Review of clinical trials on the effectiveness of cognitive rehabilitation in patients with traumatic brain injury

Leandro Mendoza Rivas1, Laura Martínez Cruz1

Abstract

Introduction: Traumatic brain injury (TBI) can impact patients’ cognitive functioning and quality of life. This study assesses the effectiveness of cognitive interventions in TBI patients and examines factors influencing their success, aiming to enhance care and customize treatments for optimal rehabilitation outcomes.

Methods: a systematic review of 31 scientific articles evaluating the effectiveness of cognitive rehabilitation in patients with traumatic brain injuries was conducted, following the PRISMA workflow. The studies covered the period from 2017 to 2021, and specific terms were used to search the PubMed and Scopus databases.

Results: the research on cognitive interventions in patients with traumatic brain injuries has involved various countries, with notable contributions from the United States, Norway, the United Kingdom, and Canada. Cognitive training has proven to be effective, showing significant improvements in symptoms and quality of life. Other therapies, such as transcranial direct stimulation and vocational rehabilitation, have also been investigated.

Conclusions: cognitive training has proven to be an effective technique in managing traumatic brain injuries, demonstrating significant improvements in composite cognitive measures and patients’ quality of life. Some therapies, such as hyperbaric oxygen therapy, have shown promising results in treating symptoms such as post-traumatic stress, depression, and anxiety in patients with traumatic brain injuries.

Keywords: Cognitive Training; Craniocerebral Trauma; Traumatic Brain Injuries; Cerebrovascular Trauma; Diffuse Brain Injuries.
Conclusiones: el entrenamiento cognitivo ha demostrado ser una técnica eficaz en el manejo de las lesiones cerebrales traumáticas, demostrando mejoras significativas en las medidas cognitivas compuestas y en la calidad de vida de los pacientes. Algunas terapias, como la oxigenoterapia hiperbárica, han mostrado resultados prometedores en el tratamiento de síntomas como el estrés postraumático, la depresión y la ansiedad en pacientes con lesiones cerebrales traumáticas.

Palabras clave: Entrenamiento Cognitivo; Traumatismo Craneoencefálico; Lesiones Cerebrales Traumáticas; Traumatismo Cerebrovascular; Lesiones Cerebrales Difusas.

INTRODUCTION

Traumatic brain injury (TBI) is a condition that can have a significant impact on individuals' cognitive functioning. It is characterized by impairments in various cognitive functions such as memory, attention, processing speed, executive function, and visuospatial skills. These cognitive difficulties can negatively affect the quality of life, functional independence, and social reintegration of TBI patients.\(^{(1,2)}\)

These injuries occur as a result of an external impact or force that affects the brain, causing structural and functional damage. The consequences of traumatic brain injury can be significant, especially in terms of cognitive functions.\(^{(3)}\)

Brain plasticity is a concept that underlies cognitive interventions for patients with traumatic brain injury. It refers to the brain's ability to change and adapt in response to experience and training. Although traumatic brain injury can cause damage to brain cells and neuronal connections, it has been shown that the brain has the capacity to reorganize and generate new neuronal connections in undamaged areas.\(^{(4)}\)

Brain plasticity is based on various neurobiological mechanisms such as synaptogenesis, neurogenesis, and dendritic remodeling. These processes allow the brain to recover and compensate for the damaged cognitive functions. In the context of cognitive interventions, the aim is to harness brain plasticity to improve cognitive skills and promote functional recovery in patients with traumatic brain injury.\(^{(5)}\)

One of the most commonly used cognitive interventions is cognitive training. This intervention is based on the principle that the brain can enhance its cognitive functioning through practice and repeated training of specific tasks. Cognitive training focuses on areas such as memory, attention, executive function, and visuospatial skills, which are often affected in patients with traumatic brain injury.\(^{(6)}\)

In addition to cognitive training, other therapeutic interventions have shown effectiveness in managing patients with traumatic brain injury. For example, hyperbaric oxygen therapy has shown benefits in improving symptoms of post-traumatic stress disorder, memory, cognitive functions, depression, anxiety, sleep, and quality of life in patients with persistent post-concussion syndrome.\(^{(7)}\)

Vocational rehabilitation also plays an important role in the management of patients with traumatic brain injury. This intervention focuses on helping patients reintegrate into the workforce by providing them with the necessary skills and support to successfully return to work. The combination of cognitive and vocational interventions has been shown to be effective in improving the employment return rate in patients with traumatic brain injury.\(^{(8)}\)

In addition to these interventions, other strategies such as transcranial stimulation and virtual rehabilitation therapy have been investigated. These interventions aim to leverage emerging technologies to provide an interactive and personalized rehabilitation environment for patients with traumatic brain injury.\(^{(9)}\)

Over the years, numerous studies and interventions have been conducted to address the cognitive difficulties associated with TBI and improve the quality of life of patients. In this article, we present a comprehensive literature review of 31 studies investigating different approaches to cognitive and therapeutic intervention in patients with TBI, addressing the following research question: What is the effectiveness of cognitive interventions in patients with traumatic brain injury, and what factors influence their effectiveness?

This research aims to evaluate the effectiveness of cognitive interventions in patients with traumatic brain injury and understand the factors that may influence their effectiveness. Identifying the most effective interventions and the factors that affect them will enable us to improve care and personalize treatments to optimize rehabilitation outcomes and patients' quality of life.

The studies included in this review cover a wide range of therapeutic approaches and samples of TBI patients from different countries. Among the reviewed studies, randomized controlled trials, observational studies, and pilot studies were found, evaluating the efficacy of interventions such as cognitive training, hyperbaric oxygen therapy, vocational rehabilitation, transcranial stimulation, virtual rehabilitation therapy, among others.

METHODS

A systematic review was conducted following the PRISMA workflow. Scientific articles of clinical studies on
the effectiveness of cognitive rehabilitation in patients with traumatic brain injuries were included. The study period ranged from 2017 to 2021.

The search was performed in the PubMed and Scopus databases. The search expression was constructed using the following MeSH terms: (Cognitive Training) AND (Craniocerebral Trauma OR Traumatic Brain Injuries OR Cerebrovascular Trauma OR Diffuse Brain Injuries).

The following filters were applied: years 2017-2021; full-text available; clinical trial, clinical trial protocol, phase I, II, III, and IV clinical trial; English and Spanish language.

Duplicate articles and those that did not fit the research topic were removed.

Finally, 31 articles were selected.

RESULTS

A total of 31 articles were included with the previously described criteria and filters. The authors and origin, trial type, sample characteristics, cognitive intervention used, and main results were analyzed. The presence of conflicts of interest was also identified.

Figure 1 presents the workflow according to the PRISMA methodology. It outlines how the criteria and filters were applied.

![Flowchart for the review of the state of the art according to PRISMA methodology](https://doi.org/10.56294/ri202225)

Table 2 displays the main results of the 31 articles studied.

DISCUSSION

When analyzing the results of the included studies, a wide variety of countries involved in the research of cognitive interventions in patients with traumatic brain injuries can be observed. Among the prominent countries are the United States, represented by studies such as Harch et al., which demonstrated significant improvements in post-traumatic stress disorder symptoms, memory, cognitive functions, depression, anxiety, sleep, and quality of life through hyperbaric oxygen therapy. Norway, represented by studies like Fure et al. and Howe et al., which showed that cognitive training combined with vocational rehabilitation increased the rate of return to work in patients with traumatic brain injuries. The United Kingdom and Canada have also made significant contributions in this field, such as the study by Elbogen et al., which demonstrated reduction in anger and maladaptive interpersonal behaviors in veterans with traumatic brain injuries and post-traumatic stress disorder.

Regarding the most used techniques, cognitive training in its various forms stands out. The study by Mahncke et al. demonstrated significant improvements in composite cognitive measures in the treatment group compared to the control group. Additionally, the study by Lu et al. showed that intensive rehabilitation training combined with hyperbaric oxygen therapy improved functional disorders and prognosis in patients with traumatic brain injuries.

https://doi.org/10.56294/ri202225
<table>
<thead>
<tr>
<th>No</th>
<th>Author (Year)</th>
<th>Country</th>
<th>Type of study</th>
<th>Sample</th>
<th>Cognitive Intervention/ Treatment/ Intervention</th>
<th>Main outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fure et al. (2021)</td>
<td>Norway</td>
<td>Randomized controlled trial</td>
<td>116 individuals with mild to moderate traumatic brain injury</td>
<td>Cognitive training and vocational rehabilitation</td>
<td>The intervention group showed a significantly higher proportion of participants returning to stable employment at 3 months compared to the treatment as usual group. No significant differences were found in other outcome measures</td>
</tr>
<tr>
<td>2</td>
<td>Harch et al. (2020)</td>
<td>United States of America</td>
<td>Randomized controlled trial</td>
<td>63 civilian and military subjects with persistent postconcussion syndrome after mild traumatic brain injury</td>
<td>Hyperbaric oxygen therapy</td>
<td>Subjects who received hyperbaric oxygen therapy experienced significant improvements in post-traumatic stress disorder symptoms, memory, cognitive functions, depression, anxiety, sleep and quality of life compared to the control group</td>
</tr>
<tr>
<td>3</td>
<td>Mahncke et al. (2021)</td>
<td>United States of America</td>
<td>Randomized controlled trial</td>
<td>Military/veteran participants with a history of mild traumatic brain injury and cognitive impairment.</td>
<td>Cognitive training based on plasticity</td>
<td>The treatment group showed significantly greater improvement in the composite cognitive measure compared to the active control group. Improvements were also seen in other measures of cognitive function</td>
</tr>
<tr>
<td>4</td>
<td>Howe et al. (2017)</td>
<td>Norway</td>
<td>Randomized controlled trial</td>
<td>Patients with mild to moderate traumatic brain injury who experienced difficulties returning to work</td>
<td>Combined cognitive and vocational interventions</td>
<td>The group that received combined cognitive rehabilitation and job support showed a higher proportion of participants returning to work at 12 months compared to the control group</td>
</tr>
<tr>
<td>5</td>
<td>Lu et al. (2021)</td>
<td>China</td>
<td>Randomized controlled trial</td>
<td>Traumatic brain injury patients</td>
<td>Early intensified rehabilitation training with hyperbaric oxygen therapy</td>
<td>Intensive rehabilitation training combined with hyperbaric oxygen therapy improved functional disorders and prognosis in patients with traumatic brain injury</td>
</tr>
<tr>
<td>6</td>
<td>Teel et al. (2018)</td>
<td>United States of America</td>
<td>Randomized controlled trial</td>
<td>Healthy participants with aerobic training</td>
<td>Aerobic workout</td>
<td>Aerobic training had no significant effect on clinical assessments of sports-related concussion in healthy participants</td>
</tr>
<tr>
<td>7</td>
<td>Fleming et al. (2017)</td>
<td>Australia</td>
<td>Randomized controlled trial</td>
<td>Participants with traumatic brain injury</td>
<td>Prospective memory rehabilitation plus metacognitive skills training</td>
<td>Prospective memory rehabilitation therapy coupled with metacognitive skills training improved cognitive skills and psychosocial integration in adults with traumatic brain injury</td>
</tr>
<tr>
<td>8</td>
<td>Han et al. (2020)</td>
<td>United States of America</td>
<td>Neuroimaging study</td>
<td>Participants with traumatic brain injury</td>
<td>Cognitive training</td>
<td>Cognitive training reorganized modular networks in the brain after traumatic brain injury</td>
</tr>
<tr>
<td>9</td>
<td>Krawczyk et al. (2019)</td>
<td>United States of America</td>
<td>Randomized controlled trial</td>
<td>Participants with chronic traumatic brain injury</td>
<td>Executive function training</td>
<td>The electronic cognitive rehabilitation program improved daily cognitive skills and daily functions in individuals with chronic traumatic brain injury</td>
</tr>
<tr>
<td>10</td>
<td>McDonald et al. (2017)</td>
<td>United States of America</td>
<td>Randomized controlled trial</td>
<td>Participants with traumatic brain injury</td>
<td>Methylphenidate and adaptive memory and attention training for persistent cognitive symptoms</td>
<td>The combination of adaptive memory and attention training and the use of methylphenidate improved cognitive function after persistent traumatic brain injury</td>
</tr>
<tr>
<td>Study ID</td>
<td>Authors and Year</td>
<td>Country</td>
<td>Study Design</td>
<td>Sample Description</td>
<td>Intervention Details</td>
<td>Outcome Details</td>
</tr>
<tr>
<td>---------</td>
<td>------------------</td>
<td>---------</td>
<td>--------------</td>
<td>--------------------</td>
<td>---------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>11</td>
<td>Freitas et al. (21), 2021</td>
<td>Brazil</td>
<td>Double-blind, randomized, placebo-controlled trial</td>
<td>36 participants with chronic, moderate, and severe traumatic brain injury</td>
<td>Transcranial direct current stimulation (tDCS) and simultaneous cognitive training on episodic memory</td>
<td>Improvements in episodic memory with active tDCS compared to sham tDCS. Differences in episodic memory scores between active IDLPFC and BTC stimulation. Reduced cortical activity measured by qEEG in the active tDCS group</td>
</tr>
<tr>
<td>12</td>
<td>Elbogen et al. (22), 2019</td>
<td>United Kingdom</td>
<td>Randomized controlled trial</td>
<td>112 dyads of veterans with TBI and PTSD</td>
<td>Cognitive rehabilitation with mobile technology and social support</td>
<td>Reduction in anger and maladaptive interpersonal behaviors in the CALM group. Improvement in PTSD symptoms in the CALM group</td>
</tr>
<tr>
<td>13</td>
<td>Corti et al. (23), 2018</td>
<td>Italy</td>
<td>Exploratory study</td>
<td>32 Italian adolescents with congenital or acquired brain damage</td>
<td>Computer-based cognitive training at home</td>
<td>Feasibility of computer-based cognitive training program CCT (Lumosity) with high adherence and no significant technical problems</td>
</tr>
<tr>
<td>14</td>
<td>Corti et al. (24), 2020</td>
<td>Italy</td>
<td>Randomized controlled trial</td>
<td>Unspecified sample of pediatric patients with acquired brain lesions</td>
<td>Computer-based cognitive training at home</td>
<td>Improvements in visuospatial working memory after training. The training-first group also showed improvements in arithmetic calculation speed</td>
</tr>
<tr>
<td>15</td>
<td>Assecondi et al. (25), 2020</td>
<td>United Kingdom</td>
<td>Randomized controlled trial</td>
<td>Patients with acquired brain damage</td>
<td>Simultaneous brain stimulation (tDCS) and working memory training on cognitive performance.</td>
<td>Results not yet available</td>
</tr>
<tr>
<td>16</td>
<td>Séguin et al. (26), 2018</td>
<td>Canada</td>
<td>Randomized controlled trial</td>
<td>Participants with pediatric TBI</td>
<td>Intensive training of attention processes</td>
<td>Improvements in working memory, inhibition and cognitive flexibility after the RST training program</td>
</tr>
<tr>
<td>17</td>
<td>Novakovic-Agopian et al. (27), 2018</td>
<td>United States of America</td>
<td>Randomized controlled trial</td>
<td>Veterans with chronic TBI and executive difficulties</td>
<td>Goal-oriented attention self-regulation</td>
<td>Significant improvements in cognitive and functional performance after goal-regulated attention training</td>
</tr>
<tr>
<td>18</td>
<td>Cisneros et al. (28), 2021</td>
<td>Canada</td>
<td>Controlled before and after study</td>
<td>Older patients with TBI</td>
<td>Multimodal cognitive rehabilitation in executive functions</td>
<td>Improvements in executive functions and ability to resume daily activities after multimodal cognitive rehabilitation program</td>
</tr>
<tr>
<td>19</td>
<td>Lu et al. (29), 2021</td>
<td>Norway</td>
<td>Randomized controlled trial</td>
<td>Construction workers with craniocerebral trauma</td>
<td>Rehabilitation training based on the concept of the International Classification of Functioning, Disability and Health (ICF)</td>
<td>Significant improvement in neurological function, cognitive function, limb motor function and self-care ability with rehabilitation training based on the ICF concept</td>
</tr>
<tr>
<td>20</td>
<td>Gilmore et al. (30), 2019</td>
<td>United States of America</td>
<td>Observational study</td>
<td>Young individuals with chronic acquired brain injury</td>
<td>Cognitive-communicative rehabilitation</td>
<td>Significant improvements in cognitive-linguistic functioning, classroom participation, and quality of life after intensive cognitive-communicative rehabilitation (ICCR) program</td>
</tr>
<tr>
<td>21</td>
<td>Du et al. (31), 2018</td>
<td>China</td>
<td>Observational study</td>
<td>60 patients with brain injury</td>
<td>Scalp acupuncture and cognitive training</td>
<td>Scalp acupuncture combined with cognitive training improved cognitive impairment in patients with brain injury</td>
</tr>
<tr>
<td>No.</td>
<td>Authors (Year)</td>
<td>Country</td>
<td>Study Design</td>
<td>Sample</td>
<td>Intervention</td>
<td>Outcome Measures</td>
</tr>
<tr>
<td>-----</td>
<td>----------------</td>
<td>---------</td>
<td>--------------</td>
<td>--------</td>
<td>-------------</td>
<td>------------------</td>
</tr>
<tr>
<td>22</td>
<td>Kim et al. (2021)</td>
<td>South Korea</td>
<td>Randomized controlled trial</td>
<td>32 patients with acquired brain injury</td>
<td>Computerized cognitive rehabilitation and traditional cognitive rehabilitation</td>
<td>Improvements in executive functions and complex attention in both computer-assisted cognitive therapy (CCR) and therapist-delivered cognitive therapy (TCR) groups</td>
</tr>
<tr>
<td>23</td>
<td>Neumann et al. (2017)</td>
<td>United States of America</td>
<td>Phase I trial</td>
<td>17 adults with moderate to severe traumatic brain injury</td>
<td>Emotional self-reflection</td>
<td>Improvements in emotional awareness and emotional regulation after emotional awareness training</td>
</tr>
<tr>
<td>24</td>
<td>Sood et al. (2018)</td>
<td>Australia</td>
<td>Randomized controlled trial</td>
<td>Unspecified sample of children with pediatric traumatic brain injury</td>
<td>Cogmed-based working memory and decision making training</td>
<td>Study protocol to evaluate the efficacy of Cogmed (working memory training) in children with pediatric traumatic brain injury</td>
</tr>
<tr>
<td>25</td>
<td>Belchev et al. (2021)</td>
<td>Canada</td>
<td>Randomized controlled trial</td>
<td>84 participants with chronic traumatic brain injury</td>
<td>Remotely delivered environmental enrichment intervention</td>
<td>Study protocol to evaluate a remotely delivered environmental enrichment program for rehabilitation of chronic traumatic brain injury</td>
</tr>
<tr>
<td>26</td>
<td>Brandt et al. (2021)</td>
<td>Norway</td>
<td>Randomized controlled trial</td>
<td>76 children with chronic pediatric acquired brain injury</td>
<td>Goal Management Training (GMT) with active control in the improvement of executive function</td>
<td>Goal management training (GMT) tailored for children was not shown to be more effective than a psychoeducational control in improving parent-reported executive function</td>
</tr>
<tr>
<td>27</td>
<td>Ettenhofer et al. (2019)</td>
<td>United States of America</td>
<td>Pilot clinical trial</td>
<td>11 participants in the intervention group and 6 on the waiting list</td>
<td>Neurocognitive Driving Rehabilitation in Virtual Environments (NeuroDRIVE)</td>
<td>The NeuroDRIVE intervention was associated with significant improvements in working memory and visual selective attention. No significant changes were observed in untrained cognitive areas, neurobehavioral symptoms, or driving skills</td>
</tr>
<tr>
<td>28</td>
<td>Cho et al. (2018)</td>
<td>United States of America</td>
<td>Correlation study</td>
<td>30 college soccer players</td>
<td>Association between the shape of the amygdala, mood and post-concussion symptoms</td>
<td>A positive correlation was found between negative mood and the shape of the laterobasal subfield of the left amygdala in college soccer players. No significant relationship was found between postconcussion symptoms and amygdala shape</td>
</tr>
<tr>
<td>29</td>
<td>Hypher et al. (2019)</td>
<td>Norway</td>
<td>Randomized controlled trial</td>
<td>80 survivors of pediatric acquired brain injury</td>
<td>Goal Management Training (GMT) in pediatric version (pGMT)</td>
<td>The objective is to determine the efficacy of a pediatric version of GMT (pGMT) in children and adolescents with acquired brain injury and executive dysfunction. Primary outcomes will measure parent-reported changes in executive function in daily life</td>
</tr>
<tr>
<td>30</td>
<td>Pinto et al. (2019)</td>
<td>Brazil</td>
<td>Randomized controlled trial</td>
<td>90 patients with central nervous system injury</td>
<td>Sensorimotor and cardiorespiratory rehabilitation associated with transcranial photobiomodulation</td>
<td>The objective is to evaluate the effects of sensorimotor and cardiorespiratory sensory rehabilitation associated with transcranial photobiomodulation in patients with central nervous system lesions</td>
</tr>
<tr>
<td>31</td>
<td>Bosch et al. (2019)</td>
<td>Australia</td>
<td>Randomized controlled trial</td>
<td>31 emergency department patients</td>
<td>Clinical practice recommendations in the management of patients</td>
<td>The NET intervention significantly improved appropriate assessment of posttraumatic amnesia. However, it did not significantly increase the performance of CT scans or the provision of written information at discharge</td>
</tr>
</tbody>
</table>
On the other hand, there were techniques that have not shown effectiveness in this context. For example, the study by Teel et al.\(^{(16)}\) showed that aerobic training had no significant effect on the clinical assessment of sports-related concussions in healthy participants. In the case of Brandt et al.\(^{(16)}\), goal management training (GMT) tailored for children was not shown to be more effective than a psychoeducational control in improving parent-reported executive function.

In addition to cognitive interventions, other therapies have been investigated, such as transcranial direct current stimulation, as evidenced by the study by De Freitas et al.\(^{(21)}\), which showed improvements in episodic memory through transcranial direct current stimulation in patients with traumatic brain injuries. Vocational rehabilitation and virtual rehabilitation therapy have also been explored, as shown in the studies by Bosch et al.\(^{(41)}\) and Novakovic-Agopian et al.\(^{(27)}\), respectively.

CONCLUSIONS
- The research on cognitive interventions in patients with traumatic brain injuries has involved a wide variety of countries, with notable participation from the United States, Norway, the United Kingdom, and Canada.
- Cognitive training has proven to be an effective technique in managing traumatic brain injuries, demonstrating significant improvements in composite cognitive measures and patients’ quality of life.
- Certain therapies, such as hyperbaric oxygen therapy, have shown promising results in treating symptoms such as post-traumatic stress, depression, and anxiety in patients with traumatic brain injuries.

REFERENCES


9 Mendoza Rivas L, et al


https://doi.org/10.56294/ri202225
FINANCING
No financing.

CONFLICT OF INTEREST
The authors declare that there are no conflicts of interest.

AUTHORSHIP CONTRIBUTION
Conceptualization: Leandro Mendoza Rivas, Laura Martinez Cruz.
Investigation: Leandro Mendoza Rivas, Laura Martinez Cruz.
Methodology: Leandro Mendoza Rivas, Laura Martinez Cruz.
Writing-original draft: Leandro Mendoza Rivas, Laura Martinez Cruz.
Writing-review and editing: Leandro Mendoza Rivas, Laura Martinez Cruz.