Interventions to Improve Cognitive Outcomes in Older Adults with Traumatic Brain Injury and Association Between Social Determinants of Health and Intervention Effectiveness: A Scoping Review*

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ABSTRACT

Background

At least one million Canadians are at risk of experiencing a traumatic brain injury (TBI) in later life, which can lead to cognitive decline. We identified interventions studied to improve cognitive outcomes in older adults with TBI, and examined how social determinants of health (SDoH) may influence their effectiveness.

Methods

We followed JBI guidance and searched five electronic databases from inception until March 2023 for studies evaluating the clinical and cost effectiveness, and safety of interventions being studied to improve cognitive outcomes in older adults with TBI. We abstracted SDoH following the PROGRESS-Plus framework.

Results

We included 20 studies and 44,462 predominantly men/male (65%) participants with a mean age of 65.9 years; studies reported 51 cognitive outcomes. Three studies reported on race or ethnicity, eight studies reported on education, and no studies differentiated gender from sex. No studies reported on the association between SDoH and intervention effectiveness. We did not identify any economic evaluations. We classified 10 interventions into four categories: non-pharmacologic cognitive strategies (number of studies [n]=16), medications (n=1), non-invasive procedures (n=2), and invasive procedures (n=1). Invasive procedures and non-pharmacologic cognitive strategies had a statistically significant positive effect on cognitive measures in one and seven studies, respectively. Non-invasive procedures (n=2) did not have significant cognitive effects. Use of hypnotics (benzodiazepines and non-benzodiazepines) was significantly associated with a shorter time to incident dementia in one study.

Conclusion

Non-pharmacologic cognitive strategies were the most-studied interventions for improving cognitive outcomes in older adults with TBI. Future research should better integrate a health equity lens and standardize outcome measurement.

Key words: traumatic brain injury (TBI), cognitive dysfunction prevention, intervention research, social determinants of health (SDoH), health equity lens, scoping review, older people, aged, PROGRESS-Plus Framework

INTRODUCTION

According to an 18-year longitudinal study, approximately one million adults in Canada will sustain at least one traumatic brain injury (TBI) in later life (aged 60 and older).(1,2) Cognitive deficits are common after TBI, especially in older adults with age-related cerebral atrophy.(3,4) For example, the incidence of TBI-related delirium in hospitalized adults with TBI is 46.3% to 69.4%.(3,5) In the long term, TBI is associated with a two- to four-fold increased risk of dementia, with impact on daily living activities.(6) It is hypothesized that TBI increases the rate of dementia via the disruption of microtubule function leading to the accumulation of misfolded tau and amyloid proteins, which are commonly found in individuals with Alzheimer's dementia and other dementias.[7] These neurotoxic proteins contribute to neuronal loss, causing neurodegeneration and associated brain atrophy.[8] A post-mortem study showed that TBI can cause neurodegeneration and progressive brain atrophy that continued at least one year after injury.[9]

A wide range of interventions have been studied in a general adult population to prevent or reduce risk of cognitive decline after sustaining a TBI including non-pharmacologic cognitive strategies (e.g., reorientation, cognitive stimulation, cognitive training), medications (e.g., donepezil, memantine, amantadine), and non-surgical (e.g., repetitive transcranial magnetic stimulation, transcranial direct current stimulation [tDCS], low-level laser therapy), and surgical procedures (e.g., burr hole washout, craniotomy).[10] These interventions could mitigate the risk of dementia in individuals who have sustained a TBI by addressing upstream factors such as TBI-related delirium or reducing the rate of cognitive decline.[3,6] However, it is unclear if these interventions are effective in older adults.[11]

Current TBI international guidelines do not provide recommendations for interventions tailored to older adults to improve their cognitive outcomes.[12,13] Older adults with TBI represent a heterogeneous population. Studies of potential interventions to improve cognitive outcomes in this group should account for participants' frailty, and apply a health equity lens to ensure interventions reduce—rather than widen—health disparities.[14–16] Moreover, as these interventions may be resource-intensive and scarce, we should elucidate the association between older adults' social determinants of health (SDoH) and intervention effectiveness to plan equitably for services within health-care systems.[17,18]

Our scoping review's objective was to identify all interventions studied to improve cognitive outcomes in older adults (≥60 years) with TBI. We assessed the reporting of SDoH and association between these SDoH and intervention effectiveness. We reported ancillary data, such as cost or safety, if available. (Please refer to the tables in supplemental materials section Appendix S1–Tables S1 to S5.)

METHODS

We developed our scoping review protocol following the recognized JBI methodology for scoping reviews.[19] We registered our protocol on Open Science Framework (https://osf.io/2hsfa/). We reported our scoping review following the PRISMA Extension for Scoping Reviews (PRISMA-ScR) and Sex and Gender Equity in Research guidelines (in supplemental materials Appendix S2 and Appendix S3).[16,20] We chose a scoping review as it is appropriate to broadly investigate a research area that is complex and heterogeneous to clarify knowledge gaps and identify future research needs.[21]

Search Strategy and Selection Criteria

We conducted a comprehensive search of MEDLINE, EMBASE, Cochrane CENTRAL and Cochrane Database of Systematic Reviews (CDSR), PsycINFO databases, and the grey literature from inception to March 20, 2023. Our search strategy was developed with an experienced information scientist (EU) and peer-reviewed by a second scientist (JM) using the Peer Review of Electronic Search Strategies checklist.[22] We did not place restrictions on publication year, status or language. The final MEDLINE search strategy can be found in Appendix S4 in the supplemental material. We identified grey literature using the Canada's Drug Agency's Grey Matters Guide (Appendix S5 in the supplemental material).[23] We searched for unpublished and ongoing trials at clinicaltrials.gov using the terms "traumatic brain injury", "cognition" and "intervention". We hand-searched references of included studies and reviews in the literature.

We included studies that assessed interventions to improve cognitive outcomes in older adults with TBI. Our population of interest was older adults (≥60 years) with TBI with or without cognitive impairment (delirium, mild cognitive impairment, dementia) as defined by study authors (e.g., clinician using Diagnostic and Statistical Manual criteria). We limited our review to studies including older adults, as previous reviews on this topic did not report on this population. Studies had to contain at least one cognitive outcome with pre-and-post assessments or a comparator group; potential outcomes included cognitive deficit or performance description, subtotal or global cognitive scale, or cognitive impairment diagnosis.[24]

We included non-pharmacologic cognitive strategies (such as those used in persons with dementia), and pharmacologic or procedural (non-surgical or surgical) interventions to improve cognitive outcomes.[25] While no guidelines exist to classify interventions within the non-pharmacologic cognitive strategies, we followed a framework established by previous Cochrane reviews.[24,25] Non-pharmacologic cognitive strategies studies are further categorized into cognitive stimulation, training, and rehabilitation.[26,27] We define cognitive stimulation as unstructured or socially engaging activities aimed at enhancing overall cognitive and social functioning.[24,26] Cognitive training refers to standardized tasks, often computer-based or therapist-led, that target specific cognitive domains such as memory, attention, or processing speed.[26,27] Cognitive rehabilitation involves personalized, goal-oriented interventions tailored to the individual's functional needs, often delivered by a trained therapist.[26,28,29,30] We did not exclude studies based on the setting or location where the interventions were delivered. Eligible study designs included quantitative studies such as interventional studies (randomized, crossover randomized or non-randomized trials, pre-post studies), observational studies (cohort, cross-sectional and case-control studies).

Protocol Deviation

We initially limited our search to studies enrolling participants of 60 years and older with mean age of 65 years and older, based on the Centres for Disease Control and Prevention definition.[31] However, we revised it to include studies with a mean age of 60 years or above, or with any subgroup of participants older than 60 years with diagnosis of TBI, following the threshold for "older persons" defined by United Nations.[32] We made this amendment during the screening process, given few studies met the initial, stricter age criterion.

Data Screening

The screening criteria were established a priori and calibrated amongst the team (YQH, HH, SW, PH) with a pilot-test on a random sample of 50 articles. After more than 95% inter-rater agreement was established, pairs of reviewers screened the titles and abstracts independently, and all discrepancies were resolved by a third reviewer (JAW). The same process was followed when screening potentially relevant full-text articles. All levels of screening were performed using our proprietary online tool, Synthesi.SR.[33]

Data Extraction and Synthesis

Two independent reviewers (YQH and either HH or SW) abstracted: (i) study characteristics (author name, study design, country, publication year, sample size and study duration); (ii) patient characteristics (age, SDoH using the place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status, and social capital [PROGRESS]-Plus framework as SDoH defined by the World Health Organization, comorbidities, and frailty); (iii) intervention characteristics (setting, duration, timing, facilitator, assessor, and mode of delivery) following the Template for Intervention Description and Replication (TIDieR) checklist; and (iv) cognitive outcomes (e.g., rate of delirium or dementia, time to emergence out of delirium, severity of dementia, cognitive testing scores, and time to behavioural symptoms of dementia).[34,35] Two reviewers (YQH and either HH or SW) charted independently the included studies, following a pre-tested data charting form (Appendix S6 in the supplemental material). To determine the mean age of participants, we calculated the mean of reported means weighted by study sample sizes.

RESULTS

Literature Search

We included 20 studies after screening 14,251 unique titles and abstracts and 680 full-text articles (Figure 1).

Study Characteristics

Sample sizes ranged from nine to 18,413 people with a median sample size of 35 (Table 1, and Appendix S1–Table S1 in the supplemental material). Publication years ranged from 1992 to 2021.[36,37] Studies were pre-post (6/20, 30%) design, retrospective cohort studies (6/20, 30%), randomized trials (6/20, 30%), and prospective cohort studies (2/20, 10%). Three studies

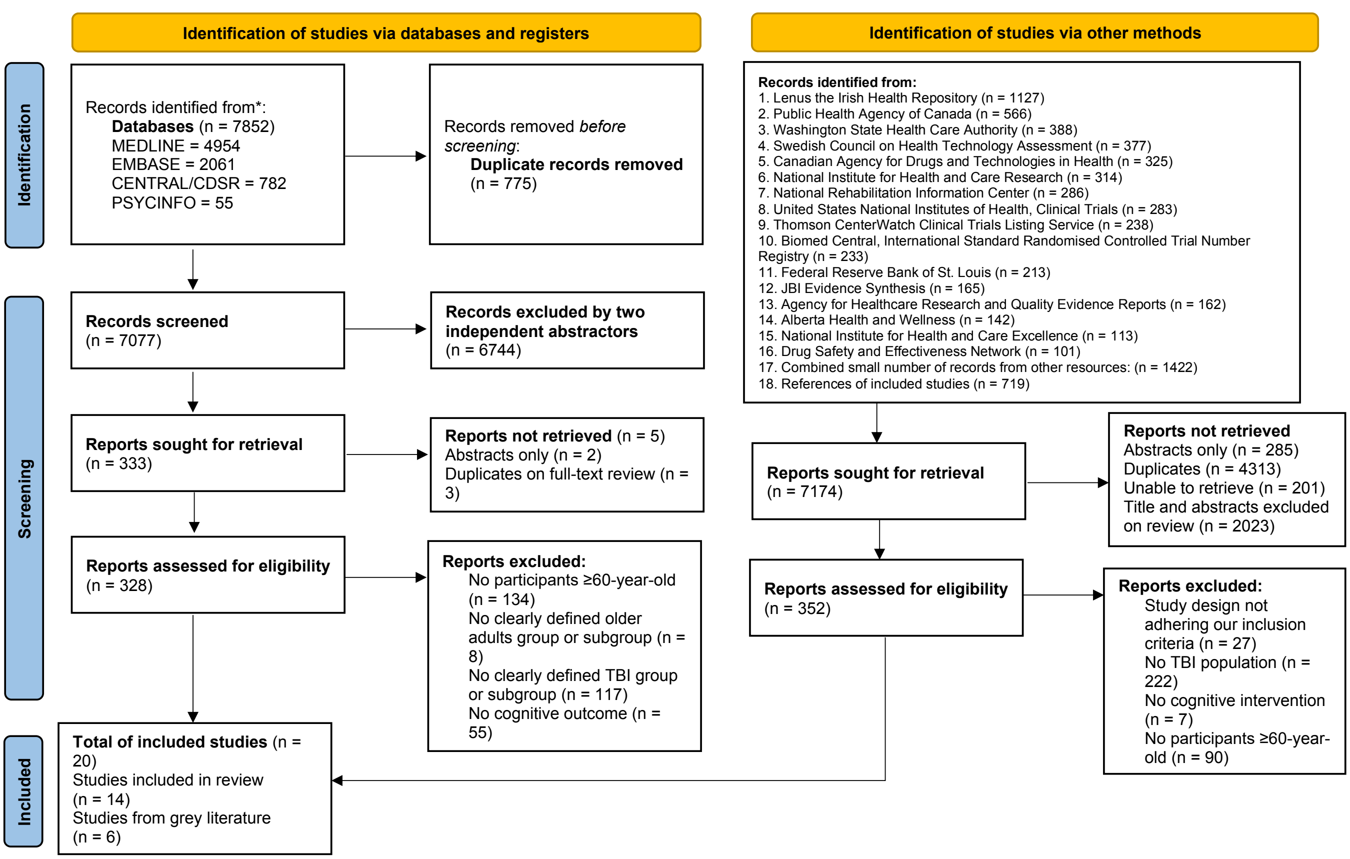

FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram

did not report follow-up timing.[38–40] The shortest follow-up period was 24 hours and the longest was nine years.[41,42] Studies assessing non-surgical and surgical procedures were from East Asia (South Korea and Japan) (Figure 2). Across included studies, 51 unique cognitive outcome measures were used. The most common scales were the cognitive subscale of Functional

TABLE 1 (part 1 of 2).
Characteristics of studies included in this scoping review describing interventions to improve cognitive outcomes in older adults with traumatic brain injury (further details can be found in Appendix S1, Tables S1 and S2 in the supplemental material)

	Non-Pharmacologic Interventions (N=16)	*Pharmacologic Interventions (N=1)*	*Non-Surgical Neuromodulation and Surgical Interventions (N=3)*	*All Interventions (N=20)*
Participant Characteristics				
Total number of participants	38534	5960	55	44549
Mean age (years)	65.5	55	66.5	65.9
Female (mean %)	40.4	49.3	30.4	41.5
Reporting of PROGRESS-PLUS Factors (social determinants of health [SDoH], number of studies reporting SDoH; mean % when available)				
Ethnic or racial minorities (number of studies; mean %)	4/16; 30.3 (ethnic) / 22.2 (racial) minorities	NR	NR	4/20; 30.3 (ethnic) / 22.2 (racial) minorities
Language used (number of studies) English French Other	English – 2/16; NR English or French – 3/16; NR Other – NR	NR	NR	English – 2/20; NR English or French – 3/20; NR Other – NR
Religion (number of studies; mean %)	NR	NR	NR	NR
Education (number of studies) Less than grade 12 (mean %) Grade 12 or above (mean %)	8/16; Less than grade 12 – 37.9 Grade 12 or above – 62.1	NR	NR	8/20 Less than grade 12 – 37.9 Grade 12 or above – 62.1
Occupation (number of studies; mean %)	NR	NR	NR	NR
Annual income (mean %)	NR	NR	NR	NR
Socioeconomic status (mean %)	NR	NR	NR	NR
Place of residence (number of studies)	3/16	NR	NR	3/20
Comorbidities (number of studies)	5/16;	NR	1/3	6/20
Frailty (number of studies) No frailty Mild frailty Moderate frailty Severe frailty	NR	NR	NR	NR
Study Characteristics				
Location (number of studies) North America Europe East Asia	N. Am. – 11/16 Europe – 3/16 East Asia – 2/16	N. Am. – 0 Europe – 0 East Asia – 1/1	N. Am. – 0 Europe – 0 East Asia – 3/3	N. Am. – 11/20 Europe – 3/20 East Asia – 6/20
Publication year (number of studies) 1990-2007 2007-2023	1990-2007 – 5/16 2007-2023 – 11/16	1990-2007 – 0 2007-2023 – 1/1	1990-2007 – 1/3 2007-2023 – 2/3	1990-2007 – 6/20 2007-2023 – 14/20

TABLE 1 (part 2 of 2).
Characteristics of studies included in this scoping review describing interventions to improve cognitive outcomes in older adults with traumatic brain injury (further details can be found in Appendix S1, Tables S1 and S2 in the supplemental material)

	Non-Pharmacologic Interventions (N=16)	*Pharmacologic Interventions (N=1)*	*Non-Surgical Neuromodulation and Surgical Interventions (N=3)*	*All Interventions (N=20)*
Setting (mean %)				
Inpatient rehabilitation	Inpatient rehabil. – 6/16	Inpatient rehabil. – 0/1	Inpatient rehabil. – 0/3	Inpatient rehabil. – 6/20
Outpatient rehabilitation	Outpatient rehabil. – 6/16	Outpatient rehabil. – 0/1	Outpatient rehabil. – 0/3	Outpatient rehabil. – 6/20
Acute care (ED, ICU, wards)	Acute care – 1/16	Acute care – 0/1	Acute care – 2/3	Acute care – 3/20
Community-based day program	Community-based day program –1/16 Outpatient specialized clinic –1/16	Community-based day program – 0/1	Community-based day program – 0/3	Community-based day program –1/20 Outpatient specialized clinic –1/20
Home	Home – 1/16 Other/NR – 0/16	Home – 0/1 Other/NR – 1/1	Home – 0/3 Other/NR – 1/3	Home – 1/20 Other/NR – 2/20
Mechanism of injury (number of studies; mean %) Falls MVCs Assault	3/16; Falls – 33.6 MVCs – 56.4 Assault – 10	NR	1/3; Falls – 50 MVCs – 50 Assault – 0	4/20; Falls – 41.8 MVCs – 53.4 Assault – 4.8

MVCs = mental or personality disorder; NA = not applicable; NR = not reported.

Independence Measure (FIM) (number of studies [n]=5), Mini Mental State Examination (MMSE) (n=4), Trail Making Test (TMT) (Trails A and B, Trails A or Trails B) (n=4), and Dementia Rating Scale (n=3) (Table 2, and Appendix S1–Table S2 in the supplemental material). Out of 20 included studies, nine studies reported cognitive scores and functional status scales (e.g., assessment of activities of daily living (ADLs) or disability rating). We contacted nine corresponding authors to clarify study details; one provided additional information specific to the older adult subgroup.[38]

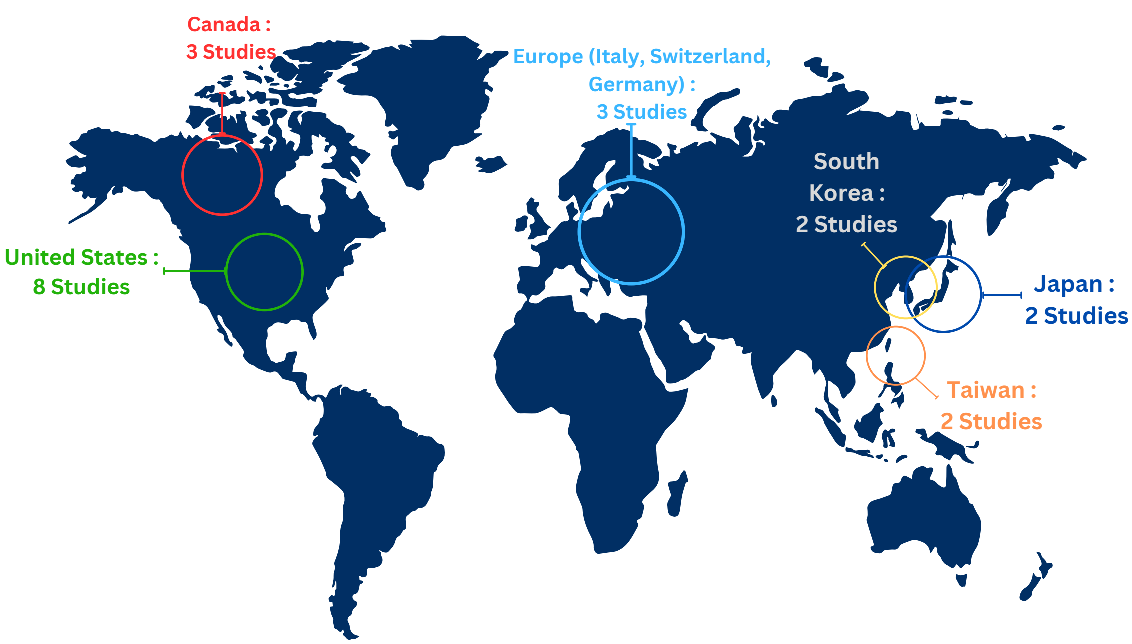

FIGURE 2. Geographic locations of included studies

TABLE 2 (part 1 of 3).
Intervention characteristics and diagnostic tools for measuring cognitive deficits or concerns in traumatic brain injury r eported in this scoping review (further details can be found in Appendix S1, Table S3 to Table S5 in the supplemental material)

First Author, Year, Country	*Intervention Description*	*TBI Diagnosis Tool*	*Participants' TBI Severity [Mean (SD)] or [Mean [95% CI]]*	*TBI Severity Measurement Tool (I.E. GCS Severity, PTA Duration)*	*Cognitive Deficit or Concern Diagnosis Tool*	*Time Since Injury*
			Non-Pharmacologic Interventions			
Whitlock, 1992, United States[36]	Acute inpatient rehabilitation (before vs after)	NR	Admission GCS score (1 older adult) = 7	GCS score	FIM; GOS; RLAS;	26 days to admission from injury
Cifu, 1996, United States[39]	Comprehensive inpatient rehabilitation program (before vs after)	NR	PTA duration = 40% of older adults' sample with unknown PTA duration, 8% with 0 days, 52% with PTA and mean duration of 45.4 days; Mean (SD) admission GCS score = 10.1 (3.9) 6% had increased intracranial pressure	PTA duration, mean admission GCS score, ICP	Disability Rating Scale, FIM, RLAS	Within 8 hours of injury
Prigatano, 1999, United States[50]	Inpatient neuro-rehabilitation (before vs after)	NR	Admitting GCS score (number of participants with score ranges): 3-8 (n=5); 9-12 (n=2); 13 to 15 (n=2).	GCS score	BNIS	NR
De Guise, 2005, Canada[53]	Integrated reality orientation program vs. usual care	A positive finding on medical imaging of the head, viewed by a radiologist, was sufficient to confirm the diagnosis of TBI	Intervention (GCS) = 9.7 (3.7) Control (GCS) = 9.2 (3.7)	GCS score	GOAT	On current hospital admission, TBI was diagnosed by ED physician or admitting physician
Frankel, 2006, United States[51]	Comprehensive inpatient rehabilitation program (before vs after)	NR	NR	Length of coma, admission, GCS score, incidence of ICP complications	DRS, FIM	NR
Graham, 2010, United States[55]	Inpatient rehabilitation program (before vs after)	Uniform Data System for Medical Rehabilitation Impairment Group Codes 02.21 and 02.22	NR	NR	FIM cognitive subscale	NR

TABLE 2 (part 2 of 3).
Intervention characteristics and diagnostic tools for measuring cognitive deficits or concerns in traumatic brain injury r
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First Author, Year, Country	*Intervention Description*	*TBI Diagnosis Tool*	*Participants' TBI Severity [Mean (SD)] or [Mean [95% CI]]*	*TBI Severity Measurement Tool (I.E. GCS Severity, PTA Duration)*	*Cognitive Deficit or Concern Diagnosis Tool*	*Time Since Injury*
Non-Pharmacologic Interventions (continued)						
Chen, 2011, United States[40]	Goal-directed attention regulation training vs brief education	NR	NR	NR	Attention and executive function: LNS from WAIS, Auditory Consonant Trigrams, DVT, DVFS, Trails B, Stroop Inhibition/ Switching; Learning and memory: HVLT, BVMTR; Motor speed of processing: Trails A test, Visual Attention Task	≥6 months from TBI
Burkard, 2014, Switzerland[49]	Implementation intention training vs usual care	NR	NR	NR	MMSE, DRS, Semi-ecological event-based PM tasks, SRT, 1-item PM measure,	NR
Li, 2015, United States[45]	Computer-based cognitive retraining vs. usual care	NR	NR	NR	MoCA version 7.1 (pre-test), MoCA version 7.2 (posttest), medication-box sorting task to test daily living activities	At least 1 year before study enrollment
Spagnolo, 2015, Italy[47]	Cognitive stimulation vs. usual care	NR	NR	NR	MMSE, Basic ADL, IADL	NR
Howrey, 2017, United States[52]	Inpatient rehabilitation vs. usual care	NR	NR	NR	Cognitive FIM	Mean in days ± SD: 18.51± 27.43
Hwang, 2020, Taiwan[48]	Computerized cognitive training vs. Tai Chi vs usual care	ICD-10 diagnosis codes S02.0-S02.1 and S06.0-S02.9	> 80% sustained a mild TBI; Mean GCS score: CCT = 11.3 ± 8.7; TC = 11.0 ± 7.0; Usual care = 11.0 ± 9.2	GCS, loss of consciousness, positive CT scan findings	MDRS, MMSE, TICS-M, TMT	Mean in months ± SD: CCT = 4.4 ± 5.5; TC = 3.1 ± 4.1; Usual care = 3.0 ± 4.5
Cisneros, 2021, Canada[44]	Multimodal cognitive training vs. usual care	World Health Organization criteria	Mild TBI = 6; Complicated Mild = 8; Moderate = 3; Severe = 4	LOC length, GCS score, brain imaging, PTA duration	Face-name association, Word list recall, Text memory measures, SEMQ, PGWBI	Mean in days ± SD: Intervention = 595.75 ± 926.67; Control = 859.33 ± 772.04
Cisneros, 2021, Canada[43]	Multimodal cognitive training vs. usual care	World Health Organization criteria	Mild TBI = 6; Complicated Mild = 8; Moderate = 3; Severe = 4	LOC length, GCS score, brain imaging, PTA duration	SET-A, D-KEFS Sorting test and Stroop four-color version, DEX	Mean in days ± SD: Intervention = 595.75 ± 926.67; Control = 859.33 ± 772.04

TABLE 2 (part 3 of 3).
Intervention characteristics and diagnostic tools for measuring cognitive deficits or concerns in traumatic brain injury r
eported in this scoping review (further details can be found in Appendix S1, Table S3 to Table S5 in the supplemental material)

First Author, Year, Country	*Intervention Description*	*TBI Diagnosis Tool*	*Participants' TBI Severity [Mean (SD)] or [Mean [95% CI]]*	*TBI Severity Measurement Tool (I.E. GCS Severity, PTA Duration)*	*Cognitive Deficit or Concern Diagnosis Tool*	*Time Since Injury*
			Non-Pharmacologic Interventions (continued)			
Oleszkiewicz, 2022, Germany[38]	Intensive (higher frequency) olfactory intervention vs. standard intensity olfactory intervention	NR	NR	NR	MoCA, COWAT, SFT	NR
Kim, 2021, South Korea[37]	Therapist-driven cognitive training vs. computerized cognitive training	Neuroimaging and clinical data	NR	NR	MMSE, CDRS	Mean in days ± SD: 25.1 ± 18.1
			Pharmacologic Interventions			
Chiu, 2015 Taiwan[42]	Hypnotics (benzodiazepines and non-benzodiazepines sleeping aids) use vs. no use	ICD-9 diagnosis codes	Not available in administrative databases	ICU admission is used as an indicator of TBI severity: 101 patients admitted to ICU	Dementia diagnosis (from ICD-9 diagnosis codes)	NR
			Surgical and Non-Surgical Neuromodulation Interventions			
Ishikawa, 2002, Japan[54]	Burr hole irrigation vs. usual care	NR	NR	NR	MMSE, HDS-R, ADL	Mean in days: 84
Kang, 2012, South Korea[41]	Transcranial direct current stimulation of the left prefrontal cortex vs. sham stimulation	NR	NR	NR	CCRTT	In older adults group mean in days ± SD: 145.54 ± 72.03
Inagawa, 2019, Japan[46]	Transcranial direct current stimulation vs. sham stimulation	NR	NR	NR	MMSE, ADAS-Cog, FAB, CDR-J	NR

ABI = Acquired Brain Injury; ADAS-Cog = Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADL = Activity of Daily Living; BNIS = Barrow Neurological Institute Screen for Higher Cerebral Functions; BNT = Boston Naming Test; BVMTR = Brief Visual Memory Test Revised; CCRTT = computerized contrast reaction time task; CDR-J = Clinical Dementia Rating-Japanese version; CDRS = Clinical Dementia Rating Scale; COWAT = Controlled Oral Word Association Test; CT = computed tomography; DEX = Dysexecutive Questionnaire; D-KEFS = Delis-Kaplan Executive Function System; DRS = Dementia Rating Scale; DVFS = Design and Verbal Fluency Switching; DVT = Digit Vigilance Test; ED = Emergency department; FAB = Frontal Assessment Battery; FIM = Functional Independence Measure; HDS-R = Hasegawa Dementia Scale–Revised; HVLT = Hopkins Verbal Learning Test; IADL = Instrumental Activity of Daily Living; ICD = International Classification of Diseases; ICP = Intracranial Pressure; ICU = Intensive Care Unit; GCS = Glasgow Coma Scale; GOAT = Galveston Orientation and Amnesia Test; GOS = Glasgow Outcome Scale; LOC = Level of Consciousness; LNS = Letter Number Sequencing; MoCA = Montreal Cognitive Assessment; MDRS = Mattis Dementia Rating Scale; MMSE = Mini-Mental State Examination; NIDRR = National Institute on Disability and Rehabilitation Research; NA = Not Applicable; NR = Not Reported; PGWBI = Psychological General Well-Being Index; PM = Prospective memory; PTA = Post Traumatic Amnesia; RLAS = Rancho Los Amigos Levels of Cognitive Functioning Scale; SD = Standard Deviation; SEMQ = Self-Evaluation Memory Questionnaire; SET-A = Six Elements Task-Adapted; SFT = Semantic fluency test; SRT = Selective Reminding Test; TBI = Traumatic brain injury; TBIMS = Traumatic Brain Injury Model Systems; TDI = combined Sniffin' Sticks score for Threshold, Discrimination and Identification; TICS-M = Telephone Interview for Cognitive Status; TMT = Trail Making Test; WAIS = Wechsler Adult Intelligence Scale.

Participants

A total of 44,549 participants were included with a mean age of 65.9 years (Table 1). Five studies selected patients who had mild-to-moderate cognitive impairment.[37,43–46] Thirty percent of studies reported on participants' comorbidities, and no studies reported on their frailty.

Participants' PROGRESS-PLUS Variables

Place of residence: Three of 20 studies reported participants' place of residence. *Race/ethnicity/culture/language:* Three studies (15%) reported on race and their participants were predominantly White (77.8%). One study reported that 30% of participants were ethnic minorities. Five studies (26.3%) reported on the language used to conduct interventions; fluency in English or French was a participant selection criterion in these studies, especially in studies involving cognitive training.

Occupation/religion/social capital: No studies reported on occupation, religion or social capital. *Gender/sex:* No studies differentiated gender from sex. Study participants were predominantly men/male (65%). *Education:* Eight studies (59.6%) reported on the level of education. Mean years of education was 12.5, or completion of high school. *Additional PROGRESS-PLUS variables:* There were no additional variables reported such as disability and time-dependent relationships. *Association:* No studies reported on the association of PROGRESS-PLUS variables and intervention effectiveness.

Setting and Caregiver Engagement

Studies took place in an outpatient (6/20) or inpatient rehabilitation program (6/20), acute care hospital (3/20), outpatient clinic (1/20), community-based day program (1/20) or participants' home (1/20). Two studies did not report the intervention setting. One study involved caregiver participation and training, and one study was conducted in the participants' home in the presence of caregivers.[47,48]

Cause of TBI, TBI Severity Markers, and TBI Severity

Eighty percent of studies did not report the cause of TBI. The most prevalently reported mechanism of injury was related to motor vehicle collisions. Overall, the mean Glasgow Coma Scale (GCS) score was 11/15 (moderate TBI severity) in eight studies that reported participants' TBI severity.

Interventions to Improve Cognitive Outcomes in Older Adults with TBI

Sixteen studies described non-pharmacologic cognitive strategies, one assessed the effects of hypnotics, and three assessed non-surgical and surgical procedures. Eleven of 20 studies (55%) reported on intervention providers, which included most frequently interdisciplinary staff (nurses, physicians, physical, occupational and recreational therapists, speech language pathologists, psychologists). Within subcategories of non-pharmacologic cognitive strategies, intervention onset timing ranged from eight hours to more than one year after TBI. Similarly, session duration was variable from 30 seconds to two hours, with frequency of eight to 45 sessions.

Non-Pharmacologic Cognitive Strategies

The most studied non-pharmacologic strategy was cognitive training (7/16), followed by rehabilitation programs without description of the cognitive activity (6/16), and cognitive stimulation (3/16) (Figure 3). Three cognitive training strategies involved use of computer-based programs (Parrot [necessitated Internet use] and RehaCom) to train domains such as attention, memory, processing speed, and executive functioning.[37,45,48] These were compared to non-computerized, therapist-led cognitive training interventions, such as Tai Chi, goal-directed attention regulation, prospective memory training, and multimodal approaches (e.g., problem-solving, goal management training, self-awareness strategies) delivered by neuropsychologists.[40,43,44,49] Within six studies on rehabilitation programs, one study's primary outcome was treatment goal attainment such as self-care (completion of basic ADLs) and communication.[50] The remaining five studies on cognitive rehabilitation reported improvements in global cognition or functional status, but provided limited detail on the specific cognitive tasks or therapeutic components involved.[7,36,39,51,52] The cognitive stimulation strategies were reality orientation, "3R program" with reality orientation, reminiscence and remotivation, or olfactory training through the medium of an electrical odour dispenser.[38,47,53]

Pharmacologic Interventions, Non-Surgical and Surgical Procedures

One study assessing hypnotics captured use of benzodiazepines and non-benzodiazepines via a medical claims database.[42] In this study, the authors did not specify which medications were used. Two studies compared tDCS of the left dorsolateral prefrontal cortex to sham stimulation.[41,46] Both studies applied two milliamp (mA) for 20 minutes per session. While Kang *et al*. measured outcomes after one session, Inagawa *et al*. tested feasibility of 10 sessions (two sessions per day for five consecutive days).[41,46] Burr hole irrigation with closed system drainage was the surgical intervention studied for evacuating blood products in older patients with TBI and chronic subdural hematoma.[54]

Outcomes and direction of effect of interventions are summarized in Appendix S1– Table S4 in the supplemental material. Within non-pharmacologic interventions, no studies (n=3) assessing cognitive stimulation interventions (reorientation, 3R program, olfactory stimulation) demonstrated statistically significant effects.[38,47,53] Six of seven (85.7%) studies on cognitive training strategies showed statistically significant positive results; these strategies were goals-directed attention regulation (n=1), computer-based (n=2), multimodal (n=2), and therapist-driven (n=1) cognitive trainings.[37,40,43–45,48,49] All (16.7%) studies (n=6) on rehabilitation showed positive effects; [36,39,50–52,55] one study — Howrey *et al*.[52] — investigated statistical power and showed positive statistically significant results. Study on medications (n=1) showed that hypnotics statistically significant decreased

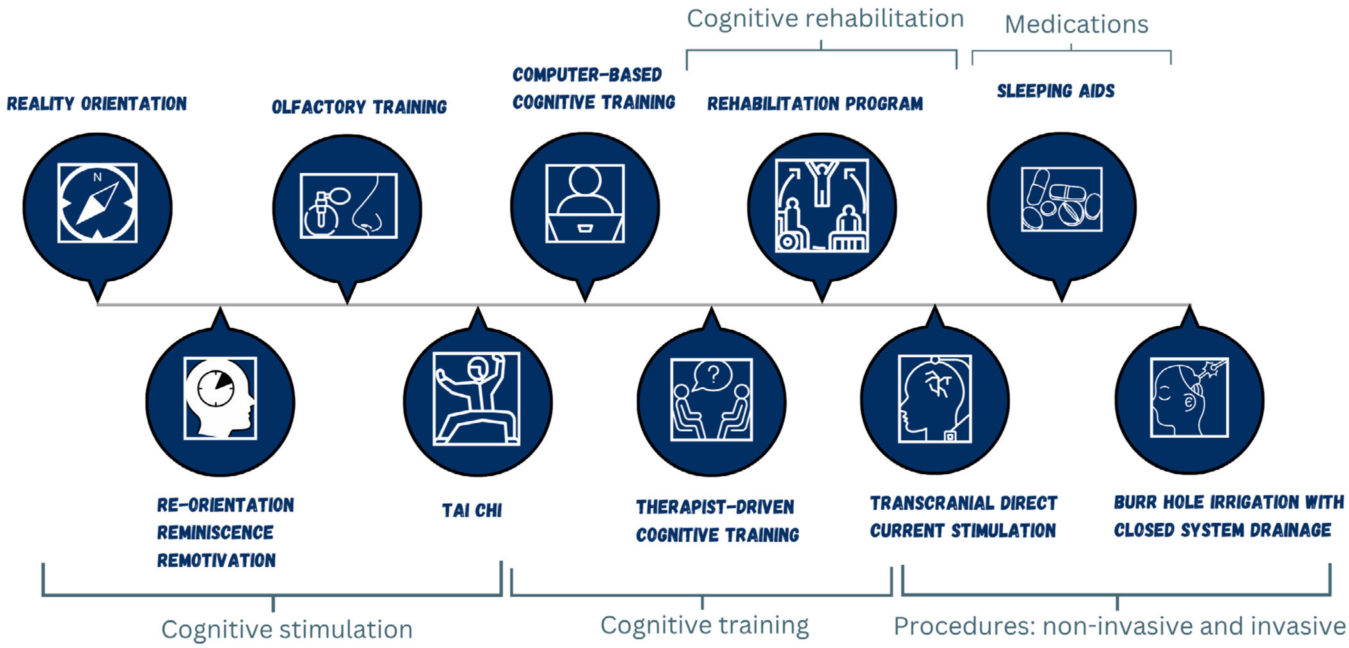

FIGURE 3. Interventions to prevent cognitive decline in older adults with traumatic brain injury identified in scoping review

dementia-free survival time.[42] Studies on tDCS (n=2) did not yield positive statistically significant results, but burr hole irrigation (n=1) led statistically significant positive effects on cognitive scores.[41,46,54]

Ancillary Outcomes

Additional outcomes from studies included length of stay, cost of care, number of treatment goals attained, discharge disposition, hematoma size with or without midline shift, olfactory function, sleep quality, perceived level of attention, fatigue and task difficulty, caregiver distress and attrition rate as a surrogate marker for safety and feasibility (Appendix S1–Table S4 in the supplemental material). Two studies reported safety outcomes for tDCS; one study had safety and feasibility as a primary outcome (Appendix S1–Table S5 in the supplemental material).[41,46] There were no serious adverse events or statistically significant differences in mild reaction symptoms (e.g., headache, neck pain) between treatment and control groups.

DISCUSSION

Our scoping review was the first knowledge synthesis that comprehensively identified the breadth of interventions studied to improve cognitive outcomes in older adults with TBI across all care settings. We found 20 studies focused on older adults with TBI. Included studies infrequently reported details on intervention delivery such as timing, duration, and frequency. Further, many outcome measures were used across studies within the same intervention categories, indicating the need for standardized outcome measures. Studies seldom reported participants' comorbidities, frailty or SDoH. Within studies on non-pharmacologic cognitive strategies (16 studies), most of those assessing cognitive training (six out of seven studies) were positive and reached statistical significance positive effects; those assessing cognitive stimulation and rehabilitation found positive results, but were not significant or analyzed statistically. Sleep-inducing medications were shown to impact adversely cognition. Studies on non-surgical procedures (tDCS) did not demonstrate significant effects, but one study on surgical procedure (burr hole irrigation) yielded significant improvement of cognitive function. Few studies on rehabilitation and tDCS reported on cost or safety.

Despite older adults being the population with the highest risk of sustaining TBI, we found only 20 studies meeting our review eligibility criteria, which covered many different interventions, outcomes, and care settings.[56] Previous scoping or systematic reviews assessed cognitive strategies in adults with TBI, but did not report specifically on older adults, highlighting a knowledge gap.[57–60] Because older adults are often excluded from the evaluation of TBI interventions, international guidelines do not offer guidance to clinicians for optimizing cognitive outcomes in older adults with TBI.[12,61] In addition, previous reviews on this topic have not assessed SDoH, or association between SDoH and outcomes. SDoH are factors produced by structural, social, economic, and political mechanisms that affect health outcomes.[62] SDoH are associated with access to—and utilization of—specialized services in general.[63] We found that few included studies in this review reported SDoH. If researchers use administrative data (which seven [35%] studies did in our review), patient-level factors like SDoH may not be adequately captured within administrative databases. When considering future TBI research—intervention studies and reviews—researchers should use a health equity lens, and consider the SDoH and their association with intervention effectiveness such as cognitive outcomes, especially as SDoH are known effect modifiers.[64–66]

In our scoping review, studies did not differentiate gender from sex and study participants were predominantly men or male. While there are sex differences related to outcomes following TBI (e.g., higher mortality and morbidity in females), there is no sex-related rationale for studies to capture more males than females.[67] It is possible that more men/male are included, as they get hospitalized more than women/females for TBI, especially in middle-aged to early older adulthood (e.g., 55- to 75-year-old; mean age found in our review was 65.9-year-old) due to motor vehicle collisions or sports-related injuries.[68] A recently published longitudinal cohort study of community-dwelling older adults (≥65 years) show a higher TBI incidence in older women than men.[1]

Moreover, most participants in our review had a high school level education. This is most likely associated with the higher likelihood of more educated individuals to seek care, at least in those experience falls, which is the most common cause of TBI in older adults. This is reflective of volunteer bias, which is comparable to prior work and further emphasized when participants are recruited from specialized-care clinics or programs and academic centers (the case for most participants in our review) with an entry barrier.[1,69] Future studies should consider using various individual and public methods of recruitment such as referrals or advertisements, and establishing contact with community organizations.[70] Evaluating SDoH and their association with access to interventions in older adults with TBI is an area for further study.

Across non-pharmacologic cognitive strategies, components of intervention delivery (timing, frequency, duration, follow-up, facilitators) and assessment (outcome scales and outcome assessors) were highly variable (e.g., hours to months, no reporting of facilitator, numerous different outcome scales used or non-blinded outcome assessor). Indeed, more than 50 unique outcome measures were reported in included studies. This wide variability in cognitive outcome measures poses a substantial challenge to evidence synthesis and cross-study comparisons, and reflects the absence of consensus on which cognitive domains are most relevant or sensitive to change in older adults following TBI.[71] As a result, it is difficult to determine whether observed differences in intervention effectiveness reflect true differences in outcomes or inconsistencies in measurement approaches. This lack of standardization also limits the feasibility of meta-analyses and the development of clinical practice guidelines. Numerous cognitive outcome measures exist, and current guidelines recommend using a battery of validated tests to comprehensively assess all cognitive domains, without endorsing any single preferred instrument.[12] Examples of commonly used multidomain cognitive screening tools include the Montreal Cognitive Assessment, the Mini-Mental State Examination, and the Addenbrooke's Cognitive Examination.[72] Studies on rehabilitation had a focus on participants' functional status prior and post the intervention, but other categories of interventions rarely included functional outcomes such as performing instrumental ADLs. It will be critical to incorporate older adults' functional history or functional assessment when conducting studies of these interventions and implementing them in clinical practice.[73] Furthermore, comparable to studies included in reviews of interventions for younger adults and guidelines on TBI management, no study included in our review investigated adjustment of intervention frequency, duration or difficulty based on the degree cognitive impairment or TBI severity.[12,25,58] This is a gap, as pre-existing cognitive impairment and TBI severity are confounding variables and should be accounted for in statistical models evaluating intervention effect sizes.[71,74] Overall, our review found a paucity of standardization on timing, frequency or facilitators of the interventions, or stratification of interventions depending on TBI severity. Studies to develop and validate core outcome measures in older adults with TBI are needed for future studies on interventions.[75] Future research on interventions that improve cognitive outcomes in those with TBI should implement a checklist such as the TIDieR or the Guidance for reporting intervention development studies in health research (GUIDED) checklists for reporting to ensure transparent and accurate reporting of interventions to facilitate replication.[35,76]

Limitations

Our findings have potential limitations. Initially, we planned to include studies with clearly defined subgroups of adults with a mean age ≥65 years.[31] However, we subsequently broadened this criterion to include studies with subgroups reporting a mean age ≥60 years and ultimately included any studies with participants aged ≥60 years. This protocol amendment was made as the literature in older adults was sparse. Although this change may have introduced heterogeneity in baseline cognitive risk, we consistently applied the revised age criterion during screening and data extraction.[32] Second, we categorized interventions within non-pharmacologic cognitive strategies following a framework presented in previous literature, but due to limited reporting of interventions such as the exact cognitive tasks completed, readers should remain cautious to findings at the category-level. For example, studies on cognitive rehabilitation reported few intervention details. As we narrowed our search to studies with at least a cognitive outcome, our findings may not be applicable to older adults with TBI who present with neuropsychiatric symptoms. Lastly, as illustrated by our equity analyses following the PROGRESS-Plus framework, the applicability of these interventions is limited as studies lacked diverse and older adults with frailty representation.

CONCLUSIONS

Our review synthesized studies reporting on interventions to improve cognitive decline in older adults with TBI. Cognitive training strategies were the most-studied interventions for improving cognitive outcomes in older adults with TBI. Limited studies reported on cost and safety. More older adults should be included in studies investigating interventions to improve cognitive outcomes in those with TBI because they represent the population most in need and those who could derive the most benefit. Older adults are heterogeneous and have different care needs and goals than younger adults. Without representation of diverse older adults, generalizability and application of research findings on these interventions will be significantly affected. Clinically, our findings suggest that structured cognitive training, especially goal-directed, multimodal, and therapist-led programs, may be prioritized in post-acute care and rehabilitation settings where older adults with TBI are treated. Standardizing cognitive outcome assessments in these settings could also support clinical decision-making, facilitate communication across care teams, and guide timely referral to specialized cognitive rehabilitation services. Further research is warranted on the standardization of intervention delivery and assessment to allow clinical guidelines and policymakers to provide evidence-based and equitable care to older adults with TBI.

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CONFLICT OF INTEREST DISCLOSURES

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SUPPLEMENTAL MATERIALS

Supplemental material linked to the online version of the paper (https://doi.org/10.5770/cgj.28.868):

- **Appendix S1:** Result tables: Table S1 to Table S5
- **Appendix S2:** Preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews (PRISMA-SCR) checklist
- **Appendix S3:** Sex and gender equity in research
- **Appendix S4:** Medline search strategy
- **Appendix S5:** Grey literature search
- **Appendix S6:** Pre-tested data charting form

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