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REVIEW ARTICLE

Update on the Efficacy of Cognitive Rehabilitation After Moderate to Severe Traumatic Brain Injury: A Scoping Review



Adeline Julien, MSc,^{a,b} Lola Danet, PhD,^{a,b} Mallaury Loisel, MSc,^b David Brauge, MD,^{b,c} Jérémie Pariente, MD, PhD,^{a,b} Patrice Péran, PhD,^b Mélanie Planton, PhD^{a,b}

From the ^aDepartment of Neurology, Toulouse University Hospital, Toulouse, France; ^bToulouse Neuroimaging Center, Université de Toulouse, Inserm, UPS, Toulouse, France; and ^cUniversity Sports Clinic, Toulouse University Hospital, Toulouse, France.

Abstract

Objectives: To identify, categorize, and analyze the methodological issues of cognitive rehabilitation of patients with moderate to severe traumatic brain injury and its efficacy.

Data Sources: Pubmed and PsycINFO were searched for studies published between 2015 and 2021 using keywords for cognitive intervention and traumatic brain injury.

Study Selection: Two independent reviewers selected articles concerning cognitive rehabilitation for adults with traumatic brain injury. Of 458 studies, 97 full-text articles were assessed and 46 met the inclusion criteria.

Data Extraction: Data were analyzed by 1 reviewer according to criteria concerning the methodological quality of studies.

Data Synthesis: Results showed a large scope of 7 cognitive domains targeted by interventions, delivered mostly in individual sessions (83%) with an integrative cognitive approach (48%). Neuroimaging tools as a measure of outcome remained scarce, featuring in only 20% of studies. Forty-three studies reported significant effects of cognitive rehabilitation, among which 7 fulfilled a high methodological level of evidence.

Conclusions: Advances and shortcomings in cognitive rehabilitation have both been highlighted and led us to develop methodological key points for future studies. The choice of outcome measures, the selection of control interventions, and the use of combined rehabilitation should be investigated in further studies.

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Cognitive disorders after a traumatic brain injury (TBI) have been well described in recent decades. Long-term memory, attention, processing speed, executive functions, and self-awareness disorders are frequent and related to the high frequency of temporal and frontal lesions. Cognitive sequelae commonly persist several years after a moderate to severe TBI, affecting vocational integration and quality of life. Cognitive rehabilitation aims to decrease acquired neurocognitive impairment and disability using various and complementary approaches. Interventions could aim to train or strengthen impaired cognitive functions and/or to implement compensatory mechanisms in addition to external aids. Metacognitive strategies are also trained in order to facilitate the transfer to different environmental contexts.

Disclosures: Jérémie Pariente is on the Scientific Board of Biogen. The other authors have nothing to disclose.

In recent years, the literature has provided quantitative data about cognitive rehabilitation after TBI, leading to a better understanding of the underlying cerebral mechanisms and the development of new interventions. Results were reported across reviews, systematic reviews, meta-analyses, and scoping reviews. The most consequent systematic review was conducted by the Cognitive Rehabilitation Task Force of the American Congress of Rehabilitation Medicine. 10 Since 2000, Cicerone et al have published 4 successive systematic reviews on the cognitive rehabilitation of patients with TBI or stroke and established evidence-based clinical recommendations. 6,10-12 Four hundred ninety-one studies have now been reviewed and classified according to the level of evidence, including 109 studies in class I, 68 in class II, and 314 in class III. For each cognitive domain, Cicerone et al¹⁰ provided several levels of recommendations: practice standards, practice guidelines, and practice options. Practice standards, derived from

the strongest evidence, have been identified for treatment of attention deficits, left visual neglect, apraxia, mild memory impairments, language and social communication deficits, mild to moderate executive functions deficits, and holistic neuropsychological rehabilitation. They concluded that future research could investigate the effect of individual characteristics, especially the role of psychological insight, residual cognitive reserve, and the presence of associated psychiatric comorbidities. They also recommended including the frequency and intensity of cognitive rehabilitation as covariates in statistical models. Furthermore, several scoping reviews addressed complementary aspects of TBI, such as societal dimensions, ¹³⁻¹⁵ neurologic and neuropsychological patterns, ¹⁶⁻¹⁸ psychological conditions associated with TBI, ¹ delivery mode of rehabilitation, ^{20,21} and state of scientific research on clinical rehabilitation. 22,23 Two scoping reviews have reported the effects of cognitive rehabilitation^{24,25} on 2 very specific approaches that focused on driving rehabilitation²⁵ and the use of repeated transcranial magnetic stimulation on cognitive functioning.²⁴

The literature about cognitive rehabilitation after TBI is vast. Reviews on this subject usually analyze the content of rehabilitation to derive recommendations for clinical practice. Here, we chose to focus on methodological criteria to determine the level of scientific evidence of these studies. The most recent substantial systematic review on this subject includes published articles up to 2014. In this article, we aimed to review the scope of interventions in cognitive rehabilitation since 2015. Moreover, we chose to select studies including only patients with TBI and to exclude the stroke population in order to limit the heterogeneity of the underlying physiopathology of cognitive disorders. We also excluded the population with mild TBI because the functional and cognitive outcomes differ from those of moderate to severe TBI.²⁶ Scoping review was an appropriate approach to map the scope and nature of research in cognitive rehabilitation after TBI, summarize research findings, and identify gaps in the existing literature. In order to guide our search, we addressed 4 main questions: (1) Which cognitive domains does cognitive rehabilitation focus on? (2) What are the characteristics of interventions in cognitive rehabilitation? (3) What are the outcome measures used by authors? (4) What is the efficacy of cognitive rehabilitation?

Methods

The scoping review was based on the framework developed by Arksey and O'Malley²⁷ including the successive stages described below.

Search strategy

A systematic search of publications listed in the Pubmed (via Medline) and PsycINFO databases was conducted in August 2021

List of abbreviations:

EEG electroencephalography

fMRI functional magnetic resonance imaging

GMT goal management training

TBI traumatic brain injury

tDCS transcranial direct current stimulation

WM working memory

using the keywords "cognitive rehabilitation" (OR "cognitive remediation," "cognitive intervention," "cognitive training," "cognitive treatment") AND "traumatic brain injury." The following terms were excluded from the systematic search: "children," "pediatric," "concussion," "mild," and "animal." The scope of the search went from January 1, 2015, to July 31, 2021.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) studies including adults or adolescents, no younger than 15 years old, with moderate to severe TBI. The Mayo Classification System criteria were used to define moderate to severe TBI: loss of consciousness lasting 30 minutes or more and/or posttraumatic anterograde amnesia lasting 24 hours or more and/or worst Glasgow Coma Scale score less than 13 in the first 24 hours and/or imaging evidence of intracranial pathology (intracerebral hematoma, subarachnoid hemorrhage, cerebral contusion, etc). 28 We also reported for each article whether brain lesions were identified by authors through computed tomography/ magnetic resonance scanning (table 1). In a context of mixed samples including several acquired brain injuries, moderate to severe TBI should be the most represented group. (2) Patients had to be included at least 3 months after the onset. (3) Interventions had to investigate the rehabilitation of cognitive functions. (4) Effects of cognitive rehabilitation had to be documented by quantitative or qualitative comparisons throughout follow-up. (5) Interventions had to be conducted in a rehabilitation center, through ambulatory care, or at home.

Reviews and study protocols were excluded from this research, as were those not written in the English language. Then, for all citations, 2 authors (AJ, ML) conducted an abstract review and excluded articles that did not meet the eligibility criteria. All remaining citations underwent a full-text review.

Data analysis

For each of the 4 research questions, criteria of analysis were defined and collected in order to classify the characteristics and level of evidence of the reviewed studies.

Cognitive domains targeted by cognitive rehabilitation

All cognitive functions targeted by rehabilitation were listed. When several cognitive functions were trained, we registered all of them. We consider interventions to be "global training" interventions when they focused on 3 or more cognitive functions or when the aim was defined with the generic term "cognitive skills."

Characteristics of cognitive rehabilitation

Types of cognitive rehabilitation were divided into 3 categories of interventions. *Cognitive training* was defined as repetitive exercises without any explicit mention of metacognitive strategy training. *Integrative cognitive intervention* referred to interventions that explicitly combined the training of cognitive functions and metacognitive strategies. Finally, *external aids training* corresponded to the use of external compensatory mechanisms such as notebooks, cell phone applications, and alarms.

We also identified *combined approaches*, which referred to cognitive rehabilitation associated with other interventions like pharmacotherapy or noninvasive brain stimulation.

Three other parameters of cognitive interventions were analyzed: the delivery mode including group vs individual sessions, the length, and the intensity. Length was studied by distinguishing

 Table 1
 Summary of reviewed studies on cognitive rehabilitation posttraumatic brain injury

Authors and Level of	Participants*	Cognitive Rehabilitation	Design	Intervention Characteristics	Neuropsychological Outcome	Significant Main Results
Evidence		Characteristics [†]	3		Measures	. j
Cho and Sohlberg ²⁹ Class III	3 TBI, including 2 severe TBI Ages: 24, 51, and 52 y	60 min 1 per wk Over 6 wk Total of 6 sessions	Intra-individual comparison: help-seeking scores before vs after CR	Group sessions NICE training protocol: Intervention protocol targeting help-seeking behaviors during wayfinding	Ecological executive assessment (executive function route-finding task) Structured role-plays with a 4-point social behavior rating scale	Absence of statistical analysis Improvements for all 3 patients of ecological measures and structured role-plays
Constantinidou ³⁰ Class II	15 moderate to severe TBI Age: 28.13 (9.21)	60 min 2 to 4 per wk 10-12 wk Average total of 27 sessions	Intergroup comparison: CP training in young adults with TBI vs CP training in young healthy adults vs CP training in older adults vs no training in healthy older adults	Individual sessions CP training	Two categorization tests designed for this study Scores on executive function, visuospatial, memory, working memory, and language tests	Improvement in CP for all treated groups No intergroup differences
Elbogen et al ³¹ Class I	112 TBI with PTSD, including 57% moderate to severe TBI Age: 36.52 (8.42)	60-90 min 3 home visits at 0, 2, 4 mo Over 6 mo	Intergroup comparison: CR with a CALM vs active control intervention including psychoeducation	Individual sessions CALM: Goal management training plus mobile devices and attentional control	Scores on executive functions tests Emotional and behavioral questionnaires	No improvement on executive performance Improvement on behavioral, emotional, and PTSD symptoms
Emmanouel et al ³² Class I	18 patients with brain injury, including 11 moderate to severe TBI [‡] Severity: Period of loss of consciousness ranging from 12 to 33 d Age: 35 (9)	30 minutes 3 to 4 per wk Total of 11 sessions	Intergroup comparison: CR	Individual sessions BMT combined with WM training	Experimental tasks: Multistep everyday tasks Scores on executive function, memory, working memory, and language tests Executive ecological assessment. Executive functioning questionnaires (self- and relative-reports).	Improvements on multistep everyday tasks for the intervention group compared to the control group (medium to large effect sizes) No interaction effects between treatment and time for all other neuropsychological measures
Goodwin et al ³³ Class III	66 patients with ABI, including 50 traumatic injuries (46 closed head injuries and 4 open head injuries) Age: 31.6 (11.75)	Intensive phase: 4 full d/wk Over 12 wk Reintegration phase: 2 or 3 full d/wk Over 12 wk Total of 24 sessions	Intra-individual comparison: Dysexecutive scores before vs after CR	Individual and group sessions Holistic neuropsychological rehabilitation including 2 phases: Intensive phase: education, practical tasks, facilitated discussion, and homework Reintegration phase	Executive functioning and behavioral questionnaire (self- and relative reports)	Lower number of self-reported and relative-reported dysexecutive symptoms
Gracey et al ³⁴ Class I	59 acquired nonprogressive brain injuries, including 27 patients with TBI Severity obtained for 55% of participants with TBI: 41% severe, 7% moderate, 7% mild Age: Detailed for each group, not for total sample Min mean age: 47.79 (14.72) Max mean age: 49.76 (12.94)	90 to 120 min Total number of sessions varied depending on the abilities of the participant	Longitudinal intergroup comparison Crossover design: Assisted intention monitoring vs control intervention (information and games)	Individual sessions AIM: Brief GMT combined with periodic SMS text messages	Proportion of daily intentions achieved by participant	Improvement of achievement intentions after the intervention phase compared to the control condition (medium effect sizes)
Hart and Vaccaro ³⁵ Class I	8 moderate to severe TBI Age: 23.8 (4.3)	8 wk No more details	Intergroup comparison: Goal intention intervention (with text messaging) vs active control group (who received unspecific text messages)	Individual sessions Goal intention intervention: Implementation of intentions with reminder messages	Assessment of emotional function, social participation, and goal attainment scaling scores	Improvement for the experimental group on self- and relative reports for social participation and social relation compared to control group (medium to large effect sizes) (continued on next page)

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Powell et al ³⁶ Class I	23 ABI (including 14 motor vehicle collisions, 1 fall, and 2 assaults) No information regarding severity Age: 44 (15)	60 min Over 8 wk Total of 6 sessions	Intra-individual comparison: problem solving, self-efficacy, and life satisfaction self-report scores before vs after CR	Individual sessions Implementation of web-based program (Prosolv program) for problem solving in daily life	Self-report questionnaires on problem solving, self-efficacy, and life satisfaction scores	No difference
Siponkoski et al ³⁷ Class I	40 moderate to severe TBI Age: 41.3 (13.3)	60 min 2 times per wk Over 3 mo Total of 20 sessions	Longitudinal intergroup comparison Crossover design: intervention phase vs control phase (standard care)	Individual sessions Neurological music therapy: intervention adapted from 2 existing music therapies (functionally oriented music therapy and music-supported training)	Scores on executive function, memory, attention, and reasoning tests	Improvement of cognitive functioning in the AB group (ie, intervention phase followed by control phase) Increase in gray matter volume (right inferior frontal gyrus) in both groups during intervention and control periods
Vander Linden et al ³⁸ Class III	16 moderate to severe TBI [‡] Age: 15 y 8 mo (1 y 7 mo)	40 min 5 per wk Over 8 wk Total of 40 sessions	Intergroup comparison: changes in gray matter volume in regions of interest related to executive functions after cognitive training vs changes in gray matter volume in control regions	Individual sessions Brain games software: Home- based cognitive training program targeting executive functions and attention	Scores on working memory, executive function, attention, and processing speed tests	No difference on frontal gray matter volume after training Significant negative correlation between changes in processing speed score and gray matter volume of putamen area
Vander Linden et al ³⁹ Class II	16 moderate to severe TBI [‡] Age: 15 y 8 mo (1 y 7 mo)	40 min 5 per wk Over 8 wk Total of 40 sessions	Intergroup comparison: computerized cognitive training vs healthy control group (no training)	Individual sessions Brain games software: Home- based cognitive training program targeting executive functions and attention	Scores on working memory, executive functions, attention, and processing speed tests Executive functioning and behavioral questionnaires (relative report)	At 6-mo follow-up, lower effect from training on executive functions was found in adolescents with diffuse axonal injuries in the deep brain nuclei compared to adolescents without diffuse axonal injuries in this area
Verhelst et al ⁴⁰ Class III	5 moderate to severe TBIs [†] Age: 16 y (9 mo)	40 min 5 per wk Over 8 wk Total of 40 sessions	Intra-individual comparison: executive performance before and after CR	Individual sessions Brain games software: Home- based cognitive training program targeting executive functions and attention	Scores on attention, working memory, and executive function tests Executive functioning and behavioral questionnaires (self- and relative reports)	Small to large effect size of intervention on all neuropsychological measures Results maintained or increased at 6-mo follow-up
Verhelst et al ⁴¹ Class II	16 moderate to severe TBIs [‡] Age: 15 y (1.8)	40 min 5 per wk Over 8 wk Total of 40 sessions	Intergroup comparison: white matter changes in TBI group vs healthy control group	Individual sessions Brain games software: Home- based cognitive training program targeting executive functions and attention	Scores on attention, working memory, and executive function tests Executive functioning and behavioral questionnaires (self- and relative reports)	Time × Group interaction effects on 1 attention score and on 1 executive function score (small to moderate effect sizes)
Attention						
Arroyo-Ferrer et al ⁴² Class III	20-year-old man with TBI [‡] Axonal damage was diagnosed using MRI	45 min 4 sessions per wk Over 6 wk Total of 16 sessions	Case report	Individual sessions EEG-based NFB intervention targeting inhibition of theta frequency band in frontal areas during exercises in virtual environments Neuropsychological intervention aiming attention, executive function, and working memory	Scores on executive function, memory, attention, and visuospatial ability tests	Improvement of visuospatial abilities, attention, and executive function after EEG-based NFB intervention compared to after neuropsychological intervention Correlative quantitative EEG changes were found
Dundon et al ⁴³ Class I	26 TBI Information regarding regions of	Not detailed	Intergroup comparison: adaptive training group vs nonadaptive	Individual sessions Dichotic listening training task	Scores on attention and memory tests	Improvement with both trainings on cognitive variables (continued on next page)
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Chiaravallotti et al ⁵¹ Class I	Min mean age: 42.22 (14.12) Max mean age: 45.78 (10.53) 69 moderate to severe TBI Age: Detailed for each group, not for total sample Min mean age: 37.17 (11.24) Max mean age: 40.68 (11.28)	45 to 60 min Twice per wk Over 5 wk Total 10 sessions	exposed to critical components of training) Intergroup comparison: treatment group vs placebo control group (non-training-oriented tasks)	the source/context of learned information Individual sessions Modified story memory technique, involving the training of mental imagery and the use of the source/context of learned information	Scores on memory tests Ecological scores on the Rivermead Behavioural Memory Test Cognitive and behavioral executive questionnaires (self- and relative reports)	default mode network (Bonferroni correction) Improvement in prose recall compared to placebo group (medium effect size) No treatment effect on standardized memory scores Improvement on Rivermead Behavioural Memory Test in the experimental group compared to placebo group
Hara et al ⁵² Class III	67-year-old man who sustained a diffuse axonal injury [‡]	6 per wk Over 2 wk Total of 12 sessions	Case report	Individual sessions Repeated transcranial magnetic stimulation (2400 pulses once a d) combined with CR (training program focused on memory and attention disorders)	Scores on memory, attention, and executive function tests Everyday memory assessment scores on Rivermead Behavioural Memory Test	Absence of statistical analysis 2-point gain on the MMSE
Leśniak et al ⁵³ Class I	65 ABI including 30 TBIs, 27 CVAs, 4 encephalitis Age: Detailed for each group, not for total sample Min mean age: 39.6 (15) Max mean age: 42.2 (14)	60 min 5 per wk Over 3 wk Total 15 sessions	Intergroup comparison: individual therapy group vs group therapy group vs no therapy group	Individual and group sessions Increased awareness of memory deficits and learning of global strategies for everyday memory	Scores on memory tests Ecological memory scores (RBMT) Self-report of everyday memory complaint	No difference between groups In individual therapy group, significant improvements on computerized memory, attention, and working memory tests In group therapy group, decrease of memory failures in daily life (relative report)
Leśniak et al ⁵⁴ Class III	15 moderate to severe TBI [‡] Age: 26.2 (7.6)	5 individual and 5 group sessions per wk Over 3 wk Total of 30 sessions	Intergroup comparison: comprehensive therapeutic program vs waiting list control condition	Group and group sessions Group sessions: Internal memory strategy training and implementation of external aids. Discussion about memory problems and their respective compensatory strategies Individual sessions: exercises using memory strategies on Rehacom software	Scores on episodic memory, working memory, and attention tests Self- and relative reports on cognitive measures	Improvement of cognitive scores (small to moderate effect sizes) Improvement on self- and relative report measures Gains maintained at 4-mo follow- up
Raskin et al ⁵⁵ Class III	20 moderate to severe TBI Age: 42.11 (13.21)	60 min 1 or 2 per wk Over 6 mo Total of sessions not specified	Longitudinal intergroup comparison Crossover design: active treatment condition vs no treatment phase at baseline and at 1-y follow-up	Individual sessions Metacognitive technique using mental imagery	Prospective memory scores Scores on attention, retrospective memory, and executive function tests Self-report questionnaires about prospective memory, everyday memory, and quality of life	Improvement of prospective memory measure after active treatment phase only Improvement on self-report questionnaire for everyday memory Improvement maintained at 1-y follow-up for all previous results
Global Training						
Buccellato et al ⁵⁶ Class III	21 ABI, including 62% mild to severe TBI Age: 41 (13.38)	30 to 40 min 3 per wk Over 6 wk Total of 18 sessions	Longitudinal comparison Crossover within-subjects design: global cognitive training phase with the Brainer Virtual Rehabilitation software vs	Individual sessions Virtual reality training using Bright Brainer Virtual Rehabilitation software (global cognitive training)	Scores on sustained attention, processing speed, working memory, and visuospatial tests Neurobehavioral symptoms inventory and mood questionnaire	No significant difference between phases
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			standard-of-care therapies			
De la Rosa-Arredondo et al ⁵⁷ Class III	26-year-old woman with severe TBI‡	1 time per wk Over 24 wk Total of 24 sessions	Case report	Individual sessions CR including 2 phases of 12 wk: phase 1 targeted sustained and selective attention and visuospatial abilities; phase 2 focused on memory and executive functions	Scores on attention, working memory, memory, visuospatial, and abstract reasoning tests	Absence of statistical analysis Improvement in selective attention, verbal fluency, visuospatial ability, and executive function scores
De Luca et al ⁵⁸ Class I	100 mild to moderate TBI Brain lesion site specified Age: 39.9 (10.1)	60 min 3 times per wk Over 8 wk Total of 24 sessions	Intergroup comparison: Virtual reality training group vs traditional CR group	Individual sessions Semi-immersive virtual reality using Nirvana BTs-N software, targeting attention, executive function, and visuospatial training	Scores on global scale, executive functions, and attention tests	Improvements on cognitive and mood scores for both traditional and virtual reality training Improvements on cognitive flexibility for virtual reality training
Eilam-Stock et al ⁵⁹ Class III	29-year-old man with a moderate TBI	30 min/d (including initial safety checks and 20 min of tDCS combined with cognitive training) 5 times per wk Over 4 wk Total of 20 sessions	Case report	Individual sessions Computerized CR with BrainHQ program (attention, processing speed, executive function, and working memory) combined with tDCS (anodal electrode on the left DLPFC and a cathodal electrode on the right DLPFC, 20 min 2 mA)	Scores on attention, working memory, processing speed, executive function, and memory tests Mood, sleep, pain, and fatigue self-report scales	Absence of statistical analysis Improvement in several cognitive domains: attention, working memory, processing speed, and semantic fluency Improvement in emotional functioning: mood, sleep, and fatigue
Hwang et al ⁶⁰ Class I	96 TBI No classification of severity 49% of participants with positive CT scan findings Age: Detailed for each group, not for total sample Min mean age: 65.8 (10.7) Max mean age: 68.1 (11.4)	Once a wk Over 6 mo Total of sessions not specified	Intergroup comparison: CCT group or TC group vs usual care group	Individual sessions Computerized cognitive training using Rehacom software (attention, memory, speed of processing, executive functioning)	Scores on global cognitive scales and executive function tests	Improvement on attention, memory scales, and global cognitive scale scores after the intervention for the CCT group compared to usual care No difference at 6-mo follow-up Improvement on conceptualization scores and global cognitive scale for the TC group compared to usual care Differences between CCT and TC were not investigated
Kanchan et al ⁶¹ Class II	10 moderate to severe TBI Age: 20-40	45 min 1 to 5 times per wk Over 6 mo Total of session not specified	Intergroup comparison: cognitive training vs passive control group (no training)	Individual sessions Brainwave-R software: cognitive strategies and techniques for brain injury rehabilitation (attention, visual processing, information processing, memory, executive function)	Scores on cognitive battery (Luria Nebraska Neuropsychological Battery Adults-Form I)	3
Kumar et al ⁶² Class III	34-year-old woman with severe TBI [‡]	2 h 3 per wk Over 2 mo Total of 18 sessions	Case report	Individual sessions Immersive environment (coffeehouse) targeting practice job activities, which involved motor, social, and cognitive skills	Score on executive function tests Self-report quality of life	Absence of statistical analysis Improvement on TMT B score after intervention compared to baseline
Maggio et al ⁶³ Class II	56 TBI [‡] Information regarding brain	30 min 5 times per wk	Intergroup comparison: Lokomat training with virtual	Individual sessions Lokomat training with or without virtual reality	Score on general cognitive status, frontal ability, and attention tests	Improvements on global cognitive scores, executive, and
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Pinard et al ⁶⁴ Class III	lesion sites Age: 35.5 (5.3) 3 severe TBI Ages ranged between 39 and 57 y	Over 8 wk Total of 40 sessions Over 15 mo Length varied for each user Total session not detailed	reality vs Lokomat without virtual reality Case report	Individual sessions Implementation and training to use a cognitive assistive technology for meal preparation called COOK (Cognitive Orthosis for coOKinq)	Qualitative scores of numbers of meals prepared per wk with the stove, number of warnings, number of interventions of security modules	attention scores for the experimental group Absence of statistical analysis For 2 of 3 participants, increased number of meals prepared per wk
Ramanathan et al ⁶⁵ Class III	54-year-old man with severe TBI‡	2.5 h/d 4 times per wk Over 3 wk Total of 12 sessions	Case report	Individual sessions (R including attention and prospective memory training and metacognitive strategy instructions	Scores on executive functions, attention, and communication tests Self-report of quality of life	Improvement on executive and attentional scores and quality of life scale Cerebral activation task: Increased activation in middle and inferior frontal gyrus and superior temporal gyrus Resting state: greater functional integration of frontal and parietal cortices, visual, and auditory association areas and portions of the cerebellar vermis Structural (DTI-measured FA; P<.01 uncorrected): increased FA in white matter tracts throughout the brain. Especially in tracts serving the prefrontal, occipito-parietal, and temporal association cortices and cerebellum
Välimäki et al ⁶⁶ Class I	90 TBI [‡] Severity defined with the presence of intracranial injury and sequelae of injuries to the head (ICD-10) Age: 41	30 min/d Over 8 wk Total of 8 sessions	Intergroup comparison: rehabilitation gaming group vs entertainment gaming (PlayStation 3) group vs passive control group (no gaming)	Individual sessions Rehabilitation gaming with Cognifit software (cognitive training platform with 3 categories of exercises: memory, spatial, and mental planning)	Scores on processing speed, visuomotor tasks, attention, executive function, and working memory tests Executive self-report questionnaire	No difference between the 3 groups
Wu et al ⁶⁷ Class III	50-year-old man, TBI with multiple contusions and lacerations, diffuse axonal injury, and scattered cerebral hemorrhages [‡]	30 min 5 times per wk Over 1 mo Total of sessions not specified	Case report	Individual sessions Comprehensive multifaced intervention including computer-assisted cognitive impairment rehabilitation system targeting memory, attention, and visuospatial defects	Score on general cognitive status	Absence of statistical analysis Global improvement of cognitive performance DTI neuroimaging: number and length of callosal fiber bundle increased, especially for fibers connecting the bilateral hemispheres
Communication Douglas et al ^{®8} Class III	13 severe TBI Age: 35.2 (9.3)	Twice per wk Over 6 wk Total of 12 sessions	Intra-individual comparison: communication scores before vs after intervention vs 3-mo follow-up	Individual sessions and with communication partner CommCope-I program: Communication-specific coping intervention	Communication specific coping scores Scores on functional communication abilities scale	Improvements in communication- specific coping strategies scores (moderate to medium effect sizes) Improvements in functional communication scores (moderate effect size) (continued on next page)

NOTE. For each study, all cognitive functions targeted by rehabilitation were listed. If several cognitive functions were trained, all were registered, but each study was classified according to the main cognitive function trained.

Abbreviations: ABI, acquired brain injury; ABT, attention builders training; AIM, assisted intention monitoring; APT, attention process training; BOLD, blood oxygen level—dependent; CALM, cognitive application for life management; CCT, computerized cognitive training; CR, cognitive rehabilitation; CT, computed tomography; CVA, cerebral vascular accident; CP, categorization performance; DLPFC, dorsolateral prefrontal cortex; DTI, diffusion tensor imaging; FA, fractional anisotropy; ICD, *International Classification of Diseases*; MAAT, memory and attention adaptation training; MACT, music attention control training; MMSE, Mini Mental State Examination; NFB, neurofeedback; NICE, Noticing you have a problem, *I*dentifying the information you need for help, *C*ompensatory strategies, *E*valuating progress; PTSD, posttraumatic stress disorder; RBMT, rivermead behavioral memory test; SMS, short messaging service; TC, Tai Chi; TMT B, trail making test - part B; T-ScEmo, treatment for impairments in social cognition and emotion regulation.

* Participants: n. TBI severity, mean age in years (SD).

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- † Cognitive rehabilitation characteristics: Length for each session; intensity (eq., number of cognitive rehabilitation sessions per week and number of weeks), total of sessions.
- Brain lesions were identified by authors through computed tomography/magnetic resonance scanning for all included patients.

very short (≤ 1 week), short (1 week to 1 month), moderate (1-3 months), and high (>3 months) duration. Intensity was classified as low (1 session per week), moderate (2 sessions per week), or high (≥ 3 sessions per week).

Behavioral examination and neuroimaging as outcome measures

Concerning behavioral outcome measures, 4 types of assessment were distinguished: (1) neuropsychological examination including standardized neuropsychological tests; (2) ecological neuropsychological examination including standardized tests and/or experimental ecological tasks with reference to daily life situations; (3) self-reporting of cognitive complaints, social participation in everyday activities, and quality of life; (4) relative reporting of patient's difficulties in daily life. We also counted the number of these types of assessment for each study in order to attest to the exhaustiveness of the assessment.

Neuroimaging outcome measures were classified as structural and/or functional imaging and/or electroencephalography (EEG).

Efficacy of cognitive rehabilitation

The efficacy of cognitive rehabilitation was analyzed according to 3 main criteria and associated subcriteria detailed below. A coding grill was used for the extraction of these methodological criteria.

The outcome measures were the first criteria. We first pointed out the results showing a significant improvement in at least 1 of the outcome measures defined by the authors. Quantitative and qualitative improvements were coded when collected. Second, if a significant and/or clinically relevant change was reported, we distinguished whether it was in the primary or secondary outcome measures.

The internal validity of reviewed studies was assessed as secondary criteria, based on the classification used by Cicerone et al in systematic reviews. According to this classification, studies were classified as class I when they were well-designed, prospective, randomized controlled trials. Class II referred to prospective, nonrandomized cohort studies, retrospective, nonrandomized case-control studies, or multiple baseline studies that allowed a direct comparison between treatment conditions. Class III included clinical series without concurrent controls or single-subject designs. In a second step, we also detailed the control group design, distinguishing active, passive, or no control group. We considered it an active control group when patients participated in usual care or unspecific activities. A passive control group referred to a waiting list or a no-treatment phase.

The statistical analysis was the third criterion. As proposed by Cicerone et al, 75 comparisons of between-group treatment conditions were considered as a higher level of methodological quality compared to within-group comparisons. We also identified whether or not the authors applied an intention-to-treat analysis. Finally, we analyzed whether the effect size and measures of variability such as confidence intervals were reported.

Charting the data

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews guidelines, ⁷⁶ a flow diagram was used in order to illustrate study selection (figure 1). The level of evidence for the efficacy of cognitive rehabilitation was also charted (figure 2). Figure 2 details the number of studies that met each precited methodological

criterion and associated subcriteria. For each study, the key characteristics of participants with TBI, cognitive rehabilitation, experimental design, intervention, neuropsychological outcome measures, and significant main results were collected and are summarized in table 1.

Results

Between January 2015 and July 2021, 458 studies were published in the Pubmed (via Medline) and PsycINFO databases. We found 31 duplicates across the 2 databases and removed them (figure 1). Four hundred twenty-seven records were reviewed by title and abstract and 330 were excluded based on the inclusion and exclusion criteria. Ninety-seven articles were assessed by full-text review. In the end, 46 studies were included in the scoping review.

Cognitive domains targeted by cognitive rehabilitation

The results showed a large scope of 7 cognitive functions targeted by interventions: executive functions (n=14, 30%), attention (n=14, 30%), memory (n=7, 15%), communication (n=4, 9%), social cognition (n=1, 2%), topographic orientation (n=1, 2%), and verbal auditory perception (n=1, 2%). Global training was proposed in 12 out of the 46 studies (26%).

Characteristics of cognitive rehabilitation

Type of cognitive interventions

In this review, integrative cognitive interventions concerned 48% of studies (n=22), cognitive training was reported in 37% of studies (n=17), and external aids training was described in 11% (n=5). Two studies did not detail the type of intervention (4%). ^{62,74} The effects of combined interventions were examined in 4 studies, ^{46,47,52,59} in which cognitive rehabilitation was associated with pharmacotherapy, ⁴⁶ repetitive transcranial magnetic stimulation, ⁵² or transcranial direct current stimulation (tDCS). ^{47,59}

Methodological parameters of cognitive rehabilitation

Among the 46 reviewed studies, we showed that individual sessions were used in 83% of the studies (n=38), whereas group sessions were only used in 11% (n=5). Six percent of the studies combined individual and group sessions (n=3).

Furthermore, the length of interventions was heterogeneous, ranging from 5 days⁴⁷ to 15 months. ⁶⁴ Fifty-four percent of studies proposed an intervention that lasted between 1 and 3 months (n=25). Shorter interventions lasting 1 week to 1 month were found in 24% of studies (n=11). Finally, cognitive rehabilitation interventions including a duration of <1 week or >3 months were found in 1 (2%) and 8 studies (18%), respectively. In 1 study, this methodological feature was not detailed (2%). ⁴³

Concerning the intensity of interventions, 26% of the reviewed studies proposed 2 sessions per week (n=12) and 44% proposed 3 or more sessions per week (n=20). Conversely, 11% included only 1 session per week (n=5). In 1 study, the intensity was variable and progressively decreased among each phase of cognitive rehabilitation. Finally, 17% did not describe this methodological point (n=8).

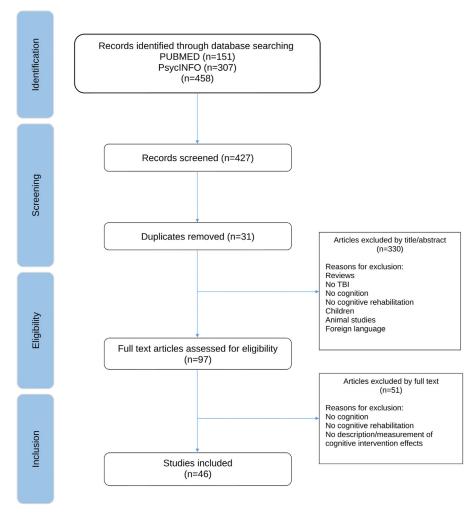


Fig 1 Flow diagram for the scoping review process with Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews guidelines.

Our results indicated that 9 out of the 46 studies did not detail both the length and intensity of the interventions (20%). Among studies that detailed length and intensity, the most common design combined 3 or more sessions per week over 1 to 3 months and was found, in this scoping review, in 10 studies.

Behavioral examination and neuroimaging as outcome measures

The effects of cognitive rehabilitation were mostly measured with standardized neuropsychological tests in 41 out of the 46 studies (89%). Ecological neuropsychological examination was used in 35% of studies (n=16). Fifty percent included a self-report questionnaire (n=23), whereby cognitive complaint was assessed in 16 studies (70%) and quality of life was measured in 7 studies (30%). Finally, reporting by relatives was used in 35% of studies (n=16).

Thirty-seven percent of studies used one of these 4 types of measures (n=17), 28% of studies used 2 types of measures (n=13), and 24% used 3 types of measures (n=11). In contrast, 11% of studies proposed an exhaustive evaluation with these 4 types of measures (n=5).

Neuroimaging outcome measures used as brain markers of cognitive rehabilitation were reported in 20% of studies (n=9),

whereas EEG was performed in only 2 studies. 42,43 More specifically, resting state functional magnetic resonance imaging (fMRI), 71 regional cerebral blood flow, 52 and brain activation during an fMRI cognitive task 47,65 were analyzed in 4 studies. Structural MRI data were reported in 4 studies. 37,38,41,67 Only 1 paper combined diffusion tensor imaging, attention-related fMRI, and resting-state fMRI sequences. 65

Efficacy of cognitive rehabilitation

According to Cicerone et al's criteria for evidence-based classes, 6 41% $^{31,32,34-37,43,45-51,53,58,60,66,72}$ of reviewed studies were classified as class I (n=19), $13\%^{30,39,41,44,61,63}$ as class II (n=6), and $46\%^{29,33,38,40,42,52,54-57,59,62,64,65,67-71,73,74}$ as class III (n=21).

Ninety-three percent of studies reported significant cognitive improvement on at least 1 outcome measure, among which 19 studies described clinical improvement on the primary outcome independently of statistical change (figure 2). Within these studies, 10 were classified as class I and involved an active control group. ^{32,34,37,40,45,46,47,50,51,60} Then, with regard to statistical analysis, these 10 studies applied between-group comparisons to assess the efficacy of treatment, among which 7 used an intention-to-treat analysis (15% of reviewed studies). ^{32,37,45,47,50,51,60} Medium to large effect sizes were reported in 5 out of these 7

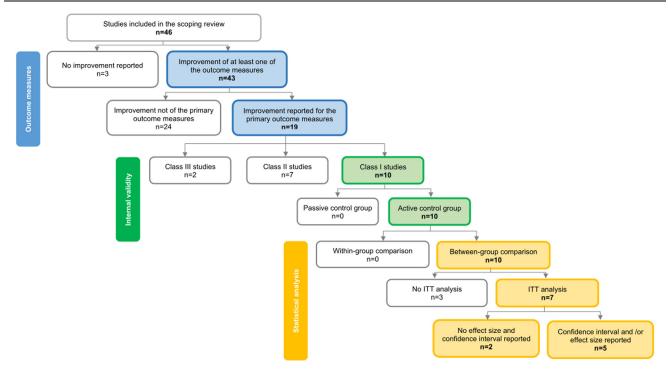


Fig 2 Flow diagram for the level of evidence in the efficacy of cognitive rehabilitation in the reviewed studies.

studies 32,37,45,51,60 and the confidence interval was reported in only 1 out of these 7 studies. 51

Discussion

This scoping review was conducted starting with 2015, after the most recent systematic review, ¹⁰ in order to identify and characterize studies evaluating cognitive rehabilitation after a moderate to severe TBI, to summarize the cognitive approach used and the domains investigated, and to analyze their efficacy.

Memory, attention, and executive functions were most often targeted in individual sessions adopting an integrative cognitive approach. Cognitive interventions were mainly temporally distributed with 3 or more sessions per week over 1 to 3 months. One or 2 behavioral outcome measures were mostly preferred by authors to assess the efficacy of intervention, whereas neuroimaging outcome measures were rarely used. The review found clinically significant effects of cognitive rehabilitation after a moderate to severe TBI in a very large part of reviewed studies (93%), among which 41% described an improvement on the primary outcome measure. The high number of positive published results could be the sign of a publication bias according to Dwan et al's conclusions in 2013.77 Nevertheless, when methodological criteria for the level of evidence were controlled (outcome measures, internal validity, and statistical analysis) a significant decrease was observed, from 93% to 15%. This significant decrease is unsatisfactory and highlights the methodological requirements for future studies. Challenges in TBI rehabilitation imply that cognitive interventions must be based on a robust experimental design to prove their efficacy and to replicate the findings on which recommendations for clinical practice could be finally derived. Therefore, this scoping review provides a complementary approach to prior systematic reviews^{6,10-12} by identifying 5 key methodological points.

Specific experimental designs for cognitive rehabilitation of patients with TBI

In this scoping review, 41% of reviewed studies were classified as class I. This result highlights a continuing upward trend of randomized controlled trials in cognitive rehabilitation. Indeed, Cicerone et al reported a percentage of class I studies ranged from 17%^{6,12} to 20%¹¹ until 2008, which increased to 36% between 2009 and 2014. Randomized controlled trials were crucial for evidence-based studies but not always relevant in rehabilitation practice, where double blind was sometimes not feasible 11 because the therapist was systematically aware of the hypothesis underlying the contents of intervention. Furthermore, experimental and control groups have to share common methodological parameters such as delivery mode and length and intensity of rehabilitation to allow between-group comparisons.⁷⁸ A major advance in the literature is the presence of an active control group to attest to the specificity of the experimental intervention and to rule out the nonspecific effects of global cognitive stimulation, such as treatment effect, motivational or novelty effect, and Hawthorne effect. 8 Statistically, the efficacy of interventions cannot be only demonstrated using within-group analysis. Improvements must be specific to the experimental intervention and thereby confirmed with between-group comparisons. Effect sizes, rarely presented in reviewed studies, are also a supplementary indicator of the efficacy of cognitive interventions and should be systematically added in the future. All of these methodological points were controlled in 1 study,⁵¹ in which the authors investigated the added effects of psychoeducation and metacognitive strategy training in an experimental group compared to an active control group with cognitive rehabilitation including non-training-oriented tasks, with a positive effect for patients. Finally, a challenge for further group studies may be the individualization of the cognitive intervention regarding cognitive profiles and complaints in order to compensate for the clinical heterogeneity of TBI. Two main solutions could be proposed for greater methodological relevance. The first is to constitute toolboxes for each cognitive domain, including standardized exercises with increasing levels of difficulty, like those developed by Visch-Brink et al⁷⁹ and Van Rijn et al⁸⁰ in aphasia therapy.81 For a single cognitive function rehabilitated, the therapist will be able to choose the modalities of presentation of the most relevant exercise to work on. The second solution is the use of single-case experimental design. Multiple baseline design includes a small number of patients (ie, classically at least 3 participants), has high feasibility, and allows for an individualized approach. The high level of evidence of single-case experimental design lies in the repeated measurements performed during the baseline and intervention phases in order to control for intra-individual variance. The participant corresponds to their own control, comparing their performance at the baseline and after the intervention. Visual and statistical analysis are used to measure the efficacy of intervention. 44,82-84

Combined cognitive interventions as an attractive perspective

Combined interventions are interesting to potentiate significant individual benefits of each therapy on cognitive functioning and to promote the generalization of improvements to daily functioning. Regarding the results of the present scoping review, combination may be considered at 3 levels: within interventions, between delivery modes of interventions, and between interventions.

Forty-eight percent of the reviewed studies used integrative rehabilitation combining both cognitive and metacognitive training. For example, Emmanouel et al,³² in a randomized controlled trial of 18 patients with TBI, showed the benefits of goal management training (GMT) associated with working memory (WM) training (GMT+WM group) in comparison with an isolated WM group on multistep everyday tasks and ecological executive measures, with small to large effect sizes for the combined approach.

The second level of combination was between group and individual sessions. Even if, in this scoping review, results showed that individual interventions remained the majority (83%), a combined approach of these 2 delivery modes was proposed in 3 studies, but its specific benefits were not analyzed. 33,53,54

The third level concerned the use of combined interventions. Only 4 studies proposed combined rehabilitation with pharmacotherapy⁴⁶ or noninvasive brain stimulation. ^{47,52,59} The heterogeneous designs and the low statistical power of these studies call for replication.

Specific effects of length and intensity of cognitive rehabilitation

The main temporality reported by this scoping review included a moderate duration (ie, ranging between 1 and 3 months) with a high intensity (ie, 3 or more sessions per week). This choice seems related to clinical relevance and feasibility in clinical research protocols. As mentioned by Cicerone et al, ¹⁰ the intensity and length of the cognitive interventions must be studied in order to determine their respective contribution to the efficacy of the rehabilitation and thus have to be integrated into statistical models. None of these 2 parameters were analyzed across all reviewed studies. Furthermore, Chiaravalloti et al⁵¹ have investigated the use of monthly booster sessions proposed over 5 months, after memory training with 10 sessions over 5 weeks. These focused on applying

trained memory strategies in daily life. Although the authors reported no effect of these booster sessions during follow-up, it seems very useful to check the implementation and efficacy of trained cognitive strategies in daily living.

In addition to length and intensity parameters, future studies should investigate the severity of cognitive impairment at inclusion, the delay from the injury, or fatigability as contributing variables in determining the dynamic of the intervention.

Selection of outcome measures as a key experimental point

The choice of outcome measures is a key methodological point as well as the categorization into classes I to III for evidencebased medicine. Assessment using standardized neuropsychological examination was the most frequently reported (89%), followed by self-report questionnaires (50%), ecological neuropsychological assessment (35%), and relative report questionnaires (35%). An exhaustive neuropsychological examination of all cognitive domains could contribute to demonstrating the benefits of therapy on trained as well as on untrained functions. Moreover, after a washout period, a follow-up assessment may show maintained benefits of rehabilitation. However, it has been well described that standardized pencil-paper neuropsychological performance test could not exactly reflect those obtained in daily contexts, especially in executive functions assessment. 85 In this way, an ecological cognitive assessment could be a sensitive measure to predict real-life performance.⁸⁶ Ecological tests such as the Test of Everyday Attention⁸⁷ or the Rivermead Behavioral Memory Test⁸⁸ were frequently proposed in the reviewed studies but remained in nonecological environments and encompassed a restricted representation of daily life tasks. Conversely, the Multiple Errands Test, 85 which was not reported here, implies daily life activities, takes place outside of the rehabilitation sites, and offers a more sensitive image of executive disorders.85 The Multiple Errands Test should be combined with person-centered assessment to improve the clinical relevance of the evaluation. The goal attainment scaling,⁸⁹ derived from occupational therapy, makes it possible to set personalized goals with the patient as well as 5 levels of predicted attainment for a sensitive evaluation of progress.90

In the scoping review, 2 authors developed ecological experimental tasks to assess the effect of executive rehabilitation. Emmanouel et al³² proposed multistep daily activities such as sending a text message or buying an airplane ticket. The number of correct steps was counted and compared among parallel scripts before and after cognitive rehabilitation. After sessions of goal management training, Gracey et al³⁴ defined with each participant several daily life intentions, such as making sure their mobile phone is with them, charged, and switched on. The daily proportion of intentions achieved by patients was studied.

Finally, several studies used cognitive complaint and quality of life questionnaires to investigate views of patients and their family in addition to the standardized neuropsychological examination. After cognitive rehabilitation, these reports provided an update on the cognitive complaint and metacognitive abilities.

Exhaustiveness and specificity of assessment constitutes a methodological key point contributing to the level of evidence of interventions. Complete outcome measures (ie, standardized examination, ecological assessment, self- and relative reports) were reported in only 5 studies.^{32,44,51,53,72}

Multiple contributions of neuroimaging in cognitive interventions

Magnetic resonance imaging was used in 20% of reviewed studies. The use of neuroimaging tools has remained scarce in recent years, which is in agreement with Galetto and Sacco, 91 who reported only 11 studies between 1985 and 2016 that used neuroimaging techniques to attest to neuroplastic changes after cognitive rehabilitation in TBI. For instance, Chiaravalloti et al⁵⁰ reported BOLD signal changes during word learning and recognition tasks, with patterns of increased and decreased cerebral activation in the frontal and parietal lobes after 10 sessions of memory rehabilitation. Some authors have suggested a disengagement of the executive control network and an activation of the default mode network after cognitive rehabilitation to explain cognitive improvement, suggesting that memory tasks became less cognitively demanding after cognitive rehabilitation. Nevertheless, no details were given about cognitive scores on task-related functional activation.

Brain imaging constituted a promising method, but further research is needed to identify potential contributions. Structural and functional MRI continue to contribute to a better understanding of TBI physiopathology. These techniques illustrate the brain reorganization and the dynamics of plasticity mechanisms that could be associated with short- and long-term cognitive changes.

Brain imaging may also participate in the identification of potential modulators of recovery trajectories after TBI⁹² such as brain reserve, including measures of specific patterns of gray matter volume, cortical thickness, synaptic integrity, or white matter microstructural properties. Neuroimaging could make multiple contributions, but at this time its use as a measure of the efficacy of an intervention should be done in combination with cognitive measures.

Study limitations

A few main limitations were identified in the scoping review. The first concerned the search strategy, which focused on only 2 databases and did not include the gray literature. As reported, the effect of publication bias could contribute to an inaccurate picture of the literature on cognitive rehabilitation. Second, only 1 reviewer performed data extraction and analysis. Though we made efforts to define criteria precisely to assess the methodological quality of the reviewed studies, there may be subjective interpretation involved in this process.

Conclusions

This scoping review highlights the persistent and growing interest in cognitive rehabilitation with major methodological improvements in the design of studies for moderate to severe TBI since 2015. This led to a higher number of studies that show an improvement in the primary outcome measures after cognitive rehabilitation. Our findings make it possible to identify 3 methodological criteria and subcriteria for determining the level of evidence of cognitive interventions and could be used in future studies. Our approach is complementary to the prior systematic

reviews^{6,10-12} that were mainly focused on the content of interventions. Methodological efforts must be continued, and combined interventions studies must be proposed. Individualized cognitive rehabilitation also remains a challenge. Outcome measures must be well selected, including neuropsychological tests in ecological and nonecological environments, patient and relative reports. Rehabilitation of social cognition and emotion regulation should be better investigated. The results of this scoping review now need to be confirmed by systematic reviews and meta-analyses.

Keywords

Brain injuries; Cognitive Remediation; Rehabilitation; Review

Corresponding author

Adeline Julien, MSc, Département de neurologie, Unité de neuropsychologie clinique, CHU de Toulouse, Place du Dr Baylac, 31059 Toulouse cedex, France. *E-mail address:* julien.ade@chutoulouse.fr.

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