Update on the efficacy of cognitive rehabilitation following moderate to severe traumatic brain injury: a scoping review

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Update on the efficacy of cognitive rehabilitation following moderate to severe traumatic brain injury: a scoping review.

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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 one 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.

Keywords: Brain injuries; Cognitive Remediation; Rehabilitation; Review.

List of abbreviations:

CRTF: cognitive rehabilitation task force
DAI: diffuse axonal injury
DMN: default mode network
EEG: electroencephalography
ECN: executive control network
fMRI: functional magnetic resonance imaging
Cognitive disorders after a traumatic brain injury (TBI) have been well described over the last 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\textsuperscript{2,3}, impacting vocational integration and quality of life\textsuperscript{4,5}. Cognitive rehabilitation aims to decrease acquired neurocognitive impairment and disability using various and complementary approaches\textsuperscript{6}. Interventions could aim to train or strengthen impaired cognitive functions and/or to implement compensatory mechanisms in addition to external aids\textsuperscript{6}. Metacognitive strategies are also trained in order to facilitate the transfer to different environmental contexts\textsuperscript{7–9}.

Over the last 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 (CRTF) of the American Congress of Rehabilitation Medicine\textsuperscript{10}. Since 2000, Cicerone and colleagues have published 4 successive systematic reviews on the cognitive rehabilitation of patients with TBI or stroke and established evidence-based clinical recommendations\textsuperscript{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 al.\textsuperscript{10} 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 impact 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 \(^{13-15}\), neurological and
neuropsychological patterns \(^{16-18}\), psychological conditions associated with TBI \(^{19}\),
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 two very specific approaches that focused on driving
rehabilitation \(^{25}\) and the use of repeated transcranial magnetic stimulation on
cognitive functioning \(^{24}\).

The literature about cognitive rehabilitation following 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 \(^{10}\). In this paper, 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 mild TBI population
because the functional and cognitive outcomes differ from 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
four main questions: (i) Which cognitive domains does cognitive rehabilitation focus on? (ii) What are the characteristics of interventions in cognitive rehabilitation? (iii) What are the outcome measures used by authors? (iv) What is the efficacy of cognitive rehabilitation?

Methods

The scoping review was based on the framework developed by Arksey & O’Malley including the successive stages described below.

1.1. Search strategy

A systematic search of publications listed in the Pubmed (via Medline) and PsycINFO databases was conducted in August 2021 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.
1.2. **Inclusion and exclusion criteria**

Inclusion criteria were: (i) 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 post-traumatic 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...) \(^\text{28}\). We also reported for each article if 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; (ii) patients had to be included at least 3 months after the onset; (iii) interventions had to investigate the rehabilitation of cognitive functions; (iv) effects of cognitive rehabilitation had to be documented by quantitative or qualitative comparisons throughout follow-up; (v) interventions had to be conducted in a rehabilitation center, 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, two 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.
1.3. Data analysis

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

1.3.1. 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 three or more cognitive functions, or when the aim was defined with the generic term “cognitive skills.”

1.3.2. Characteristics of cognitive rehabilitation

Types of cognitive rehabilitation were divided into three 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 non-invasive brain stimulation (NIBS).

Three other parameters of cognitive interventions were analyzed: the delivery mode including group versus individual sessions, the length and the intensity. Length was studied by distinguishing very short (1 week or less), short (1 week to 1 month), moderate (1 to 3 months) and high (more than 3 months) duration. Intensity was classified as low (1 session per week), moderate (2 sessions per week) or high (3 or more sessions per week).

### 1.3.3. Behavioral examination and neuroimaging as outcome measures

Concerning behavioral outcome measures, four types of assessment were distinguished: (i) *neuropsychological examination* including standardized neuropsychological tests; (ii) *ecological neuropsychological examination* including standardized tests and/or experimental ecological tasks with reference to daily life situations; (iii) *self-reporting* of cognitive complaints, social participation in everyday activities and quality of life; (iv) *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).

1.3.4. Efficacy of cognitive rehabilitation

The efficacy of cognitive rehabilitation was analyzed according to three main criteria and associated sub-criteria 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 one 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, non-randomized 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-subjects 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 criteria. As proposed by Cicerone et al.\textsuperscript{29}, 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 (ITT) analysis. Finally, we analyzed whether the effect size and measures of variability such as confidence intervals were reported.

1.4. Charting the data

In accordance with the PRISMA-Scr guidelines\textsuperscript{30}, 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 pre-cited methodological criterion and associated sub-criteria. For each study, the key characteristics of TBI participants, cognitive rehabilitation, experimental design, intervention, neuropsychological outcome measures and significant main results were collected and 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 two 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.

2.1. 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%).

2.2. Characteristics of cognitive rehabilitation
2.2.1. 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 (4%) did not detail the type of intervention
31,32. The effects of combined interventions were examined in 4 studies 33–36, in which
cognitive rehabilitation was associated with pharmacotherapy 36, repetitive
transcranial magnetic stimulation (rTMS) 33 or transcranial direct current stimulation
(tDCS) 34,35.

2.2.2. 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 (n=3) of the studies combined individual and group sessions.

Furthermore, the length of interventions was heterogeneous, ranging from 5 days 34
to 15 months 37. Fifty-four percent of studies (n=25) proposed an intervention which
lasted between 1 and 3 months. Shorter interventions lasting 1 week to 1 month were
found in 24% of studies (n=11). Finally, cognitive rehabilitation interventions including
a duration of less than 1 week or longer than 3 months were found in 1 (2%) and 8 studies (18%), respectively. In one study (2%), this methodological feature was not detailed.

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

Our results indicated that 9 out of the 46 studies (20%) did not detail both the length and intensity of the interventions. 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.

2.3. 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 (n=23) included a self-report questionnaire, 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 (n=17) used one of these 4 types of measures, 28% of studies (n= 13) used 2 types of measures and 24% (n=11) used 3 types of measures. In contrast, 11% of studies (n=5) proposed an exhaustive evaluation with these 4 types of measures.

Neuroimaging outcome measures used as brain markers of cognitive rehabilitation were reported in 20% (n=9) of studies, whereas EEG was performed in only two studies \(^{38,40}\). More specifically, resting state functional magnetic resonance imaging (fMRI) \(^{41}\), regional cerebral blood flow \(^{33}\) and brain activation during an fMRI cognitive task \(^{34,42}\) were analyzed in 4 studies. Structural MRI data were reported in 4 studies \(^{43-46}\). Only one paper combined diffusion tensor imaging, attention-related fMRI and resting-state fMRI sequences \(^{47}\).

2.4. Efficacy of cognitive rehabilitation

According to Cicerone’s criteria for evidence-based classes \(^{6}\), 41% (n= 19) of reviewed studies were classified as class I, 13% (n=6) \(^{39,46,62-65}\) as class II and 46% (n=21) \(^{31-33,35,37,40,41,43,45,47,66-76}\) as class III.

Ninety-three percent of studies reported significant cognitive improvement on at least one 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 \(^{34,36,42,44,48,49,52-54,56}\). Then, with regard to statistical analysis, these 10 studies applied
between-groups comparisons to assess the efficacy of treatment, among which 7 used an intention-to-treat analysis (15% of reviewed studies)\textsuperscript{34,42,44,49,52,53,56}. Medium to large effect sizes were reported in 5 out of these 7 studies\textsuperscript{44,49,52,53,56} and the confidence interval was reported in only one out of these 7 studies\textsuperscript{49}.

Discussion

This scoping review was conducted starting with 2015, after the most recent systematic review\textsuperscript{10}, in order to identify and characterize studies evaluating cognitive rehabilitation following 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 two behavioral outcome measures were mostly preferred by authors to assess the efficacy of intervention, while 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 and colleagues’ conclusions in 2013\textsuperscript{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 by identifying five key methodological points.

3.1. Specific experimental designs for cognitive rehabilitation of TBI patients

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% to 20% until 2008, which increased to 36% between 2009 and 2014. RCTs were crucial for evidence-based studies but not always relevant in rehabilitation practice, where double blind was sometimes not feasible 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, length and intensity of rehabilitation to allow between-groups comparisons. 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. 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 these methodological points were controlled in one study, 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 al. and Van Rijn et al. in aphasia therapy. 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 (SCED). Multiple baseline design includes a small number of patients (i.e. classically at least 3 participants), has high feasibility and allows for an individualized approach. The high level of evidence of SCED 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 \(^{63,82-84}\).

3.2. **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 three 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. \(^52\), in a randomized controlled trial of 18 TBI patients, showed the benefits of goal management training associated with working memory training (GMT + WM group) in comparison with an isolated WM group on multistep everyday tasks and ecological executive measures, with small to large effects 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 two delivery modes was proposed in 3 studies, but its specific benefits were not analyzed \(^{61,73,74}\).
The third level concerned the use of combined interventions. Only 4 studies proposed combined rehabilitation with pharmacotherapy \textsuperscript{36} or NIBS \textsuperscript{33–35}. The heterogeneous designs and the low statistical power of these studies call for replication.

3.3. **Specific effects of length and intensity of cognitive rehabilitation**

The main temporality reported by this scoping review included a moderate duration (i.e. ranging between 1 and 3 months) with a high intensity (i.e. 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. \textsuperscript{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 two parameters were analyzed across all reviewed studies. Furthermore, Chiaravalotti et al. \textsuperscript{49} 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.

3.4. 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 evidence-based 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 wash-out 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. In this way, an ecological cognitive assessment could be a sensitive measure to predict real-life performance. Ecological tests such as the Test of Everyday Attention or the Rivermead Behavioral Memory Test were frequently proposed in the reviewed studies but remained in non-ecological environments and encompassed a restricted representation of daily life tasks. Conversely, the Multiple Errands Test (MET)
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. MET should be combined with person-centered assessment to improve the clinical relevance of the evaluation. The Goal Attainment Scaling (GAS), 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.

In the scoping review, two authors developed ecological experimental tasks to assess the effect of executive rehabilitation. Emmanouel et al. proposed multistep daily activities such as sending a text message or buy 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 al. 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 (i.e. standardized examination, ecological assessment, self- and relative-reports) were reported in only 5 studies.
3.5. **Multiple contributions of neuroimaging in cognitive interventions**

Magnetic resonance imaging was used in 20% of reviewed studies. The use of neuroimaging tools still remained scarce in recent years, which is in agreement with Galetto and Sacco, 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, Chiaravalotti et al. 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 (ECN) and an activation of the default mode network (DMN) 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 TBI 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.

3.6. Study limitations

A few main limitations were identified in the scoping review. The first concerned the search strategy, which focused on only two databases and did not include the gray literature. As reported, the impact of publication biases could contribute to an inaccurate picture of the literature on cognitive rehabilitation. Second, only one reviewer performed data extraction and analysis. While 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. In consequence, this led to higher number of studies that show an improvement in the primary outcome measures after cognitive rehabilitation. Our findings make it possible to identify three methodological criteria and sub-criteria 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\textsuperscript{6,10–12} which 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 non-ecological 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 confronted with systematic reviews and meta-analyses.


84. Lane-Brown A, Tate R. Evaluation of an Intervention for Apathy After Traumatic Brain Injury: A Multiple-Baseline, Single-Case Experimental Design. *J Head Trauma Rehabil*. Published online 2010:11. doi:10.1097/HTR.0b013e3181d98e1d


List of figure legends

**Figure 1:** Flow diagram for the scoping review process with PRISMA-Scr guidelines.
Figure 2: Flow diagram for the level of evidence in the efficacy of cognitive rehabilitation in the reviewed studies.
Table 1: Summary of reviewed studies on cognitive rehabilitation post-traumatic brain injury

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.

<table>
<thead>
<tr>
<th>Executive functions</th>
<th>Authors and level of evidence</th>
<th>Participants</th>
<th>Cognitive rehabilitation characteristics</th>
<th>Design</th>
<th>Intervention characteristics</th>
<th>Neuropsychological outcome measures</th>
<th>Significant main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho et al. 75</td>
<td>Class III</td>
<td>3 TBI, including 2 severe TBI</td>
<td>60 minutes per week</td>
<td>Intra-individual comparison: help-seeking scores before vs. after CR.</td>
<td>Group sessions</td>
<td>NICE training protocol (Noticing you have a problem, Identifying the information you need for help, Compensatory strategies, Evaluating progress): Intervention protocol targeting help-seeking behaviors during wayfinding.</td>
<td>Ecological executive assessment (Executive function route-finding task). - Absence of statistical analysis - Improvements for all three patients of ecological measures and structured role-plays.</td>
</tr>
<tr>
<td>Study</td>
<td>Class</td>
<td>TBI Type</td>
<td>Age (Mean ± SD)</td>
<td>Duration</td>
<td>Frequency</td>
<td>Sessions</td>
<td>Intergroup Comparison</td>
</tr>
<tr>
<td>------------------------</td>
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<td>----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Constandinidou et al.</td>
<td>II</td>
<td>15 moderate to severe TBI</td>
<td>28.13 (9.21)</td>
<td>60 minutes</td>
<td>2 to 4 per week</td>
<td>10-12 weeks</td>
<td>Intergroup comparison: Categorization performance (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.</td>
</tr>
<tr>
<td>Elbogen et al.</td>
<td>I</td>
<td>112 TBI with PTSD, including 57% moderate to severe TBI</td>
<td>36.52 (8.42)</td>
<td>60-90 minutes</td>
<td>3 home visits at 0, 2, 4 months</td>
<td>Over 6 months</td>
<td>Intergroup comparison: CR with a cognitive application for life management (CALM) vs. active control intervention including psychoeducational training.</td>
</tr>
<tr>
<td>Emmanouel et al.</td>
<td>I</td>
<td>18 brain-injured patients, including 11 moderate to severe TBI</td>
<td>35 (9)</td>
<td>30 minutes</td>
<td>3 to 4 per week</td>
<td>Total of 11 sessions</td>
<td>Intergroup comparison: CR combining goal management training (GMT) + working memory training (WMT) vs. control intervention including GMT only.</td>
</tr>
<tr>
<td>Study</td>
<td>Class</td>
<td>Participant Details</td>
<td>Intervention Details</td>
<td>Outcome Details</td>
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<tr>
<td>Goodwin et al.</td>
<td>Class III</td>
<td>66 ABI patients, including 50 traumatic injuries (46 closed head injuries and 4 open head injuries)</td>
<td>Intensive phase: 4 full days a week Over 12 weeks</td>
<td>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. - Re-integration phase.</td>
<td>Executive functioning and behavioral questionnaire (self- and relative-reports). Lower number of self-reported and relative-reported dysexecutive symptoms.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gracey et al.</td>
<td>Class I</td>
<td>59 acquired non-progressive brain injuries, including 27 patients with TBI</td>
<td>90 to 120 minutes Total number of sessions varied depending on the abilities of the participant</td>
<td>Longitudinal intergroup comparison - Cross-over design: Assisted intention monitoring vs. control intervention (information and games). Individual sessions Assisted intention monitoring (AIM): Brief GMT combined with periodic SMS text messages.</td>
<td>Proportion of daily intentions achieved by participant. Improvement of achievement intentions after the intervention phase compared to the control condition (medium effect sizes).</td>
<td></td>
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</tr>
</tbody>
</table>

Age: Detailed for each group. Not for total sample.  
Min. mean age: 47.79 (14.72)  
Max. mean age: 49.76 (12.94)
<table>
<thead>
<tr>
<th>Authors</th>
<th>Class</th>
<th>Type of TBI</th>
<th>Age (years)</th>
<th>Time (weeks)</th>
<th>Intergroup Comparison</th>
<th>Interventions</th>
<th>Assessment</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hart et al. 55</td>
<td>Class I</td>
<td>8 moderate to severe TBI</td>
<td>23.8 (4.3)</td>
<td>8</td>
<td>No more details</td>
<td>Goal intention intervention (with text messaging) vs. active control group who received unspecific text messages.</td>
<td>Individual sessions</td>
<td>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).</td>
</tr>
<tr>
<td>Powell et al. 57</td>
<td>Class I</td>
<td>23 ABI (including 14 motor vehicle crashes, 1 fall and 2 assaults)</td>
<td>44 (15)</td>
<td>Over 8 weeks</td>
<td>Total of 6 sessions</td>
<td>Intra-individual comparison: problem solving, self-efficacy and life satisfaction self-report scores before vs. after CR.</td>
<td>Individual sessions</td>
<td>No difference</td>
</tr>
<tr>
<td>Siponkoski et al. 44</td>
<td>Class I</td>
<td>40 moderate to severe TBI</td>
<td>41.3 (13.3)</td>
<td>Over 3 months</td>
<td>Total of 20 sessions</td>
<td>Longitudinal intergroup comparison - Cross-over design: intervention phase vs. control phase (standard care).</td>
<td>Individual sessions</td>
<td>Improvement of cognitive functioning in the AB group.</td>
</tr>
<tr>
<td>Vander Linden et al. 45</td>
<td>Class III</td>
<td>16 moderate to severe TBI ‡</td>
<td>15 years 8 months (1)</td>
<td>Over 8 weeks</td>
<td>Total of 40 sessions</td>
<td>Intergroup comparison: changes in gray matter volume in regions of interest related to executive functions after cognitive</td>
<td>Individual sessions</td>
<td>Scores on working memory, executive function, attention and processing speed tests.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Brain games software: Home-based cognitive training program</td>
<td></td>
<td>No difference on frontal gray matter volume after training.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Scores on executive function, memory, attention and reasoning tests.</td>
<td></td>
<td>Significant negative</td>
</tr>
</tbody>
</table>
Vander Linden et al. 55 Class II
16 moderate to severe TBI ‡

Age: 15 years 8 months (1 year 7 months)

40 minutes
5 per week
Over 8 weeks
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.

At 6-month 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. 76 Class III
5 moderate to severe TBIs ‡

Age: 16 (9 months)

40 minutes
5 per week
Over 8 weeks
Total of 40 sessions

Intra-individual comparison: executive performances 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.

Small to large effect size of intervention on all neuropsychological measures.

Results maintained or increased at 6-month follow-up.

Verhelst et al. 46 Class II
16 moderate to severe TBIs ‡

Age: 15 (1.8)

40 minutes
5 per week
Over 8 weeks
Total of 40 sessions

Intergroup comparison: white matter changes in TBI patient 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.

Time X group interaction effects on one attention score and on one executive function score (small to moderate effect sizes).
<table>
<thead>
<tr>
<th>Attention</th>
<th>Arroyo-Ferrer et al. 40</th>
<th>Class III</th>
<th>20-year-old man with TBI ‡</th>
<th>45 minutes</th>
<th>Case report</th>
<th>Individual sessions</th>
<th>Scores on executive function, memory, attention and visuospatial ability tests.</th>
<th>Improvement of visuospatial abilities, attention and executive functions after EEG-NFB intervention compared to after neuropsychological intervention.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Axonal damage was diagnosed using MRI</td>
<td>4 sessions per week</td>
<td>Over 6 weeks</td>
<td>Total of 16 sessions</td>
<td>EEG-based neurofeedback (EEG-NFB) intervention targeting inhibition of theta frequency band in frontal areas during exercises in virtual environments.</td>
<td>Neurropsychological intervention aiming attention, executive functions and working memory.</td>
<td>Correlative quantitative EEG changes were found.</td>
<td></td>
</tr>
<tr>
<td>Dundon et al. 38</td>
<td>26 TBI</td>
<td>Class I</td>
<td>Not detailed</td>
<td>Intergroup comparison: adaptive training group vs. non-adaptive training group vs. no training control group.</td>
<td>Individual sessions</td>
<td>Dichotic listening training task.</td>
<td>Scores on attention and memory tests.</td>
<td>Improvement with both trainings on cognitive variables.</td>
</tr>
<tr>
<td></td>
<td>Information regarding regions of damage for 23/26 participants...</td>
<td>Age: 37.3 (±9.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interaction between group and time was not significant.</td>
<td></td>
</tr>
<tr>
<td>Dymowski et al. 63</td>
<td>3 severe TBI ‡</td>
<td>Class II</td>
<td>Ages: 21, 27 and 53</td>
<td>60 minutes</td>
<td>Single case design repeated across subjects: baseline phase vs. attention training phase, and attention training phase vs. individualized strategies training phase.</td>
<td>Individual sessions</td>
<td>Computerized attention training: Attention process training 3 (APT-3)</td>
<td>Scores on processing speed and attention tests.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2-3 per week</td>
<td></td>
<td></td>
<td>Questionnaire of attentional complaint (self- and relative-reports).</td>
<td></td>
</tr>
</tbody>
</table>
Fitzgerald et al. 53

Class I
11 moderate to severe TBI ‡

Age: Detailed for each group. Not for total sample.
Min. mean age: 27.2 (5.6)
Max. mean age: 33.78 (13.33)

Intergroup comparison: error awareness training vs. no feedback group.
Individual sessions
Computer-based intervention program for improving error awareness: participants received feedback on errors.

Scores on global functioning, executive function and attention tests.

Self- and relative-reports on dysexecutive questionnaires.

Improvement of error awareness scores (large effect size in the experimental group).
No change in group who did not receive feedback.

McDonald et al. 36

Class I
72 TBI: 36 mild,
8 complicated mild,
8 moderate,
23 severe

Age: Detailed for each group. Not for total sample.
Min. mean age: 37.2 (12.0)
Max. mean age: 43.1 (12.3)

Intergroup comparison: cognitive behavioral therapy vs. repetitive cognitive tasks combined with methylphenidate or placebo.
Individual sessions
Memory and attention adaptation training (MAAT): metacognitive intervention.
Attention builders training (ABT): Repetitive cognitive tasks.

Scores on memory, attention, executive function and processing speed tests.

Improvement in scores for learning, working memory and divided attention after combined MAAT/ methylphenidate intervention.
Better memory improvement scores after MAAT compared to ABT intervention.

Sacco et al. 34

Class I
32 severe TBI

Age: 37.7 (10.4)

Intergroup comparison: real tDCS group vs. placebo tDCS group.
Individual sessions
Computerized rehabilitation of divided attention combined with unilateral or bilateral tDCS on dorsolateral prefrontal cortex (depending on the hemispheric

Scores on visuospatial, semantic fluency, divided attention, working memory and long-term memory tests.

Improvement in divided attention score in experimental group.
No change over the pretreatment phase and within the control
Vakili et al. 58

31 TBI
Average length of post-traumatic amnesia (days):

Intervention group: 41.87 (43.87)
Control group: 43.64 (35.64)

Age: Detailed for each group. Not for total sample.
Min. mean age: 27.73 (11.43)
Max. mean age: 28.63 (6.54)

Class I

2 hours Once a week Over 8 weeks Total of 8 sessions

Intergroup comparison:
Video games group vs. passive control group (usual care).

Group sessions
Sessions combined "Medal of Honor: Rising Sun" games on PlayStation 2 (first-person shooter action video game) and psychoeducational program with compensatory strategies.

Game performance on Playstation 2.

Attentional blink task.

Scores on attention tests.

Self-report questionnaires of quality of life, self-efficacy and executive functioning.

Improvement in game performance, attentional blink and attentional task, implying processing speed.
No change in behavioral and self-efficacy scales scores.

Jones et al. 48

15 ABI, including 9 moderate to severe TBI

45 minutes 1 session per week Over 3 weeks Total of 3 sessions

Intergroup comparison:
Music attention control training group (MACT) vs. attention process training (APT)

Individual sessions
Music attention control training (MACT): Structured music-based auditory training exercises to practice attention functions.

Scores on attention and executive tests.

Improvement in one of the three attention and executive tests (TMT B) after the intervention for the MACT group compared to the APT group.

APT:
Computer-based tasks to address focused, sustained, selective, alternating and divided...
<table>
<thead>
<tr>
<th>Class I</th>
<th>18 TBI: 3 mild, 3 moderate, 12 severe</th>
<th>TBI: 3 mild, 3 moderate, 12 severe</th>
<th>45 to 60 minutes</th>
<th>Intergroup comparison: treatment group vs. placebo control group (memory exercises but not exposed to critical components of training).</th>
<th>Individual sessions</th>
<th>BOLD signal on fMRI, word learning task and word recognition task.</th>
<th>Improvement in prose recall compared to placebo group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Detaile d for each group. Not for total sample.</td>
<td>Age: Detailed for each group. Not for total sample.</td>
<td>Age: Detailed for each group. Not for total sample.</td>
<td>Twice per week</td>
<td>Modified story memory technique, involving the training of mental imagery and the use of the source/context of learned information.</td>
<td>Scores on memory tests.</td>
<td>fMRI: Changes in activation in executive control network and default mode network (Bonferroni correction).</td>
<td></td>
</tr>
<tr>
<td>Min. mean age: 42.22 (14.12)</td>
<td>Min. mean age: 45.78 (10.53)</td>
<td>Min. mean age: 45.78 (10.53)</td>
<td>Over 5 weeks</td>
<td>Total 10 sessions</td>
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<tr>
<td>Class I</td>
<td>69 moderate to severe TBI</td>
<td>69 moderate to severe TBI</td>
<td>45 to 60 minutes</td>
<td>Intergroup comparison: treatment group vs. placebo control group (non-training-oriented tasks).</td>
<td>Individual sessions</td>
<td>Scores on memory tests.</td>
<td>Improvement in prose recall compared to placebo group.</td>
</tr>
<tr>
<td>Age: Detaile d for each group. Not for total sample.</td>
<td>Age: Detailed for each group. Not for total sample.</td>
<td>Age: Detailed for each group. Not for total sample.</td>
<td>Twice per week</td>
<td>Modified story memory technique, involving the training of mental imagery and the use of the source/context of learned information.</td>
<td></td>
<td>Ecological scores on the Rivermead Behavioural Memory Test.</td>
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</tr>
<tr>
<td>Min. mean age:</td>
<td>Min. mean age:</td>
<td>Min. mean age:</td>
<td>Over 5 weeks</td>
<td>Total 10 sessions</td>
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<td>No treatment effect on standardized memory scores.</td>
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<td>Improvement on Rivermead Behavioural</td>
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<tr>
<td>Age: Detailed for each group. Not for total sample.</td>
<td>65 ABI including 30 TBI, 27 CVAs, 4 encephalitis.</td>
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<tr>
<td>Min. mean age:</td>
<td>39.6 (15)</td>
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<tr>
<td>Max. mean age:</td>
<td>60 minutes 5 per week Over 3 weeks Total 15 sessions</td>
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<tr>
<td>Lesniak et al. 81</td>
<td>67-year-old man who sustained a diffuse axonal injury ‡</td>
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<tr>
<td>Class III</td>
<td>6 per week Case report Individual sessions rTMS (2400 pulses once a day) combined with CR (training program focused on memory and attention disorders).</td>
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<tr>
<td>Hara et al. 33</td>
<td>Memory Test in the experimental group compared to placebo group.</td>
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<tr>
<td>Intergroup comparison: individual therapy group vs. group therapy group vs. no therapy group.</td>
<td>Scores on memory tests. No difference between groups.</td>
<td></td>
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<tr>
<td>Increased awareness of memory deficits and learning of global strategies for everyday memory.</td>
<td>Ecological memory scores (RBMT).</td>
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<tr>
<td>Self-report of everyday memory complaint.</td>
<td>In individual therapy group, significant improvements on computerized memory, attention and working memory tests.</td>
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<tr>
<td>In group therapy group, decrease of memory failures in daily life (relatives-report).</td>
<td>- Absence of statistical analysis -</td>
<td></td>
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<td>2-point gain on the MMSE.</td>
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<tr>
<td>Study</td>
<td>Class</td>
<td>Age</td>
<td>Duration</td>
<td>Frequency</td>
<td>Interventions</td>
<td>Scores on cognitive</td>
<td>Gains</td>
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</tr>
<tr>
<td>Lesniak et al.</td>
<td>III</td>
<td>26.2 (7.6)</td>
<td>3 weeks</td>
<td>5 sessions</td>
<td>Individual sessions: exercises using memory strategies on Rehacom software.</td>
<td>Improvement of cognitive scores (small to moderate effect sizes).</td>
<td>Gains maintained at 4-month follow-up.</td>
</tr>
<tr>
<td>Raskin et al.</td>
<td>III</td>
<td>42.11 (13.21)</td>
<td>6 months</td>
<td>1 or 2 per week</td>
<td>Longitudinal intergroup comparison with mental imagery.</td>
<td>Improvement of prospective memory measure after active treatment phase only.</td>
<td>Improvement on self-report questionnaire for everyday memory.</td>
</tr>
<tr>
<td>Buccellato et al.</td>
<td>III</td>
<td>42 to 48</td>
<td>6 weeks</td>
<td>30 to 40 minutes</td>
<td>Longitudinal comparison - Cross-over within-subjects design: Global cognitive training phase with the Brainer Virtual</td>
<td>No significant difference between phases.</td>
<td>Improvement maintained at 1-year follow-up for all previous results.</td>
</tr>
<tr>
<td>Study Details</td>
<td>Rehabilitation</td>
<td>Cognitive Training</td>
<td>Neurobehavioral Symptoms Inventory and Mood Questionnaire</td>
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</table>

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Case Report</th>
<th>Intergroup Comparison: Virtual Reality Training Group vs. Traditional CR Group</th>
<th>Improvement in Selective Attention, Verbal Fluency, Visuospatial Ability and Executive Function Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>De la Rosa-Arredondo et al.</td>
<td>26-year-old woman with severe TBI</td>
<td>Individual sessions: Virtual reality training group vs. traditional CR group.</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Total of 24 sessions</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Phase 1 targeted sustained and selective attention and visuospatial abilities.</td>
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<td></td>
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<td>Phase 2 focused on memory and executive functions.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Scores on attention, working memory, memory, visuospatial and abstract reasoning tests.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Case Report</th>
<th>Intergroup Comparison: Virtual Reality Group vs. Traditional CR Group</th>
<th>Improvement in Cognitive and Mood Scores for Both Traditional and Virtual Reality Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Luca et al.</td>
<td>100 mild to moderate TBI</td>
<td>Individual sessions: Semi-immersive virtual reality using Nirvana BTs-N software, targeting attention, executive function and visuospatial training.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total of 24 sessions</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Scores on global scale, executive functions and attention tests.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improvement in cognitive flexibility for virtual reality training.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Case Report</th>
<th>Individual Sessions: Computerized CR with BrainHQ program (attention, processing speed, executive functions and working memory) combined with tDCS (anodal electrode on the left DLPFC and a cathodal electrode on the right DLPFC, 20 min 2</th>
<th>Improvement in several cognitive domains: attention, working memory, processing speed and semantic fluency.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eilam-Stock et al.</td>
<td>29-year-old man with a moderate TBI</td>
<td>5 times per week</td>
<td></td>
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<td>Over 4 weeks</td>
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<tr>
<td></td>
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<td>Total of 20</td>
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</tr>
</tbody>
</table>
### Hwang et al. 56

**Class I**

- **96 TBI**
- **Once a week**
- **Over 6 months**
- **No classification of severity.**
- **49% of participants with positive CT scan findings.**

**Intergroup comparison:**
- Computerized cognitive training (CCT) group or tai chi (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 in emotional functioning:** mood, sleep and fatigue.

### Kanchan et al. 39

**Class II**

- **10 moderate to severe TBI**
- **45 min**
- **1 to 5 times per week**
- **Over 6 months**

**Age:**
- **Total of sessions not specified**

**Intergroup comparison:**
- Computerized cognitive training vs. passive control group (no training).

**Individual sessions**
- Brainwave-R software: cognitive strategies and techniques for brain injury

**Scores on cognitive battery (Luria Nebraska Neuropsychological Battery Adults - Form I).**

**Improvement for all impaired cognitive areas in the experimental group.**
<table>
<thead>
<tr>
<th>Study</th>
<th>Class</th>
<th>Age</th>
<th>Intervention Details</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kumar et al.</td>
<td>III</td>
<td>34-year-old woman with severe TBI ‡</td>
<td>20-40 sessions session not specified, rehabilitation (attention, visual processing, information processing, memory, executive functions)</td>
<td>Differences between experimental group and passive control group after training.</td>
</tr>
<tr>
<td>Maggio et al.</td>
<td>II</td>
<td>56 TBI ‡</td>
<td>30 minutes 5 times per week, Lokomat training with virtual reality vs. Lokomat without virtual reality</td>
<td>Score on general cognitive status, frontal ability and attention tests. Improvements on global cognitive scores, executive and attention scores for the experimental group.</td>
</tr>
<tr>
<td>Pinard et al.</td>
<td>III</td>
<td>3 severe TBI</td>
<td>Over 15 months Length varied for each user</td>
<td>Qualitative scores of numbers of meals prepared per week with the stove, number of warnings, number of interventions of security modules. For two of three participants, increased number of meals prepared per week.</td>
</tr>
<tr>
<td>Ramanathan et al.</td>
<td>IV</td>
<td>54-year-old man</td>
<td>2.5 hours per day 4 times per day</td>
<td>Scores on executive and attentional functions and quality of life</td>
</tr>
<tr>
<td>Class III</td>
<td>severe TBI ‡</td>
<td>week</td>
<td>attention and prospective memory training and metacognitive strategy instructions.</td>
<td>tests.</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>------</td>
<td>-----------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Over 3 weeks</td>
<td>Total of 12 sessions</td>
<td>Self-report of quality of life.</td>
</tr>
</tbody>
</table>

| Resting state: greater functional integration of frontal and parietal cortices, visual and auditory association areas and portions of the cerebellar vermis. |

<table>
<thead>
<tr>
<th>Class I</th>
<th>90 TBI ‡</th>
<th>30 minutes per day</th>
<th>Intergroup comparison: Rehabilitation gaming group vs. entertainment gaming (PlayStation 3) group vs. passive control group (no gaming).</th>
<th>Individual sessions</th>
<th>Scores on processing speed, visuomotor tasks, attention, executive functions and working memory tests.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Over 8 weeks</td>
<td>Rehabilitation gaming with Cognifit software (cognitive training platform with three categories of exercises: memory, spatial and mental planning).</td>
<td>Executive self-report</td>
<td>No difference between the three groups.</td>
</tr>
</tbody>
</table>

Valimaki et al. 

Structural (DTI-measured FA; p < 0.01 uncorrected): increased FA in white matter tracts throughout the brain. Especially in tracts serving the prefrontal, occipito-parietal and temporal association cortices and cerebellum.
and sequelae of injuries to the head (ICD-10).

Age: 41

**Wu et al.**

<table>
<thead>
<tr>
<th>Class III</th>
<th>50-year-old man, TBI with multiple contusions and lacerations, diffuse axonal injury and scattered cerebral hemorrhages ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>30 minutes, 5 times per week, Over 1 month, Total of sessions not specified</td>
</tr>
<tr>
<td>Type</td>
<td>Case report</td>
</tr>
<tr>
<td>Interventions</td>
<td>Individual sessions</td>
</tr>
<tr>
<td>Description</td>
<td>Comprehensive multifaceted intervention including computer-assisted cognitive impairment rehabilitation system targeting memory, attention and visuospatial defects.</td>
</tr>
<tr>
<td>Outcome</td>
<td>Score on general cognitive status.</td>
</tr>
</tbody>
</table>

**Douglas et al.**

<table>
<thead>
<tr>
<th>Class III</th>
<th>13 severe TBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>35.2 (9.3)</td>
</tr>
<tr>
<td>Time</td>
<td>Twice per week, Over 6 weeks, Total of 12 sessions</td>
</tr>
<tr>
<td>Type</td>
<td>Intra-individual comparison: communication scores before vs. after intervention vs. 3-month follow-up.</td>
</tr>
<tr>
<td>Interventions</td>
<td>Individual sessions and with communication partner</td>
</tr>
<tr>
<td>Description</td>
<td>CommCope-I program: Communication-specific coping intervention.</td>
</tr>
<tr>
<td>Outcome</td>
<td>Communication specific coping scores.</td>
</tr>
<tr>
<td>Scores</td>
<td>Scores on functional communication abilities scale.</td>
</tr>
</tbody>
</table>

**Communication**

- 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.

Improvements in communication-specific coping strategies scores (moderate to medium effect sizes).

Improvements in functional communication scores (moderate effect size).
<table>
<thead>
<tr>
<th>Study</th>
<th>Class</th>
<th>TBI Level</th>
<th>Age (Mean±SD)</th>
<th>Treatment Duration</th>
<th>Treatment Details</th>
<th>Scores/Improvements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosco et al.</td>
<td>III</td>
<td>19 severe TBI</td>
<td>38.5 (10.6)</td>
<td>1.5 hours</td>
<td>Group sessions: Longitudinal comparison - Cross-over within-subjects design: Cognitive pragmatic treatment</td>
<td>Scores on attention, memory, executive function and logical reasoning tests. Overall improvement in pragmatic scores.</td>
</tr>
<tr>
<td>Gabbatore et al.</td>
<td>III</td>
<td>15 severe TBI ‡</td>
<td>36.7 (8.73)</td>
<td>1.5 hours</td>
<td>Group sessions: Longitudinal comparison - Cross-over within-subjects design: Cognitive pragmatic treatment</td>
<td>Improvement in comprehension and production scores. Improvement in long-term verbal memory and cognitive flexibility.</td>
</tr>
<tr>
<td>Sacco et al.</td>
<td>III</td>
<td>8 severe TBI</td>
<td>36.37 (8.6)</td>
<td>1.5 hours</td>
<td>Group sessions: Longitudinal comparison - Cross-over within-subjects design: Cognitive pragmatic treatment</td>
<td>Scores on communicative pragmatic tests. Improvement in comprehension and production scores.</td>
</tr>
</tbody>
</table>
### Social Cognition

<table>
<thead>
<tr>
<th>Study</th>
<th>Class</th>
<th>Age</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Westerhof-Evers et al.</td>
<td>Class I</td>
<td>43.2 (13)</td>
<td>60 minutes, 1 or 2 per week, Total of 16 to 20 sessions</td>
<td>Intergroup comparison: social cognition and emotional regulation protocol training vs. active control treatment (computerized cognitive training). Individual sessions T-ScEmo protocol including 3 modules (i, enhancing emotion perception, ii, perspective taking and theory of mind, iii, basic and goal-directed social behavior). Scores on social cognition tests. Scores on attention and executive function tests. Self- and relative-reports: dysexecutive symptoms, social monitoring, empathy.</td>
<td>Improvement for the experimental group on facial affect recognition, theory of mind compared to the control group. Improvement in relative-reported empathic behavior, and societal participation.</td>
</tr>
</tbody>
</table>

### Topographic orientation

<table>
<thead>
<tr>
<th>Study</th>
<th>Class</th>
<th>Age</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boccia et al.</td>
<td>Class III</td>
<td>49-year-old man with extensive head trauma and a coma (period of 1 week)</td>
<td>Over 8 weeks</td>
<td>Case report</td>
<td>Individual session Imagery-based treatment including two phases (i, imagery training in order to rapidly generate mental images, ii, generating and retrieving mental images). Scores on working memory, cognitive map test and 3D mental rotation tests. Ecological navigational tasks in real environment.</td>
</tr>
</tbody>
</table>

### Verbal auditory perception

<table>
<thead>
<tr>
<th>Study</th>
<th>Class</th>
<th>Age</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al.</td>
<td>Class III</td>
<td>65-year-old patient with TBI</td>
<td>Over 2 months</td>
<td>Case report</td>
<td>Individual sessions Speech therapy and cognitive rehabilitation (cognitive domains not specified). Scores on global cognitive scale and aphasia test.</td>
</tr>
</tbody>
</table>
* Participants: n, TBI severity, mean age in years (SD)

† Cognitive rehabilitation characteristics: Length for each session; intensity (e.g. 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.

ABI: acquired brain injury
BOLD: blood-oxygen-level dependent
CR: cognitive rehabilitation
CT scan: computed tomography scan
CVA: cerebral vascular accidents
DTI: diffusion tensor imaging
FA: fractional anisotropy
ICD: international classification of diseases
MMSE: mini mental state examination
PTSD: post-traumatic stress disorder