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Meta-analysis of Cognitive Rehabilitation Interventions in Veterans and Service Members With Traumatic Brain Injuries

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Main Objective: Cognitive difficulties are some of the most frequently experienced symptoms following mild-to-moderate traumatic brain injuries (TBIs). There is meta-analytic evidence that cognitive rehabilitation improves cognitive functioning after TBI in nonveteran populations but not specifically within the veteran and service member (V/SM) population. The purpose of the current meta-analysis was to examine the effect of cognitive rehabilitation interventions for V/SMs with a history of mild-to-moderate TBI. **Design and Main Measures:** This meta-analysis was preregistered with PROSPERO (CRD42021262902) and used the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist for reporting guidelines. Inclusion criteria required studies to have (1) randomized controlled trials; (2) used adult participants (aged 18 years or older) who were US veterans or active-duty service members who had a history of mild-to-moderate TBI; (3) cognitive rehabilitation treatments designed to improve cognition and/or everyday functioning; (4) used objective neuropsychological testing as a primary outcome measure; and (5) been published in English. At least 2 reviewers independently screened all identified abstracts and full-text articles and coded demographic and effect size data. The final search was run on February 24, 2023, using 4 databases (PubMed, PsycINFO, Web of Science, and Google Scholar). Study quality and bias were examined using the revised Cochrane Risk-of-Bias Tool for Randomized Trials. **Results:** We identified 8 articles meeting full criteria (total participants = 564; 97% of whom had a history of mild TBI). Compared with control groups, participants

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showed a small, but significant, improvement in overall objective neuropsychological functioning after cognitive rehabilitation interventions. Interventions focusing on teaching strategies had a larger effect size than did those focusing on drill-and-practice approaches for both objective neuropsychological test performance and performance-based measures of functional capacity. **Conclusion:** There is evidence of cognitive improvement in V/SMs with TBI histories after participation in cognitive rehabilitation. Clinician-administered interventions focusing on teaching strategies may yield the greatest cognitive improvement in this population. **Key words:** *cognitive remediation*, *cognitive training*, *traumatic brain injury*

TRAUMATIC BRAIN INJURIES (TBIs) have been labeled the "signature injury" of post-9/11 veterans and military service members (V/SMs). Between 2000 and 2019, more than 400 000 active-duty SMs sustained a TBI, with the majority (82.8%) categorized as mild injuries and 11% categorized as moderate.[1] A random representative sample of post-9/11 veterans found that 17.3% met criteria for TBI acquired during military service.[2] Although most symptoms of mild TBI usually resolve within 90 days in civilian populations,[3] postconcussive symptoms may persist longer in military populations and often interfere with optimal functioning.[4,5] While there is more variability in recovery from moderate TBI, between 48% and 75% of participants with moderate TBI reported favorable outcomes on the Glasgow Outcome Scale-Extended and 32% reported no disability.[6,7]

TBIs can have a significant impact on both individuals and family members/caregivers, resulting in increased impairment in daily activities, depression, anxiety, social isolation, and decreased quality of life.[8] In addition, TBIs are costly to healthcare systems (eg, for veterans, the presence of TBI confers 3 times higher healthcare costs[2]). Common symptoms after mild-to-moderate TBIs include headaches, changes in mood, and cognitive symptoms.[5] Cognitive dysfunction appears to result in higher healthcare utilization, as individuals with cognitive impairment require 3 times as many hospitalizations as those without cognitive impairment.[9] As such, it is important to know the most efficacious treatments of cognitive impairments among V/SMs with a history of mild-to-moderate TBI, as well as any moderating factors of treatment response.

There is meta-analytic evidence for successful post-TBI cognitive rehabilitation in the general population, including attentional-based skills training,[10] memory skills training,[11] and problem-solving training,[12] with postintervention improvements observed on neuropsychological test performance and subjective cognitive symptoms. However, it is not well understood whether these postintervention improvements translate into meaningful changes in everyday functioning or how long they last.[12] It is also not clear whether these interventions are efficacious in V/SMs, whose TBIs often occur in the context of psychological trauma and who may have higher rates of comorbidities.[13] One previous review of cognitive rehabilitation treatments in V/SM populations found support for cognitive rehabilitation.[14] The present study provides an update and expansion to this review by performing a meta-analysis of cognitive rehabilitation for V/SMs with a history of mild-to-moderate TBI and incorporating analyses of study quality. We examined changes in performance on both neuropsychological tests and functional measures. In addition, we built on previous research by examining effects on everyday functioning and, when possible, durability of the treatment effects. Finally, we examined moderating factors (eg, type of treatment, treatment length, age) through subgroup analyses and meta-regression.

METHODS

This meta-analysis was preregistered with PROSPERO (CRD42021262902) and used the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist for reporting guidelines[15] (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765, for the PRISMA checklist). All deviations from the preregistration are explicitly noted in the Supplemental Digital Content (available at: http://links.lww.com/JHTR/A765).

We developed sets of key words related to the following elements: (A) cognitive rehabilitation and other behavioral/neuropsychological interventions; (B) traumatic brain injury/acquired brain injury; and (C) veteran/military populations. Preliminary searches were conducted in several databases to gauge the precision of the search, scan article metadata for additional relevant key words, and refine final inclusion and exclusion criteria. The final Boolean search string was as follows: (("cognitive training" or "cognitive strategy training" or "cognitive skills training" or "cognitive rehabilitation" or "cognitive remediation" or "cognitive intervention" or "memory training" or "attention training" or "executive function training" or "executive functioning training" or "problem solving training" or "problem solving therapy" or "neurorehabilitation" or "neuropsychological training") AND ("TBI" or "traumatic brain injury" or "head injury" or "brain injury" or "concussion" or "postconcussive syndrome" or "post-concussive syndrome")) AND (veteran or military or army or navy or "air force" or "marine corps" or "service member" or "active duty").

The final inclusion criteria required studies to have (1) randomized controlled trials; (2) used adult participants (aged 18 years or older) who were US veterans or active-duty service members who had a history of mild-to-moderate TBI; (3) cognitive rehabilitation treatments designed to improve cognition and/or everyday functioning; (4) used objective neuropsychological testing as a primary outcome measure; and (5) been published in English. Samples of mixed populations (eg, including civilians, mixed causes of cognitive impairment) were used if TBI or V/SM groups were reported separately. Because of the small number of studies in this area, we included 3 studies of samples with mixed mild and moderate TBI severity; in these studies, a minority of participants had moderate TBI (≤25%). Exclusion criteria included (1) severe TBI, (2) nonmilitary population, and (3) trials using only self-report outcomes. We excluded studies of severe TBI due to differences in mechanisms, symptom trajectory, prognosis, and treatment needs, resulting in minimal overlap in the rehabilitation literature.[16–20]

Data screening, extraction, and coding

At least 2 reviewers (T.A., S.P., C.H.) independently screened all identified abstracts and full-text articles, with discrepancies resolved through discussion. At least 2 reviewers (T.A., B.E., C.H.) independently extracted demographic and effect size data from articles meeting full criteria. We extracted all available summary effect size data; when multiple effect sizes were reported, we preferentially used raw mean values and standard deviations. When available, we preferentially used or calculated pre/postintervention change scores for both groups, rather than using only postintervention scores. When studies reported insufficient information to determine study eligibility or calculate an effect size, we contacted authors for information. Studies were reviewed for possible overlapping samples; we used the study with the largest sample size or most comprehensive reporting of neuropsychological outcome measures.

In addition, we coded studies for the following information: type of neuropsychological test domain (eg, attention, memory), measures of functional capacity and self-reported everyday functioning, and whether the intervention focused on teaching strategies (strategy-based interventions) or drill-and-practice approaches to cognitive rehabilitation. We coded each neuropsychological test as described in Strauss et al[21] (see Table 1 for included neuropsychological tests). Strategy-based interventions were defined as interventions teaching strategy use with the goal of improving daily functioning even in the absence of improvement in cognitive functioning. Drill-and-practice interventions were defined as interventions with the goal of strengthening or restoring the impaired skills to improve cognitive functioning through the use of repeated drills or cognitive excercises[22,23] (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765, for full definitions).

Statistical analysis

We entered raw or standardized scores for all groups in a study (eg, intervention group vs control group) directly into Comprehensive Meta-Analysis 2.0 (CMA) using Hedges and Olkin's random-effects model to calculate the overall effect size for both the primary and subgroup analyses. For studies with multiple outcomes, a meta-analysis for the results of the individual study was conducted to give one effect size based on recommendations provided by Borenstein et al.[24] We considered the mean effect sizes as significant if $P < .05$ or if the 95% CI did not include zero; if discrepancies occurred, we used the 95% CI. All effect sizes were transformed into Cohen's d for the analyses, with the classification of small ($d = 0.2$), medium ($d = 0.5$), and large ($d = 0.8$) effects based on Cohen's recommendations.[25] Moderator analyses (meta-regression) were used if there are at least 10 studies per moderator category.[24] Exploratory moderator analyses were conducted if there were at least 8 studies without statistically significant heterogeneity between studies.[26]

To estimate how unpublished null results could lower the effect sizes, we used Rosenthal's fail-safe N-analysis, which estimates how many missing studies with statistically insignificant results are needed to reduce the statistical significance to nonsignificant in the meta-analysis.[24] In addition, we report a power analysis to determine whether there were enough studies to power both the primary and subgroup analyses used in the meta-analysis.[27] We also visually inspected funnel plots and performed a trim-and-fill analysis for outlier studies among both the primary and subgroup analyses. We assessed heterogeneity using estimates of Q, τ^2, and I^2. Three studies included a minority of moderate TBI severity participants (6%, 21%, and 25%).[28,29,30] One of the 3 studies included mild, moderate, and severe TBIs, but the primary author of this study provided data with only the participants having TBI of mild and moderate severity.[28]

RESULTS

Search and sample characteristics

The final searches were run on September 8, 2022, and February 24, 2023, using key words related to "cognitive rehabilitation interventions," "traumatic brain injuries," and "veteran or military populations" (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765, for full search structure, databases used, and preliminary search methods), with reference treeing

TABLE 1 *Neuropsychological test domains*

Domain	Tests coded in meta-analysis	*n* (%) of studies
Attention	Integrated Visual and Auditory Continual Performance Test, Paced Auditory Serial Addition Test, Trail Making Test-A, WAIS-III Auditory Consonant Trigrams,[a] WAIS-III Letter Number Sequencing,[a] WAIS-IV Digit Span, WAIS-IV Letter Number Sequencing, WAIS-IV Symbol Search	8 (100%)
Memory	Brief Visual Memory Test–Revised,[a] California Verbal Learning Test-2nd edition, Hopkins Verbal Learning Test-Revised, Memory for Intentions Screening Test, RBANS Immediate and Delayed Memory, Rey Auditory Verbal Learning Test,[a] Ruff Light Trails Test	7 (88%)
Executive functions	Controlled Oral Word Association Test/FAS, D-KEFS Color-Word Inhibition, D-KEFS Trail Making, EXAMINER: Flanker and set-shifting tests,[a] Verbal Fluency/FAS, Trail Making Test-B, Wisconsin Card Sorting Test-64 items	7 (88%)
Language	RBANS Language	1 (13%)
Visual perception	RBANS Visuospatial	1 (13%)
Performance-based functional capacity[b]	Goal Processing Scale, Performance subtests, Timed Instrumental Activities of Daily Living, UCSD Performance-Based Skills Assessment, Brief Version, Virtual Reality Tactical Driving Quotient, Virtual Reality Operational Driving Quotient	4 (50%)

Abbreviations: D-KEFS, Delis-Kaplan Executive Function System; RBANS, Repeatable Battery for the Assessment of Neurological Status; UCSD, University of San Diego; WAIS-III, Wechsler Adult Intelligence Scale-3rd edition; WAIS-IV, Wechsler Adult Intelligence Scale-4th edition.

[a]Used in a composite and subtest scores are unavailable.

[b]Functional based capacity examples were not provided by Strauss et al[22] and instead based on recent literature reviews of the topic.

(ie, searching articles pulled for full-text screening and examining their references and cited by lists) completed on February 24, 2023. We screened the titles and abstracts of 636 unique articles (see Figure 1). After initial screening, we examined 88 articles.

Following full-text screening, we identified 8 articles meeting full criteria (total participants: $N = 564$; intervention: $n = 303$; control: $n = 261$; see Table 2 for included studies and descriptions).[28–34] All included articles were peer reviewed (ie, no preprints or unpublished works met all inclusion criteria). The sample size ranged from 17 to 119 (median $n = 40.5$). The average age of study participants was 36.7 years (SD = 6.8; see Table 3 for demographic information for all included studies); intervention and control participants did not differ in age. Average education did not differ between intervention and control participants. On average, participants had 14.2 years of education (SD = 1.2). Between 81% and 100% (mean = 88.3%, SD = 11.4%) of participants were male. Limited racial and ethnic information was reported by the majority of studies, limiting available information for the meta-analytic sample. Using data collected by more than 1 study, on average, 65.4% (SD = 9.7%) of participants identified as White, 15.5% (SD = 2.5%) as African American, 7% (SD = 5.0%) as Other, and 21.5% (SD = 12.5%) reported Hispanic ethnicity. The average length of time since TBI was 6 years (mean = 71.8 months; SD = 52.0; range, 5-189 months). There was limited information on preintervention cognitive treatments, which were only reported in 2 studies. One study reported that 14% of the sample had previous cognitive rehabilitation treatment, and one study reported that 24% of the sample had previous TBI rehabilitation treatment and 12% were currently in TBI rehabilitation treatment (see Table 2).

Intervention lengths ranged from 4 to 15 weeks (mean = 9.5, SD = 3.7). Four studies used a strategy-based approach, 3 studies used a drill-and-practice approach, and 1 study had 3 intervention conditions (1 drill-and-practice approach, which we included with the other drill-and-practice interventions, and 2 combinations of strategy-based and drill-and-practice approaches, which we considered separately). Sufficient information was provided to use pre/postintervention change scores for 7

TABLE 2 *Demographic and treatment information for all studies included in the meta-analysis*

Study	Sample characteristics	Treatment description	Length/intensity of treatment	Strategy-based or drill-and-practice	Outcomes included in meta-analyses	Cohen's *d* (95% CI)
Cooper et al (2017)[4]	Intervention sample size: A: 30; B: 30; C: 32 Control sample size: 34 Total sample size: 126 Average age: 31.3 y Education: 35% >12 y of education % male: 100% Race/ethnicity:77% White, 23% Other, 29% Hispanic ethnicity TBI severity: 100% mild % previous treatment: Not provided	A: Commercially available brain fitness or brain training computer games targeting attentional processes and general cognitive activation	10 h of in-clinic, computerized cognitive rehabilitation treatment per week throughout the 6-wk treatment trial	Drill-and-practice	PASAT	$d = -0.07$ (−0.78 to 0.44)
		B: Individual and group therapy (cognitive rehabilitation) and 3 h of weekly computer-based training targeting attentional processes and general cognitive activation	5 h of individual therapy sessions, 2 h of group therapy sessions, and 3 h of weekly computer-based homework (10 h total) per week for 6 wk	Mixed (clinician administered)	PASAT	$d = -0.03$ (−0.62 to 0.56)
		C: Individual and group therapy (cognitive rehabilitation, mindfulness, and CBT) and 3 h of weekly CBT, mindfulness, and computer-based training targeting attentional processes and general cognitive activation	4 h of individual therapy sessions, 3 h of group therapy sessions, 3 h of CBT, mindfulness, and computer-based training (10 h total) per week for 6 wk	Mixed (clinician administered)	PASAT	$d = 0.10$ (−0.49 to 0.69)

(*continues*)

TABLE 2 *Demographic and treatment information for all studies included in the meta-analysis* (Continued)

Study	Sample characteristics	Treatment description	Length/intensity of treatment	Strategy-based or drill-and-practice	Outcomes included in meta-analyses	Cohen's *d* (95% CI)
Ettenhofer et al (2019)[28]	Intervention sample size: 11 Control sample size: 6 Total sample size: 17 Average age: 51.7 y Education: 16.9 y % male: 65% Race/ethnicity: 65% White, 18% African American, 5% Latino, 12% Other TBI severity: 75% mild, 25% moderate Previous treatment: Not provided	Virtual driving practice, including component cognitive skills pertinent to driving (eg, dual processing, response inhibition, working memory), and performing composite driving skills (eg, road hazards, yielding)	Six 90-min sessions (9 h total) conducted over a 4-wk period	Drill-and-practice	TMT-A WAIS-IV Coding WAIS-IV DS CVLT-II Trials 1-5 CVLT-II SDFR CVLT-II LDFR COWAT, Letters COWAT Animals TMT-B VR TDQ VR ODQ	$d = -1.63$ (−2.77 to −0.49) $d = -2.56$ (−3.89 to −1.23) $d = -0.69$ (−1.71 to 0.32) $d = 0.81$ (−0.22 to 1.84) $d = 0.07$ (−0.92 to 1.06) $d = 0.31$ (−0.69 to 1.23) $d = -0.13$ (−1.12 to 0.86) $d = 0.81$ (−0.22 to 1.84) $d = -0.18$ (−1.17 to 0.81) $d = -0.19$ (−1.39 to 1.01) $d = -0.56$ (−0.82 to −0.31)

(*continues*)

TABLE 2 *Demographic and treatment information for all studies included in the meta-analysis* (Continued)

Study	Sample characteristics	Treatment description	Length/intensity of treatment	Strategy-based or drill-and-practice	Outcomes included in meta-analyses	Cohen's *d* (95% CI)
Jak et al (2019)[29]	Intervention sample size: 51 Control sample size: 49 Total sample size: 100 Average age: 34.4 y Education: 13.7 y % male: 98% Race/ethnicity: 47% White, 13% African American, 9% Asian, 23% Hispanic/Latino, 4% Native Hawaiian/Pacific Islander, 2% Native American/Native Alaskan, 2% Other TBI severity: 94% mild, 6% moderate Previous treatment: 14% had prior cognitive rehabilitation	All standard components and structure of CPT with elements from CogSMART including compensatory cognitive strategies for attention (eg, breaks, self-talk, environmental adjustments), memory and prospective memory (eg, calendar use, routines, linking tasks, automatic places), and executive functioning (eg, goal setting, problem-solving)	60-75 min individual sessions delivered weekly for 12 wk	Strategy-based (clinician administered)	WAIS-IV DS WAIS-IV PSI CVLT-II Trials 1-5 CVLT-II SDFR CVLT-II LDFR D-KEFS C-WI D-KEFS TM Switching WCST-64 Total Errors	$d = 0.33$ (−0.07 to 0.72) $d = 0.19$ (−0.21 to 0.58 $d = 0.03$ (−0.36 to 0.42) $d = 0.28$ (−0.12 to 0.67) $d = 0.13$ (−0.26 to 0.53) $d = 0.14$ (−0.25 to 0.52) $d = 0.13$ (−0.27 to 0.52) $d = 0.73$ (0.09 to 1.12)
Mahncke et al (2021)[31]	Intervention sample size: 41 Control sample size: 42 Total sample size: 83 Average age: 33.8 y Education: 14.4 y % male: 81% Race/ethnicity: 77% White TBI severity: 100% mild Previous treatment: 24% had previous TBI treatment, 12% were currently in TBI treatment	Brain plasticity-based computerized cognitive training (BrainHQ) program targeting speed/accuracy of information processing	5 h of self-delivered training per week for 13 wk	Drill-and-practice	Cognitive Composite TIADL	$d = 0.43$ (−0.07 to 9.2) $d = -0.04$ (−0.53 to 0.45)

(*continues*)

TABLE 2 *Demographic and treatment information for all studies included in the meta-analysis* (Continued)

Study	Sample characteristics	Treatment description	Length/intensity of treatment	Strategy-based or drill-and-practice	Outcomes included in meta-analyses	Cohen's *d* (95% CI)
Nelson et al (2013)[33]	Intervention sample size: 21 Control sample size: 24 Total sample size: 45 Average age: 32.9 y Education: 12.9 y % male: 100% Race/ethnicity: Not provided TBI severity: 100% mild Previous treatment: Not provided	Interactive metronome therapy: the patient executes various repeated movements in time to a beat, while a computer provides precision feedback on performance targeting planning, sequencing, and processing information	15 h over ∼7 wk (length ranged from 5 to 17 wk)	Drill-and-practice	IVA-CPT RBANS Attention WAIS-IV Coding WAIS-IV DS WAIS-IV LNS WAIS-IV SS RBANS Immediate Memory RBANS Delayed Memory D-KEFS C-WI D-KEFS TM RBANS Language RBANS Visuospatial	$d = 0.03$ (−0.55 to 0.6) $d = 0.60$ (0.20 to 1.2) $d = 0.46$ (−0.13 to 1.05) $d = 0.19$ (−0.22 to 0.60) $d = -0.28$ (−0.85 to 0.31) $d = 0.31$ (−0.28 to 0.88) $d = 0.09$ (0.12 to 1.32) $d = 0.72$ (0.06 to 1.25) $d = 0.29$ (−0.56 to 0.60) $d = 0.17$ (0.05 to 0.25) $d = 0.39$ (−0.21 to 0.96) $d = 0.06$ (−0.52 to 0.64)
Novakovic-Agopian et al (2021)[34]	Intervention sample size: 21 Control sample size: 19 Total sample size: 40 Average age: 45.3 y Education: 14.4 y % male: 88% Race/ethnicity: 67% White TBI severity: 100% mild Previous treatment: Not provided	Cognitive rehabilitation training that targets executive control functions and metacognitive goal management strategies	2 h of group training per week, 3 h of individual sessions (total) over 5 wk	Strategy-based (clinician administered)	WM composite Sustained attention composite Recall composite Delayed composite Inhibition composite MF composite GPS Overall Performance Score	$d = 0.48$ (0.19 to 0.63) $d = 0.77$ (0.17 to 1.4) $d = 0.14$ (−0.44 to 0.72) $d = 0.17$ (−0.4 to 0.75) $d = 0.64$ (0.05 to 1.23) $d = 0.09$ (−0.49 to 0.67) $d = 0.69$ (0.01 to 1.12)

(*continues*)

TABLE 2 *Demographic and treatment information for all studies included in the meta-analysis* (Continued)

Study	Sample characteristics	Treatment description	Length/intensity of treatment	Strategy-based or drill-and-practice	Outcomes included in meta-analyses	Cohen's *d* (95% CI)
Storzbach et al (2017)[34]	Intervention sample size: 50 Control sample size: 69 Total sample size: 119 Average age: 35.1 y Education: 13.7 y % male: 95% Race/ethnicity: 66% White TBI severity: 100% mild Previous treatment: Not provided	Group-based compensatory cognitive rehabilitation treatment emphasizing compensatory strategies in prospective memory, attention, learning and memory, and executive functioning	2 h of group training per week for 10 wk	Strategy-based (clinician administered)	WAIS-IV DS WAIS-IV Coding HVLT-Total Recall HVLT Retention D-KEFS, TM D-KEFS CF D-KEFS PF UPSA-B	$d = 0.37$ (−0.5 to 0.80) $d = 0.03$ (−0.39 to 0.45) $d = 0.44$ (0.14 to 0.87) $d = 0.44$ (0.13 to 0.87) $d = 0.06$ (−0.37 to 0.48) $d = 0.07$ (−0.35 to 0.49) $d = 0.44$ (0.01 to 0.49) $d = 0.58$ (0.06 to 0.90)
Twamley et al (2014)[30]	Intervention sample size: 16 Control sample size: 18 Total sample size: 34 Average age: 32.0 y Education: 13.6 y % male: 94% Race/ethnicity: 58.6% White, 35.4% Hispanic TBI severity: 79% mild, 21% moderate Previous treatment: Not provided	Manualized, 12-wk, multimodal compensatory cognitive training intervention emphasizing habit learning and compensatory strategies in prospective memory, attention, learning and memory, and executive functioning	2 h/wk (1-h CogSMART and 1-h standard supported employment) for 12 wk	Strategy-based (clinician administered)	WAIS-III DS CVLT-II Trials 1-5 CVLT-II LDFR MIST Summary MIST 24-h D-KEFS LF D-KEFS CF D-KEFS CS WCST-64	$d = -0.45$ (−1.12 to 0.23) $d = -0.08$ (−0.75 to 0.59) $d = -0.09$ (−0.77 to 0.58) $d = -0.08$ (−0.74 to 0.61) $d = 0.73$ (0.04 to 1.43) $d = 0.28$ (−0.40 to 0.95) $d = 0.27$ (−0.41 to 0.95) $d = 0.16$ (−0.51 to 0.84) $d = -0.30$ (−0.97 to 0.38)

Abbreviations: ACT, Auditory Consonant Trigrams; BVMT-R, Brief Visual Memory Test–Revised; CBT, cognitive behavioral therapy; CF, Category Fluency; COWAT, Controlled Oral Word Association Test; CogSMART, Cognitive Symptom Management and Rehabilitation Therapy; CPT, Continuous Performance Test; CS, Switching Fluency; CVLT-II, California Verbal Learning Test-2nd edition; C-WI, Color-Word Inhibition; DF, Design Fluency; D-KEFS, Delis-Kaplan Executive Function System; DR, Delayed Recall; DS, Digit Span; DVT, Digital Vigilance Test; GPS, Goal Processing Scale; HVLT-R, Hopkins Verbal Learning Test-Revised; IVA-CPT, Integrated Visual and Auditory Continuous Performance Test; LDFR, Long Delay Free Recall; LF, Letter Fluency; LNS, Letter Number Sequencing; MF, mental flexibility subdomain score; MIST, Memory for Intentions Screening Test; ODQ, Operational Driving Quotient; PASAT, Paced Auditory Serial Addition Test; PSI, Processing Speed Index; RAVLT, Rey Auditory Verbal Learning Test; RBANS, Repeatable Battery for the Assessment of Neurological Status; RULIT, Ruff Light Trails Test; SDFR, Short Delay Free Recall; SS, Symbol Search; TBI, traumatic brain injury; TDQ, Tactical Driving Quotient; TIADL, Timed Instrumental Activities of Daily Living; TM, Trail Making; TMT, Trail Making Test; UPSA-B, University of San Diego (UCSD) Performance-Based Skills Assessment, Brief Version; VF, Verbal Fluency; VR, Virtual Reality; WAIS-III, Wechsler Adult Intelligence Scale-3rd edition; WAIS-IV, Wechsler Adult Intelligence Scale-4th edition; WCST-64, Wisconsin Card Sorting Test-64 items; WMS-III, Wechsler Memory Scale, 3rd edition.

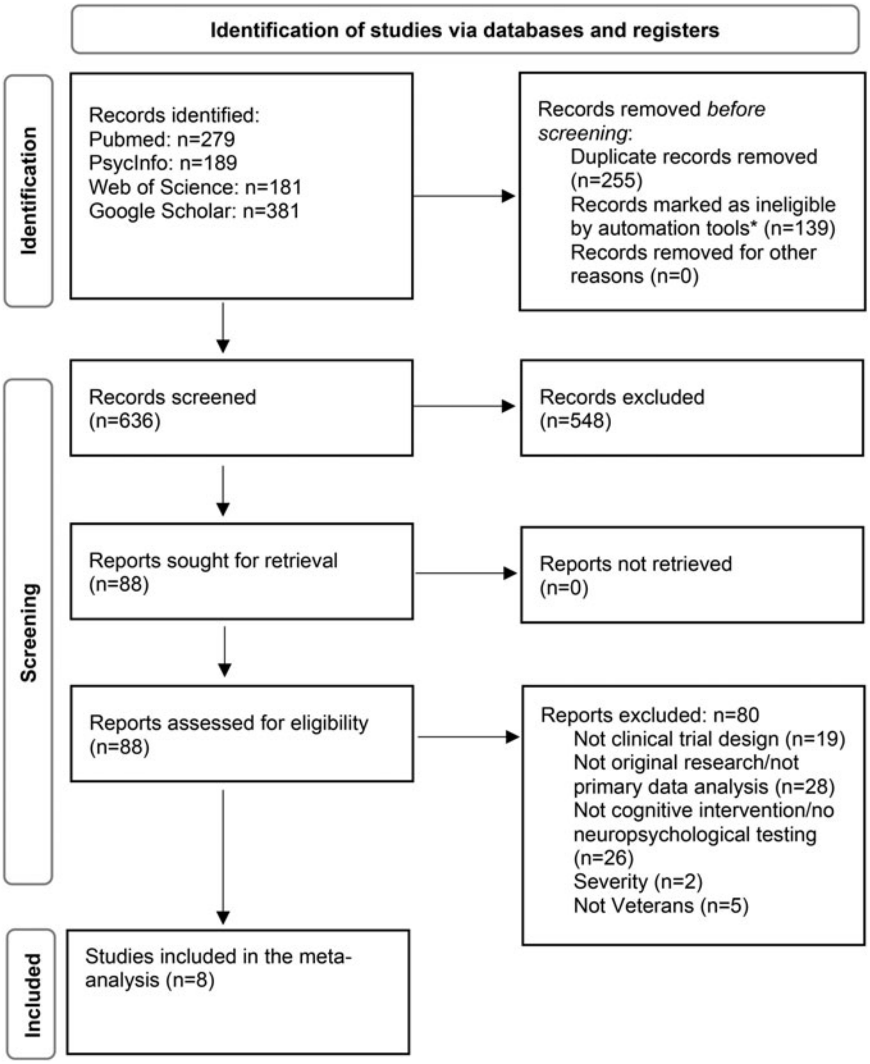

Figure 1. PROSPERO flow chart. Asterisk (*) indicates this number was marked ineligible by automation tools and then each record was manually reviewed by the first author to check the record was ineligible.

studies. We ran a post hoc sensitivity analysis comparing results with and without the study with only postintervention scores, which revealed minimal differences (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765, for sensitivity analysis results). Sensitivity analysis did not reveal a difference when including these studies compared with using only samples with mild injury severity (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765). Agreement between coders was greater than 96% and $\kappa = 0.85$ for all aspects of the screening and coding process; there was 100% agreement for full article inclusion and article coding after discussion.

Risk of bias assessment

Two reviewers (T.A., C.H.) independently coded for study quality using the revised Cochrane Risk-of-Bias Tool for Randomized Trials, second edition[35] (RoB 2), as well as additional indicators of study quality (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765).

Results of the risk of bias

Overall, there was low concern for study bias (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765). Two studies had baseline differences between the intervention and control groups, probably due to small sample sizes.

Overall analysis

Compared with control groups, participants showed a small, but statistically significant, improvement in objective neuropsychological functioning after cognitive rehabilitation interventions ($k = 8$, $d = 0.22$; 95% CI,

TABLE 3 *Overall demographic characteristics*

	Intervention	Control	Total[a]
All studies			
Number of participants	303	261	564
Average age, mean (SD), y	35.6 (6.2)	36.1 (8.4)	36.7 (6.8)
Average education, mean (SD), y	14.2 (1.8)	14.0 (0.6)	14.2 (1.2)
Average % male, mean (SD)			88.3% (11.4)
Average racial demographics[b]			65.4% (9.7) White, 15.5% (2.5) *African American*, 9% (0) *Asian*, 4% (0) *Native Hawaiian/Pacific Islander*, 2% (0) *Native American/Native Alaskan*, 7% (5) *Other*
Average ethnic demographics[b]			21.1% (12.5) Hispanic ethnicity
Length of intervention, mean (SD), range, wk			9.5 (3.7), range 4-15
Strategy-based			
Number of participants	106	115	221
Average age, mean (SD), y	33.2 (2.7)	34.4 (0.4)	36.3 (4.2)
Average education, mean (SD), y	13.4 (0.3)	13.9 (0.2)	13.9 (0.3)
Average % male, mean (SD)			93.8% (3.63)
Average racial demographics[b]			63.9% (3.8) White, 13% (0) *African American*, 9% (0) *Asian* 4% (0) *Native Hawaiian/Pacific Islander*, 2% (0) *Native American/Native Alaskan*
Average ethnic demographics[b]			29.2% (6.2) Hispanic ethnicity
Length of intervention, mean (SD), range, wk			9.8 (2.9), range = 5-12
Drill-and-practice			
Number of participants	149	105	254
Average age, mean (SD), y	37.5 (7.4)	37.4 (10.9)	37.1 (8.6)
Average education, mean (SD), y	15.0 (2.2)	14.2 (0.8)	14.7 (1.7)
Average % male, mean (SD)			86.5 (14.6)
Average racial demographics[b]			73% (5.7) White, 18% (0) *African American*, 17.5% (5.5) *Other*
Average ethnic demographics[b]			17% (12) Hispanic ethnicity
Length of intervention, mean (SD), range, wk			9.3 (4.4), range = 4-15

[a]Some studies only gave overall information for demographic factors. As such, the total score differs somewhat from the intervention and control group-only information.
[b]Detailed demographics are available by study in Table 2. Racial/ethnic categories *italicized* indicate the information was reported in fewer than 4 studies.
[c]Demographic information for the mixed and restorative interventions are reported together as only one study included a mixed intervention[4] and then demographic information was not reported separately.

0.01 to 0.43; P = .04; see Figure 2) and small, but not statistically significant, effect on performance-based measure of functional capacity (k = 4, d = 0.16; 95% CI, −0.48 to 0.81; P = .62). There was no evidence of significant heterogeneity between studies for the primary analysis (Q_7 = 8.14; P = .32; I^2 = 14.03). We found no evidence of publication bias (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765), though only one additional study with null findings would be needed for the improvement in objective neuropsychological testing to no longer be significant.

Cognitive domains

There were significant effects on memory (k = 6, d = 0.42; 95% CI, 0.13 to 0.70; P = .01) and executive functioning (k = 6, d = 0.26; 95% CI, 0.01 to 0.51; P = .04) but not on attention (k = 7, d = 0.12; 95% CI, −0.12 to 0.35; P = .33; see Figure 2). Data in other domains (language, visuospatial) were not sufficient to examine due to being included in only one study.

Strategy-based interventions

Studies focusing on teaching strategies had a small, but statistically significant, effect on objective neuropsy-

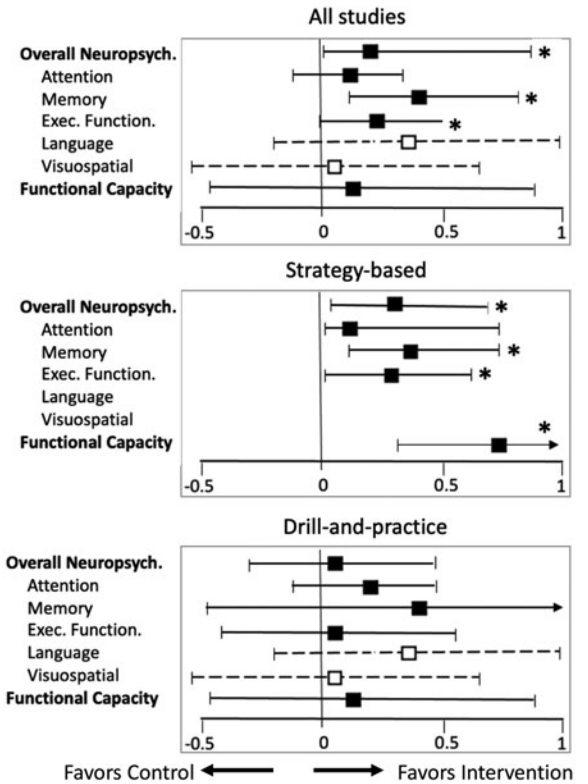

Figure 2. Forest plot for overall and subgroup analyses. Boxes represent pooled effect as Cohen's *d* and the lines indicate 95% CI. Asterisk (*) indicates statistically significant results ($P < .05$). Dashed line with open square indicates result from one study.

chological performance ($k = 4$, $d = 0.37$; 95% CI, 0.08 to 0.67; $P = .01$) and a moderate-to-large effect on performance-based measures of functional capacity ($k = 2$, $d = 0.72$; 95% CI, 0.03 to 1.07; $P < .01$). There was no evidence of significant heterogeneity ($Q_3 = 2.38$, $P = .50$, $I^2 < 0.01$). We found no evidence of publication bias (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765). Three missing null studies would be needed for the statistically significant finding of improvement in objective neuropsychological performance to no longer be significant.

Drill-and-practice interventions

Studies using a drill-and-practice approach had a negligible effect on objective neuropsychological test performance that was not statistically significant ($k = 4$, $d = 0.10$; 95% CI, −0.26 to 0.46; $P = .59$). Small (nonsignificant) improvements on measures of functional capacity favored the control groups ($k = 2$, $d = -0.45$; 95% CI, −1.39 to 0.44; $P = .32$). There was no evidence of significant heterogeneity ($Q_3 = 3.95$, $P = .27$, $I^2 < 0.01$). We found no evidence of publication bias (see Supplemental Digital Content, available at: http://links.lww.com/JHTR/A765).

Mixed interventions

One study used 3 different treatment groups, with 2 using both drill-and-practice and strategy-based elements. There was a small, but not statistically significant, effect of these mixed interventions on neuropsychological performance ($k = 1$ but with 2 groups with different treatments, $d = 0.30$; 95% CI, −0.38 to 0.45; $P = .88$).

Types of control group

Four studies used active control groups, and 4 studies used nonactive control groups (wait-list control, treatment as usual/usual care). There was greater improvement in interventions using active conditions as control groups ($d = 0.37$; 95% CI, 0.08 to 0.67; $P = .01$) than studies using nonactive control groups (not statistically significant; $d = 0.11$; 95% CI, −0.19 to 0.40; $P = .48$).

Exploratory meta-regression

We used meta-regression to examine the relationship between neuropsychological outcomes and participant demographic factors (age, education, time since TBI, and presence of comorbid posttraumatic stress disorder [PTSD]) as covariates in 4 independent models, with neuropsychological test performance change scores as the outcome. There was no significant effect for the percentage of the sample with comorbid PTSD ($b = -0.004$; 95% CI, −0.01 to 0.01; SE = 0.01; $P = .42$), age ($b = 0.01$; 95% CI, −0.04 to 0.07; SE = 0.03; $P = .64$), education ($b = 0.03$; 95% CI, −0.39 to 0.46; SE = 0.22; $P = .88$), or time since TBI ($b = -0.002$; 95% CI, −0.01 to 0.01; SE = 0.01; $P = .59$). There was also no relationship between length of the intervention and neuropsychological test performance ($b = 0.01$; 95% CI, −0.06 to 0.88; SE = 0.04; $P = .70$).

Durability of treatment effects

Four studies included postintervention follow-up visits to measure durability of treatment effects, with 3 studies repeating objective measures after a 12-week no-contact/no-training period. When limiting analysis to the studies with sufficient data, treatment effects on overall neuropsychological test performance at 10- or 12-week follow-up ($d = 0.45$; 95% CI, 0.01 to 0.90; $P = .04$) were similar to treatment effects immediately posttreatment ($d = 0.40$; 95% CI, 0.33 to 0.77; $P = .03$).

DISCUSSION

TBIs are a prevalent concern for V/SM populations, and there is a need to identify efficacious treatments. The present meta-analysis examined the effects of cognitive rehabilitation in veterans with a history of mild-to-moderate TBI. Compared with control participants, we found evidence of small effect size improvements for cognitive rehabilitation on objective neuropsychological performance, with small effect size improvements on memory and executive functioning tests, but no significant change in attention performance. Interventions using strategy-based approaches yielded larger effects than drill-and-practice interventions. We found the effect of the active intervention was larger in studies using active control groups. This finding was unexpected, as more robust control conditions are typically associated with lower effect sizes.[36] One possible reason may be inconsistency of participant blinding of active control conditions, due to difficulty in providing an active control condition that is not easily identifiable to the study participants as the control condition. Another reason is that many of the inactive control conditions, particularly treatment as usual conditions, consisted of a high level of clinical contact and specialty appointments. There was no effect of length of the intervention on neuropsychological test performance, nor did individual factors (age, education, time since TBI, presence of comorbid PTSD) moderate outcomes, although this finding may be due to minimal statistical power and limited variability in the studies. In the studies that included follow-up assessments, participants maintained treatment gains in global neuropsychological performance 3 months postintervention. Although this finding merits replication, these studies provide preliminary evidence of sustained benefit of the interventions on objective neuropsychological test performance. It should be noted that 97% of the participants included in this meta-analysis had a history of mild TBI, so these findings may not generalize to individuals with more severe TBIs.

Findings from this analysis are comparable with a recent meta-analysis of cognitive rehabilitation in nonveteran populations, which found a small treatment effect ($d = 0.30$) for cognitive rehabilitation treatments of acquired brain injuries (eg, TBI and stroke), with a smaller and statistically nonsignificant effect for studies only examining participants with TBI.[37] The larger effect size seen in our analysis is somewhat surprising, as many pharmacological and psychotherapeutic trials find lower treatment gains in veteran populations than in civilian populations.[38] However, veterans receive their care in a very different healthcare system and their injuries may have been more likely to be witnessed, resulting in earlier specialized care and rehabilitation.

Subgroup analyses found strategy-based treatments to have a small, but statistically significant, effect on objective neuropsychological performance ($d = 0.37$) and a large, but statistically significant, effect on performance-based measures of functional capacity ($d = 0.72$). There were no significant effects for either objective neuropsychological test performance or performance-based measures of functional capacity for drill-and-practice interventions. These findings are important, as the Institute of Medicine's report on TBI encourages interventions to focus on functional outcomes as many decontextualized treatments do not translate into increased daily functioning.[39]

These findings are also consistent with the best practice guidelines recommended by Cicerone et al,[40] based on the evaluation of 491 studies of cognitive rehabilitation after TBI or stroke, as well as the 2023 INCOG 2.0 guidelines for cognitive rehabilitation treatments following brain injuries.[41] In the most recent edition of the Cicerone et al[40] living review/practice guidelines, drill-and-practice, computer-assisted programs are reported to have emerging efficacy, but current practice guidelines state these programs should be managed by a rehabilitation clinician, rather than solely computer-delivered. While the INCOG 2.0 guidelines include both drill-and-practice treatments and strategy training, the guidelines recommend that drill-and-practice treatments should focus on real-world activities.[41] They recommend teaching internal compensatory strategies for mild-to-moderate memory deficits, training in external compensatory strategies for more severe impairment,[42] and metacognitive strategy use for mild-to-moderate attention deficits.[43] Computer-based training without a therapist was not recommended. As there are benefits to both drill-and-practice and computer-based programs (eg, greater flexibility in adapting the program or having the program adjust to participant abilities, easily scalable, reduced costs due to in-home and self-administered treatments), their recommendation of the use of drill-and-practice treatments that focus on real-world activities, strategy development and use, facilitated by a TBI-experienced clinician, may increase the efficacy of these programs, particularly for functional capacity in veterans. Further research can explore the benefit of interventions utilizing both strategy training and drill-and-practice treatments on cognitive domains.

There are several strengths to the current analysis. First, while there was a wide range of types of interventions, intervention lengths, and varying amounts of comorbid mental health concerns, there was a low amount of systematic heterogeneity between studies. As such, we believe there can be greater confidence in the findings of this study. Second, all studies used normed neuropsychological tests, and the age and demographic factors of the study participants included in this study are well matched to the normative samples of these tests.

LIMITATIONS

There were also limitations in the primary studies included in the analysis, as well as in our statistical analyses. The studies included in this analysis used different neuropsychological batteries, with few studies measuring multiple domains, thus precluding further analysis at the domain level. In addition, mild TBIs are frequently comorbid with other mental health concerns, including PTSD, depression, and anxiety. These conditions were inconsistently measured and described in the primary studies. There was limited information on the previous treatment experiences of participants, with only 2 studies providing information on previous cognitive rehabilitation and only one study describing previous or concurrent mood treatment. Future meta-analyses will benefit from primary studies providing details on their sample's treatment history.

There are also some limitations in our analysis due to lower power of meta-regressions, as well as the restricted age and education range in the primary studies. Although the recommended number of studies sufficient for meta-regressions typically varies between 10 and 25, there is some evidence that 8 studies may provide sufficient information in the absence of significant heterogeneity.[26] It is possible we were unable to detect whether age or education moderated treatment response due to limited range of these variables in the primary studies. In addition, we likely were underpowered to detect an effect with only 8 studies. Future meta-analyses with additional studies and greater between-study variability will be able to evaluate the moderating effects of these treatments. The average age of participants in the included studies (35.6 years) was also lower than the average age of veterans reporting TBI (49.9 years).[44,44] As such, our findings may not apply to older veterans. However, there are also advantages to our restricted age range, in that there is a low possibility of cognitive impairments due to age-related decline or dementia rather than those secondary to TBI.

On the basis of the results of this meta-analysis, we conclude that clinician-administered cognitive rehabilitation interventions with a focus on teaching strategies produce greatest cognitive improvement in V/SMs with a history of mild-to-moderate TBI. As many of these treatments are transdiagnostic and symptom-based, rather than cause-specific, further research will benefit from examining the effect of cognitive rehabilitation treatments in veterans with non-TBI causes of cognitive impairment. As other types of treatments are studied, such as neuromodulation or psychopharmacology, next steps will include comparison of these treatments as monotherapy and combination therapy.

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