the memory domain they tested.

Only studies including group means (SD) of neuropsychological memory scores were included. In cases of several reported scores for various measures for one memory domain in an individual

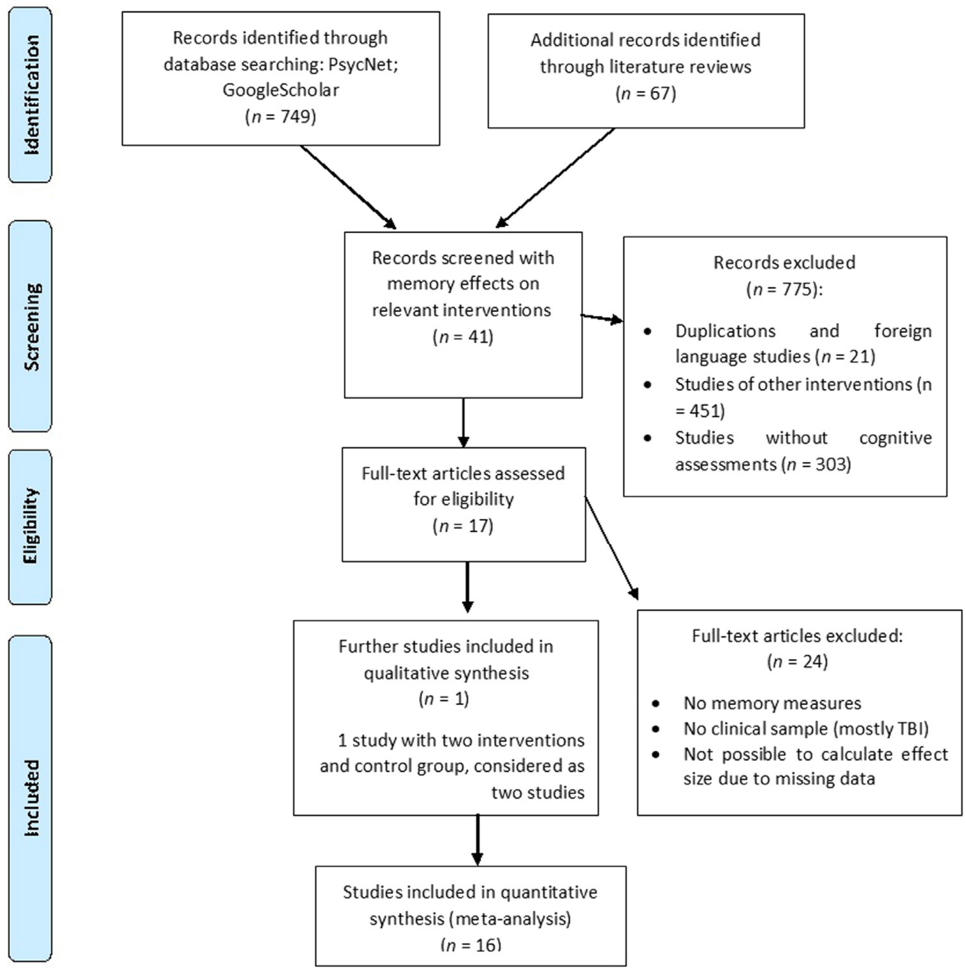

Fig. 1. Flow chart of the literature search process according to PRISMA guidelines. TBI, traumatic brain injury.

study, we extracted all data but used the most commonly cited test for the most relevant measure (based on the authors' review of the literature). Thus, for each published study, it was possible to have 6 effect sizes. Finally, if there were multiple effect sizes for a specific domain and they were derived from equally relevant tests, we used the highest effect size reflecting the most robust effect. The following variables were included in a coding sheet: study identification number, first author, year of publication, number of total participants, number of clinical and non-clinical participants, name of intervention 1, name of intervention 2 or control, number of participants in each group, duration of intervention, group or individual intervention, time from injury, injury severity, mean age and age range of participants, language of testing, and which cognitive tests were used for each memory domain. We initially created a coding sheet with all tests and results, even if there were multiple test results for a single category, but following the method detailed above, we created a final coding sheet including one pre-intervention score (mean [SD]) and one post-intervention score (mean [SD]) for each cognitive function tested within a single study. All studies were coded, and the data were extracted independently by the authors. Inter-rater reliability was 100%. All data were extracted from papers.

2.6. Statistical analyses

Analyses of effect sizes were calculated according to Morris [36] because of intervention studies containing groups with uneven sample sizes and varying pre-test means and SDs, thus needing to weight the estimation of the population effect size. Effect-size calculation was based on the recommended formula: mean pre- to post-treatment change minus the mean pre- to post-treatment control group change divided by the pooled pretest SD with a bias adjustment [36]. Effect-size calculations were first carried out using the "psychometrica" website [37], then entered onto an Excel sheet for total effect sizes and homogenous effect calculations.

Studies with insufficient and missing data were excluded from the meta-analysis. Given the heterogeneity of TBI assessments, sample characteristics, and implementation of treatments within domains in the included studies, we chose *a priori* to use random-effects models [38].

Effect sizes were also calculated according to Rosenthal [39]. To assess homogeneity/heterogeneity, we examined the data by using the Q test [40,41] and I^2 [42]. Accordingly, if the Q value was not significant, then the effect sizes were considered homogeneous, and the mean effect size was considered the best estimation for the data. However, if the Q was significant, moderators should be suggested, because the effect sizes were considered heterogeneous.

3. Results

Our final meta-analysis included 16 studies of 17 key interventions, which yielded 44 effect sizes for the 6 memory domain categories. Initially, the memory domain most improved by intervention was entered into a meta-analysis comprising all the published studies. Of note, 12 of the 16 studies of 17 interventions included additional measures with high ecological validity (e.g., quality of life and everyday memory functioning and self/family inventories). These measures are assumed to reflect transfer of training to daily-life functioning better than the objective measures. The encouraging result is that 11 of the 12 studies reported significant improvement with these measures, which strengthens the clinical significance of the observed objective effects.

The results revealed participants with significant improvement in memory domains, with a medium effect size of 0.61. Results were deemed homogenous, generating a Q value of 13.27 ($P < 0.05$) and $I^2 = 0$. A funnel plot of included studies did not show any asymmetry, so significant publication bias was not likely (Fig. 2).

Therefore, the second stage was to determine which intervention was most successful, and whether each intervention type could be classified as having a homogenic, significant effect on memory domains. The largest number of studies ($n = 7$) included internal interventions, 4 studies included mixed interventions and 6 studies included external interventions. Studies were divided into 3 meta-analyses reviewing the different intervention types; all intervention categories demonstrated moderating, homogeneous and significant results. Mixed interventions improved memory domains significantly, demonstrating the highest effect size of 0.79 ($df = 3$, 95% CIL = 0.16, 1.09, $Q = 2.76$, $P < 0.05$, $I^2 = 0$) (Table 1). Internal interventions demonstrated the lowest effect size of 0.52 ($df = 6$, 95% CIL = 0.1, 1.02) and were deemed homogenous ($Q = 3.61$, $P < 0.05$, $I^2 = 0$). External interventions demonstrated a moderate effect size of 0.60 ($df = 5$, 95% CIL = 0.43, 1.35) and were also deemed homogeneous ($Q = 3.52$, $P < 0.05$, $I^2 = 0$). The smaller variability of each intervention separately suggests intervention type as a moderator affecting intervention efficiency.

In the third stage, after comparing efficacy across interventions, we investigated the second factor, injury severity: which severity could be classified as most affected by interventions, regardless of intervention type, and whether each severity could be classified as having a homogeneous improvement effect. As in most studies, meta-analyses of injury severity included moderate-severe severity. When studies were separated into 2 meta-analyses reviewing the 2 levels of injury severity (mild-moderate severity, $n = 5$; moderate-severe, $n = 12$), homogeneous results were generated. Moderate-severe injury severity demonstrated the greatest mean effect size, 0.65 ($df = 11$, 95% CIL = 0.81, 0.91), which was homogeneous across interventions ($Q = 7.49$, $P < 0.05$, $I^2 = 0$) (Table 2). Mild-moderate severity demonstrated a slightly lower effect size, 0.61 ($df = 5$, 95% CIL = –0.06, 0.91, although still homogeneous ($Q = 5.74$, $P < 0.05$, $I^2 = 12.91$). The smaller variability of each severity level suggests that injury severity is also a moderator affecting intervention efficiency.

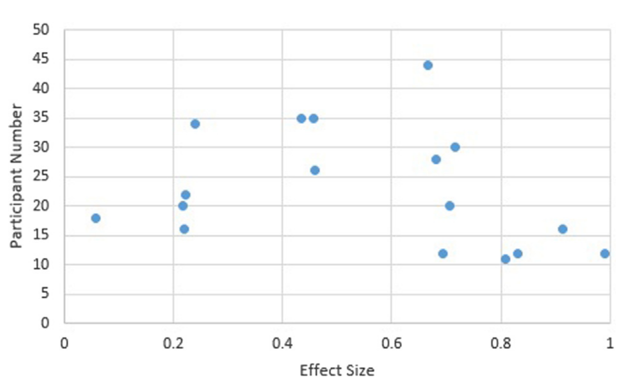

Fig. 2. Funnel plot showing effect sizes for interventions delineated by sample size.

The third stage of the current study was to test the hypothesis that these 2 factors, intervention and injury severity, interact with each other. In other words, Does the effectiveness of a particular type of intervention depend on the injury severity? All interactions demonstrated homogeneous and significant results (Fig. 3). Mixed interventions demonstrated the highest effect size both for mild-moderate severity, 0.79 ($df = 2$, 95% CIL = 0.13, 1.06), and moderate-severe severity, 0.81 ($df = 1$, 95% CIL = 0.35, 1.27) (Table 3). However, given that 2 studies were included in the latter category, this finding should be interpreted with caution. Overall, studies were considered homogeneous (mild-moderate: $Q = 2.73$, $P < 0.05$, $I^2 = 26.66$; moderate-severe: $Q = 0$, $P < 0.05$, $I^2 = 0$). Internal interventions for mild-moderate severity demonstrated the lowest effect size, 0.36 ($df = 1$, 95% CIL = 0.03, 0.95), and were deemed homogeneous ($Q = 1.07$, $P < 0.05$, $I^2 = 6.52$). Internal interventions for moderate-severe demonstrated a moderate effect size, 0.60 ($df = 5$, 95% CIL = 0.43, 1.35), and studies were considered homogeneous ($Q = 6.71$, $P < 0.05$, $I^2 = 25.58$). External interventions for moderate-severe likewise demonstrated a moderate effect size, 0.60 ($df = 5$, 95% CIL = 0.43, 1.35), and studies were considered homogeneous ($Q = 3.52$, $P < 0.05$, $I^2 = 0$).

The final stage was to examine whether the effectiveness of a particular intervention type depends on the memory domain. However, because the number of studies in each category was rather low, we had insufficient data to conduct statistical analyses. Therefore, the data presented in Table 4 are for descriptive purposes only.

4. Discussion

This is the first meta-analysis to collate the most prominent memory remediation interventions for TBI and examine their effect by type and injury severity. Other similar meta-analyses in the field have generally focused on heterogenic populations [5], improving a variety of cognitive abilities [43,44], using specific cognitive interventions [45], or using a mix of subjective and objective outcome measures. We sought to investigate the effect of several types of memory remediation treatments on objective and standardized memory outcomes, exclusively in TBI populations. We were interested in whether memory functions were differentially affected by type of intervention and injury severity in adults. We used 16 studies of 17 interventions; 10 studies used randomized controlled trials, and 7 did not. Four studies used blinded assessment, and 13 did not mention the assessment method.

The first and most significant finding was that participants improved memory functions, which resulted in a homogeneous moderate to large effect size. This finding provides statistical validation for conclusions of recent qualitative reviews [14,22,46].

Of the cognitive memory-remediation interventions studied, all showed moderate to large effect sizes, which indicates their success in ameliorating memory impairments as compared with control or less effective interventions. Mixed intervention type, regardless of injury severity, was the most effective in targeting and reducing memory impairments of people with TBI, generating a large effect size. This was followed by external, and finally with a slightly smaller effect size, internal interventions. These findings are consistent with reports that rather than injury severity, success for increasing independent functioning in TBI patients depends on the number of compensations used [47]. With mixed interventions, a wider array of strategies was used, thus increasing the number of compensations. Furthermore, our findings strengthen the systematic review of cognitive rehabilitation research [14,26]

Table 1
Effect sizes and methodology of studies by intervention type.

Author	Intervention Type	Mean age & participants number	Total no. of sessions	No. of sessions per week	Session duration	Intervention 1	Intervention 2/ Control	Injury severity	Memory test	Memory domain	Effect size
Freeman et al., 1992 [55]	Mixed	43 and 2 months $n = 12$	8	Three	120 min	Compensatory and executive training skills: monitoring skills, note-taking, meaningfulness, visual association.	No training	Mild-Moderate	Paragraph memory task	Verbal LTM memory	0.99
Twamley et al., 2014 [56]	Mixed	31 and 10 months $n = 34$	12	Nan	Nan	cogSMART - internal memory skills (e.g., systematic search, association, chunking) and external skills (calendar, to-do list)	No training	Mild-Moderate	Digit span	Immediate verbal memory	0.24
Thickpenny-Davis et al., 2007 [57]	Mixed	26 and 4 months $n = 11$	8	Twice	60 min	Memory program: errorless learning, strategies for encoding, storing, retrieval, Diary training	No training	Severe	CVLT	Immediate verbal memory	0.81
Tiersky et al., 2005 [58]	Mixed	46 and 10 months $n = 20$	33	Three	50 min	Cognitive remediation: Information processing skills, notebook use, note-taking, environment modifications	No training	Mild-moderate	RAVLT	Immediate verbal memory	0.71
								Mixed interventions, mean effect size			0.79
Serino et al. (2006) [59]	Internal	34 $n = 18$	16	Four	NaN	General Stimulation training (simple decision tasks, low executive demands)	Working memory training	Moderate	2-back	Working Memory	0.058
Milders et al., 1998 [60]	Internal	35 and 10 months $n = 26$	8	Once every two weeks	90 min	Phonetic and semantic associations	No training	Severe	Visual face memory test	LTM Visual memory	0.46
Constantinidou et al., 2009 [61]	Internal	29 and 10 months $n = 35$	65	Five	30 min	Categorization rehabilitation program	Standard rehabilitation program	Moderate to severe	CVLT-R	LTM verbal memory	0.44
O'Neil-Pirozzi et al., 2010 [62]	Internal	47 and 2 months $n = 44$	12	Twice	90 min	Internal memory strategy training	No training	Severe	HVLT	LTM verbal memory	0.67
Kaschel et al., 2002 [63]	Internal	39 and 3 months $n = 12$	30	Three	Nan	Imagery-based training	Control pragmatic memory training	Severe	RBMT	LTM verbal memory	0.99
De Luca et al., 2014 [64]	Internal	36 and 3 months $n = 35$	24	Three	Nan	Cognitive PC training	No training	Moderate to severe	RAVLT	Immediate verbal memory	0.46
								Internal interventions, mean effect size			0.52
Schmitter-Edgecombe, 1995 [65]	External	28 and 4 months $n = 16$	16	Twice	60 min	Notebook training	Supportive therapy	Moderate to severe	Observed everyday memory failure	General Memory	0.22
Goldstein et al., 1996 [66]	External	34 and 2 months $n = 30$	15	2-3	Nan	Face-Name associations	Computerized face-name associations	Severe	Face memory test	Visual face memory	0.72
Hart et al., 2002 [67]	External	31 and 6 months $n = 20$	13	Nan	Nan	Portable voice organizer training	Supportive therapy	Moderate to severe	Recall therapy goals	Prospective memory	0.22
Raskin et al., 2009 [68]	External	43 and 4 months $n = 16$	24	Twice	60 min	Specific prospective memory training for maintaining goal in mind	No training	Moderate to severe	Prospective errors (ProM)	Prospective memory	0.91
McDonald et al., 2011 [69]	External	47 $n = 12$	Nan	Nan	Nan	Google calendar training	Dairy training	Moderate to severe	% of intended actions	Prospective memory	0.83
Berg et al., 1991 [42]	External	34 and 7 months $n = 28$	18	Three	60 min	Specific memory strategy training of individual problems	No training	Severe	Acquisition of faces test, RAVLT	Immediate verbal and visual memory	0.68
								External interventions, mean effect size			0.60

CVLT: California Verbal Learning Test; CVLT-R: California Verbal Learning Test-Research edition; HVLT: Hopkins Verbal Learning Test; LTM: long-term memory; ProM: prospective memory; RAVLT: Rey Auditory Verbal Learning Test; RBMT: Rivermead Behavioral Memory Test.

Table 2
Effect sizes and methodology of studies sorted by injury severity.

Author	Injury severity	Mean age & participants number	Total no. of sessions	No. of sessions per week	Session duration	Intervention 1	Intervention 2/ Control	Intervention type	Memory test	Memory domain	Effect size
Serino et al. (2006) [59]	Moderate	34 $n=18$	16	Four	NaN	General Stimulation training (simple decision tasks, low executive demands)	Working memory training	Internal	2-back	Working Memory	0.058
Freeman et al., 1992 [55]	Mild-moderate	43 and two months $n=12$	8	Three	120 min	Compensatory and executive training skills: monitoring skills, note-taking, meaningfulness, visual association	No training	Mixed	Paragraph memory task	Verbal LTM memory	0.99
Twamley et al., 2014 [56]	Mild-moderate	31 and 10 months $n=34$	12	Nan	Nan	cogSMART - internal memory skills (e.g. systematic search, association, chunking) and external skills (calendar, to-do list)	No training	Mixed	Digit span	Immediate verbal memory	0.24
O'Neil-Pirozzi et al., 2010 [62]	Mild-moderate	47 and two months $n=44$	12	Twice	90 min	Internal memory strategy training	No training	Internal	HVLT	LTM verbal memory	0.67
Tiersky et al., 2005 [58]	Mild-moderate	46 and 10 months $n=20$	33	Three	50 min	Cognitive remediation: Information processing skills, notebook use, note-taking, environment modifications	No training	Mixed	RAVLT	Immediate verbal memory	0.71
									Mean effect size		0.61
Schmitter-Edgecombe, 1995 [65]	Moderate-severe	28 and 4 months $n=16$	16	Twice	60 min	Notebook training	Supportive therapy	External	Observed everyday memory failure	General Memory	0.22
Milders et al., 1998 [60]	Severe	35 and 10 months $n=26$	8	Once every two weeks	90 min	Phonetic and semantic associations	No training	Internal	Visual face memory test	LTM visual memory	0.46
Goldstein et al., 1996 [66]	Severe	34 and 2 months $n=30$	15	2-3	Nan	Face-Name associations	Computerized face-name associations	External	Face memory test	Visual face memory	0.72
Constantinidou et al., 2009 [61]	Moderate-severe	29 and 10 months $n=35$	65	Five	30 min	Categorization rehabilitation program	Standard rehabilitation program	Internal	CVLT-R	LTM verbal memory	0.44
Hart et al., 2002 [67]	Moderate-severe	31 and 6 months $n=20$	13	Nan	Nan	Portable voice organizer training	Supportive therapy	External	Recall therapy goals	Prospective memory	0.22
Raskin et al., 2009 [68]	Moderate-severe	43 and 4 months $n=16$	24	Twice	60 min	Specific prospective memory training for maintaining goal in mind	No training	External	Prospective errors (ProM)	Prospective memory	0.91
O'Neil-Pirozzi et al., 2010 [62]	Moderate-severe	47 and 2 months $n=44$	12	Twice	90 min	Internal memory strategy training	No training	Internal	HVLT	LTM verbal memory	0.67
Thickpenny-Davis et al., 2007 [57]	Severe	26 and 4 months $n=11$	8	Twice	60 min	memory program: errorless learning, strategies for encoding, storing, retrieval, Diary training	No training	Mixed	CVLT	Immediate verbal memory	0.81
Kaschel et al., 2002 [63]	Severe	39 and 3 months $n=12$	30	Three	Nan	Imagery-based training	Control pragmatic memory training	Internal	RBMT	LTM verbal memory	0.99
De Luca et al., 2014 [64]	Moderate-severe	36 and 3 months $n=35$	24	Three	Nan	Cognitive PC training	No training	Internal	RAVLT	Immediate verbal memory	0.46

Table 2 (*Continued*)

Author	Injury severity	Mean age & participants number	Total no. of sessions	No. of sessions per week	Session duration	Intervention 1	Intervention 2/ Control	Intervention type	Memory test	Memory domain	Effect size
McDonald et al., 2011 [69]	Moderate-severe	47 $n = 12$	Nan	Nan	Nan	Google calendar training	Dairy training	External	% of intended actions	Prospective memory	0.83
Berg et al., 1991 [42]	Severe	34 and 7 months $n = 28$	18	Three	60 min	Specific memory strategy training of individual problems	No training	External	Acquisition of faces test, RAVLT	Immediate verbal and visual memory	0.68
									Mean effect size		0.65

CVLT: California Verbal Learning Test; CVLT-R: California Verbal Learning Test-Research edition; HVLT: Hopkins Verbal Learning Test; LTM: long-term memory; ProM: prospective memory; RAVLT: Rey Auditory Verbal Learning Test; RBMT: Rivermead Behavioral Memory Test.

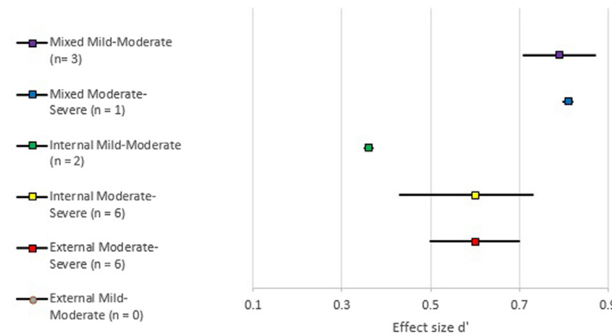

Fig. 3. Forest plot showing effect sizes and confidence intervals for the various interventions and injury severity on memory functions.

recommending memory strategy training, adopting both internal and external compensatory supports for reducing memory impairments during recovery from TBI.

Our finding of higher efficiency of external than internal interventions is consistent with findings that internal interventions showed smaller improvements than a control group [31] and reports that external strategies are most efficient among clinical approaches [48,49]. This observation might be due to the fact that internal, more than external, interventions are less convenient when adapting to everyday functioning in naturalistic settings and generalizing strategies to other tasks [50]. As well, internal strategies might be more difficult to implement because they demand more cognitive effort [51]; therefore, external strategies are easier to learn and use. In addition, the difference in efficiency of the interventions validates the theoretical distinction of the "internal" versus "external" strategy classification. Although this distinction is frequently used [9,19,52], this is the first statistical evidence of its theoretical distinction because each category results in a different effect size.

The similar moderate effect size of both interventions confirms that regardless of intervention type, intervention groups show greater change than controls in memory and use of strategies [53].

When all the interventions were considered, moderate-severe injury severity was most affected. These patients demonstrated the ability to undergo a significant change following the interventions. An explanation for this finding may be that baseline functioning level for more severely injured individuals is lower, so improvement and change potential is greater, specifically when measuring pre–post differences. Of note, the effect size was smaller for individuals with mild-moderate TBI but only slightly. These findings highlight the effectiveness of interventions for all patients, regardless of their injury severity. These findings might correspond to results indicating low correlation between injury severity and quality of life [7], thus arguing that rehabilitation services provided to patients are beneficial in terms of help in transition toward better coping and outpatient settings.

Regarding the interaction of intervention type and memory domain, stating conclusively whether intervention types have different effects on different memory domains is difficult because of the low number of interventions in each category. Although descriptive data might suggest uneven distribution, some patterns may be seen. For example, we found only studies of external interventions for training prospective memory. Additionally, we found only studies of internal and mixed interventions, neglecting external interventions, for training working memory. This observation might suggest assuming a certain type of training to target a specific memory domain.

The present study found interesting mediating qualities for the interaction of both factors, intervention type and injury severity. First, the analysis identified mixed interventions as most effective, regardless of injury severity. Here, we expand clinical recommen-

Table 3
Effect sizes and methodology of studies sorted by interaction of intervention type and injury severity.

Author	Intervention Type	Injury severity	Mean age & participants number	Total no. of sessions	No. of sessions per week	Session Duration	Intervention 1	Intervention 2/ Control	Memory test	Memory domain	Effect size
Freeman et al., 1992 [55]	Mixed	Mild-Moderate	43 and 2 months $n = 12$	8	Three	120 min	Compensatory and executive training skills: monitoring skills, note-taking, meaningfulness, visual association	No training	Paragraph memory task	Verbal LTM memory	0.99
Twamley et al., 2014 [56]	Mixed	Mild-Moderate	31 and 10 months $n = 34$	12	Nan	Nan	cogSMART- internal memory skills (e.g. systematic search, association, chunking) and external skills (calendar, to-do list)	No training	Digit span	Immediate verbal memory	0.24
Tiersky et al., 2005 [58]	Mixed	Mild-Moderate	46 and 10 months $n = 20$	33	Three	50 min	Cognitive remediation: Information processing skills, notebook use, note-taking, environment modifications	No training	RAVLT	Immediate verbal memory	0.71
							Mixed interventions for mild-moderate mean effect size				0.79
Thickpenny-Davis et al., 2007 [57]	Mixed	Severe	26 and 4 months $n = 11$	8	Twice	60 min	memory program: errorless learning, strategies for encoding, storing, retrieval, Diary training	No training	CVLT	Immediate verbal memory	0.81
							Mixed intervention for moderate-severe mean effect size				0.81
Serino et al. (2006) [59]	Internal	Moderate	34 $n = 18$	16	Four	NaN	General Stimulation training (simple decision tasks, low executive demands)	Working memory training	2-back	Working Memory	0.058
O'Neil-Pirozzi et al., 2010 [62]	Internal	Mild-Moderate	47 and 2 months $n = 44$	12	Twice	90 min	Internal memory strategy training	No training	HVLT	LTM verbal memory	0.67
							Internal interventions for mild-moderate mean effect size				0.36
Milders et al., 1998 [60]	Internal	Severe	35 and 10 months $n = 26$	8	Once every two weeks	90 min	Phonetic and semantic associations	No training	Visual face memory test	LTM Visual memory	0.46
Constantinidou et al., 2009 [61]	Internal	Moderate-Severe	29 and 10 months $n = 35$	65	Five	30 min	Categorization rehabilitation program	Standard rehabilitation program	CVLT-R	LTM verbal memory	0.44
O'Neil-Pirozzi et al., 2010 [62]	Internal	Severe	47 and 2 months $n = 44$	12	Twice	90 min	Internal memory strategy training	No training	HVLT	LTM verbal memory	0.67
Berg et al., 1991 [42]	Internal	Severe	34 and 7 months $n = 22$	18	Three	60 min	"Drill and Practice" memory tasks and games	No training	Acquisition of faces test, RAVLT	Immediate verbal and visual memory	0.22
Kaschel et al., 2002 [63]	Internal	Severe	39 and 3 months $n = 12$	30	Three	Nan	Imagery-based training	Control pragmatic memory training	RBMT	LTM verbal memory	0.99
De Luca et al., 2014 [64]	Internal	Moderate to severe	36 and 3 months $n = 35$	24	Three	Nan	Cognitive PC training	No training	RAVLT	Immediate verbal memory	0.46
							Internal interventions for moderate-severe mean effect size				0.60
Schmitter-Edgecombe, 1995 [65]	External	Moderate to severe	28 and 4 months $n = 16$	16	Twice	60 min	Notebook training	Supportive therapy	Observed everyday memory failure	General Memory	0.22

Table 3 (*Continued*)

Author	Intervention Type	Injury severity	Mean age & participants number	Total no. of sessions	No. of sessions per week	Session Duration	Intervention 1	Intervention 2/ Control	Memory test	Memory domain	Effect size
Goldstein et al., 1996 [66]	External	Severe	34 and 2 months $n = 30$	15	2-3	Nan	Face-Name associations	Computerized face-name associations	Face memory test	Visual face memory	0.72
Hart et al., 2002 [67]	External	Moderate to severe	31 and 6 months $n = 20$	13	Nan	Nan	Portable voice organizer training	Supportive therapy	Recall therapy goals	Prospective memory	0.22
Raskin et al., 2009 [68]	External	Moderate to severe	43 and 4 months $n = 16$	24	Twice	60 min	Specific prospective memory training for maintaining goal in mind	No training	Prospective errors (ProM)	Prospective memory	0.91
McDonald et al., 2011 [69]	External	Moderate to severe	47 $n = 12$	Nan	Nan	Nan	Google calendar training	Dairy training	% of intended actions	Prospective memory	0.83
Berg et al., 1991 [42]	External	Severe	34 and 7 months $n = 28$	18	Three	60 min	Specific memory strategy training of individual problems	No training	Acquisition of faces test, RAVLT	Immediate verbal and visual memory	0.68
							External interventions for moderate-severe mean effect size				0.60

CVLT: California Verbal Learning Test; CVLT-R: California Verbal Learning Test-Research edition; HVLT: Hopkins Verbal Learning Test; LTM: Long-Term Memory; ProM: Prospective Memory; RAVLT: Rey Auditory Verbal Learning Test; RBMT: Rivermead Behavioral Memory Test.

Table 4
Descriptive data (effect sizes and number of studies) for studies by interaction of intervention type and memory domain.

Memory domain Intervention type	Internal Effect size (*n*)	External Effect size (*n*)	Mixed Effect size (*n*)
Working memory	0.058 (1)	–	0.239 (1)
Long-term visual	0.468 (2)	0.339 (2)	–
Long-term verbal	0.671 (4)	0.219 (2)	0.99 (2)
Immediate visual	–	0.68 (1)	–
Immediate verbal	0.456 (1)	0.68 (1)	0.809 (1)
Prospective memory	–	0.871 (2)	–

dations, so that not only mild TBI will benefit from mixed interventions [14,26] but also moderate-severe TBI will benefit even greater from mixed interventions.

Second, moderate-severe patients with TBI were most affected by the intervention, regardless of type. This observation is consistent with the second clinical recommendation [14,26], emphasizing the use of external strategies for individuals with severe TBI. Our findings show that both internal and external strategies were beneficial for those with moderate-severe TBI. Furthermore, we demonstrate that internal strategies were beneficial, beyond the use of a specific strategy.

Our third finding indicates that people with mild-moderate injury severity benefited least from internal interventions. This finding is somewhat inconsistent with recommendations that internal memory strategy training is effective for individuals with mild memory impairment [12]. Our findings indicate such intervention is effective, although significantly less than other strategies and specifically for patients with mild TBI. This observation might be due to the reliance of such strategies on high cognitive processes and demands and therefore even people with mild TBI may find such strategies more challenging than less cognitively demanding strategies [54]. However, this conclusion is only partial, considering that we did not find studies using external strategies for patients with mild-moderate TBI. Although researchers indicate that individuals with mild TBI may benefit from external aids, these interventions are not systematically implemented [54]. In any case, the insufficient number of studies of external interventions for patients with mild TBI gives a partial picture of the effectiveness of memory-remediating strategies, thus challenging the possibility of drawing conclusions for this population's ability to benefit from interventions.

We need to acknowledge a number of limitations in the present study. Given the small number of studies that conformed to our strict inclusion criteria, we did not separate studies by age, sex and intervention duration of the sample studied. These potential moderators should be evaluated in future studies. Another limitation was the dearth of external intervention studies of patients with mild TBI, thus limiting our ability to compare the efficiency of different intervention types for this population. Additionally, by reviewing only studies with quantitative measures, we did not include studies of qualitative data. Hence, the picture depicted here may not fully reflect the entire situation.

Many intervention studies were not included in the analyses because of their lack of standardized memory tests. Ideally, further research should address studies of randomized clinical trials with blinded assessment while differentiating between distinct injury severity categories.

5. Conclusion

The present study has demonstrated that memory-remediation interventions can be successful in improving memory impairments in individuals with TBI. Individuals with moderate-severe TBI seem to benefit most from such interventions. Combined internal and external cognitive interventions seem to have the most positive effect on cognitive memory symptomology. Thus, a wide range of intervention is more effective because this addresses individual variability for severity and memory deficits.

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Disclosure of interest

The authors declare that they have no competing interest.

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