ERABI
EVIDENCE-BASED REVIEW
of moderate to severe
ACQUIRED BRAIN INJURY

REHABILITATION OF PROBLEM SOLVING, EXECUTIVE & GENERAL COGNITIVE FUNCTIONING

POST ACQUIRED BRAIN INJURY

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Conflict of Interest

In the context of ERABI development, the term "conflict of interest" (COI) refers to situations in which an author or ERABI staff member's financial, professional, intellectual, personal, organizational or other relationships may compromise their ability to independently conduct this evidence-based review. No limiting conflicts were identified.

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Greetings from Dr. Robert Teasell,

Professor and Chair-Chief of Physical Medicine and Rehabilitation

The Collaboration of Rehabilitation Research Evidence (CORRE) team is delighted to present the Evidence-Based Review of moderate to severe Acquired Brain Injury (ERABI) *Rehabilitation of Problem Solving, Executive & General Cognitive Functioning Post Acquired Brain Injury.* Through collaboration of researchers, clinicians, administrators, and funding agencies, ERABI provides an up-to-date review of the current evidence in brain injury rehabilitation. ERABI synthesizes the research literature into a utilizable format, laying the foundation for effective knowledge transfer to improve healthcare programs and services.

We offer our heartfelt thanks to the many stakeholders who are able to make our vision a reality. Firstly, we would like to thank the Ontario Neurotrauma Foundation, which recognizes ERABI's capacity to lead in the field of brain injury evidence-based reviews and is committed to funding it. We would also like to thank the co-chairs of ERABI, Dr. Mark Bayley (University of Toronto) and Dr. Shawn Marshall (University of Ottawa) for their invaluable expertise and stewardship of this review. Special thanks to the authors for generously providing their time, knowledge and perspectives to deliver a rigorous and robust review that will guide research, education and practice for a variety of healthcare professionals. We couldn't have done it without you! Together, we are building a culture of evidence-based practice that benefits everyone.

We invite you to share this evidence-based review with your colleagues, patient advisors that are partnering within organizations, and with the government agencies with which you work. We have much to learn from one another. Together, we must ensure that patients with brain injuries receive the best possible care every time they require rehabilitative care – making them the real winners of this great effort!

Robert Teasell, MD FRCPC

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PREFACE

About the Authors

ERABI is internationally recognized and led by a team of clinicians and researchers with the goal of improving patient outcomes through research evidence. Each ERABI module is developed through the collaboration of many healthcare professionals and researchers.

Dr. Shawn Marshall is a physician specializing in Physical Medicine and Rehabilitation (Physiatrist). He is the Division Head of Physical Medicine and Rehabilitation at the University of Ottawa and The Ottawa Hospital where he manages both in-patients and out-patient clinics for patients with concussion to severe traumatic brain injury. Dr. Marshall has a Master's degree in Clinical Epidemiology and is a Full Professor at the University of Ottawa in the Department of Medicine.

Amber Harnett, MSc, RN (candidate), CNF scholar, completed her MSc in pathology at Western University and is currently a first-year nursing student in the accelerated BScN program at Western University. Passionate about supporting and advocating for those with brain injuries, she also works as a research coordinator to improve the rehabilitation system through research synthesis, guideline development, knowledge translation, education and outreach, in the CORRE lab at Parkwood Institute.

Penny Welch-West has been working as a Speech-Language Pathologist since 1998 and enjoys a very varied practice ranging from Rehabilitation through Complex/Continuing and Palliative Care. This work includes teaching, assessment and treatment in the areas of dysphagia (swallowing), voice, articulation, language, cognitive-communication and Augmentative and Alternative Communication (AAC).

Shannon Janzen, MSc, is a research associate and the project coordinator for the Evidence-Based Review of Acquired Brain Injury (ERABI). Her research interests focus on the integration of best evidence into clinical practice to optimize patient outcomes, with an emphasis on knowledge translation initiatives.

Dr. Robert Teasell is Professor of Physical Medicine and Rehabilitation, Schulich School of Medicine and Dentistry, Western University and a Clinical Researcher at Lawson Research Institute in London, Ontario. He is a clinician at Parkwood Institute, St. Joseph's Health Care London.

Purpose

The Evidence-Based Review of Acquired Brain Injury (ERABI) is a systematic review of the rehabilitation literature of moderate to severe acquired brain injuries (ABI). It is an annually updated, freely accessible online resource that provides level of evidence statements regarding the strength of various rehabilitation interventions based on research studies. The ERABI is a collaboration of researchers in London, Toronto and Ottawa. Our mission is to improve outcomes and efficiencies of the rehabilitation system through research synthesis, as well as from providing the foundational research evidence for guideline development, knowledge translation, and education initiatives to maximize the real-world applications of rehabilitation research evidence.

Key Concepts

Acquired Brain Injury

For the purposes of this evidence-based review, we used the definition of ABI employed by the Toronto Acquired Brain Injury Network (2005). ABI is defined as damage to the brain that occurs after birth and is not related to congenital disorders, developmental disabilities, or processes that progressively damage the brain. ABI is an umbrella term that encompasses traumatic and non-traumatic etiologies.

TABLE 1 | Defining Acquired Brain Injury

Included in ABI definition	Excluded from ABI definition

Traumatic Causes
- Motor vehicle accidents
- Falls
- Assaults
- Gunshot wounds
- Sport Injuries

Non-traumatic Causes
- Tumours (benign/meningioma only)
- Anoxia
- Subarachnoid hemorrhage (non-focal)
- Meningitis
- Encephalitis/encephalopathy (viral, bacterial, drug, hepatic)
- Subdural Hematoma

Vascular and Pathological Incidents
- Intracerebral hemorrhage (focal)
- Cerebrovascular accident (i.e., stroke)
- Vascular accidents
- Malignant/metastatic tumours

Congenital and Developmental Problems
- Cerebral Palsy
- Autism
- Developmental delay
- Down's syndrome
- Spina bifida with hydrocephalus

Progressive Processes
- Alzheimer's disease
- Pick's disease
- Dementia
- Amyotrophic Lateral Sclerosis
- Multiple Sclerosis
- Parkinson's disease
- Huntington's disease

Given that 'ABI' can have multiple definitions, studies with an 'ABI' population can be equally heterogeneous in terms of the sample composition. Such studies may include any combination of persons with TBI, diffuse cerebrovascular events (i.e., subarachnoid hemorrhage) or diffuse infectious disorders (i.e., encephalitis or meningitis). The vast majority of individuals with ABI have a traumatic etiology; therefore, much of the brain injury literature is specific to TBI. The terms ABI and TBI have been used intentionally throughout ERABI to provide more information about populations where relevant.

Moderate to Severe Brain Injury

ABI severity is usually classified according to the level of altered consciousness experienced by the patient following injury (Table 2). The use of level of consciousness as a measurement arose because the primary outcome to understand the severity of an injury is the Glasgow Coma Scale. Consciousness levels following ABI can range from transient disorientation to deep coma. Patients are classified as having a mild, moderate or severe ABI according to their level of consciousness at the time of initial assessment. Various measures of altered consciousness are used in practice to determine injury severity. Common measures include the Glasgow Coma Scale (GCS), the duration of loss of consciousness (LOC), and the duration of post-traumatic amnesia (PTA). Another factor used to distinguish moderate and severe brain injury is evidence of intracranial injury on conventional brain imaging techniques which distinguish severity of injury from a mild or concussion related brain injury.

TABLE 2 | Defining Severity of Traumatic Brain Injury, adapted from Veterans Affairs Taskforce (2008) and Campbell (2000)

Criteria	Mild	Moderate	Severe	Very Severe
Initial GCS	13-15	9-12	3-8	Not defined
Duration LOC	< 15minutes*	<6 hours	6-48 hours	>48 hours
Duration PTA	< 1hour*	1-24 hours	1-7 days	>7 days
	*This is the upper limit for mild traumatic brain injury; the lower limit is any alteration in mental status (dazed, confused, etc.).			

Methods

An extensive literature search using multiple databases (CINAHL, PubMed/MEDLINE, Scopus, EMBASE, and PsycINFO) was conducted for articles published in the English language between 1980–March 2020 that evaluate the effectiveness of any intervention/treatment related to ABI. The references from key review articles, meta-analyses, and systematic reviews were reviewed to ensure no articles had been overlooked. For certain modules that lacked research evidence the gray literature, as well as additional databases, were searched in order to ensure the topic was covered as comprehensively as possible.

Specific subject headings related to ABI were used as the search terms for each database. The search was broadened by using each specific database's subject headings, this allowed for all other terms in the database's subject heading hierarchy related to ABI to also be included. The consistent search terms used were "head injur*", "brain injur*", and "traumatic brain injur*". Additional keywords were used specific to each module. A medical staff librarian was consulted to ensure the searches were as comprehensive as possible.

Every effort was made to identify all relevant articles that evaluated rehabilitation interventions/ treatments, with no restrictions as to the stage of recovery or the outcome assessed. For each module, the individual database searches were pooled, and all duplicate references were removed. Each article title/abstract was then reviewed; titles that appeared to involve ABI and a treatment/intervention were selected. The remaining articles were reviewed in full.

Studies meeting the following criteria were included: (1) published in the English language, (2) at least 50% of the study population included participants with ABI (as defined in Table 1) or the study independently reported on a subset of participants with ABI, (3) at least three participants, (4) ≥50% participants had a moderate to severe brain injury (as defined in Table 2), and (5) involved the evaluation of a treatment/intervention with a measurable outcome. Both prospective and retrospective studies were considered. Articles that did not meet our definition of ABI were excluded.

Interpretation of the Evidence

The levels of evidence (Table 3) used to summarize the findings are based on the levels of evidence developed by Sackett et al. (2000). The levels proposed by Sackett et al. (2000) have been modified; specifically, the original ten categories have been reduced to five levels. Level 1 evidence pertains to high quality randomized controlled trials (RCTs) (PEDro ≥6) and has been divided into two subcategories, level 1a and level 1b, based on whether there was one, or more than one, RCT supporting the evidence statement.

The evidence statements made in evidence-based reviews are based on the treatment of groups rather than individuals. There are times when the evidence will not apply to a specific case; however, the majority of patients should be managed according to the evidence. Ultimately, the healthcare professional providing care should determine whether an intervention is appropriate and the intensity with which it should be provided, based on their individual patient's needs. Furthermore, readers are asked to interpret the findings of studies with caution as evidence can be misinterpreted. The most common scenario occurs when results of a trial are generalized to a wider group than the evidence allows. Evidence is a tool, and as such, the interpretation and implementation of it must always be done with the known limitations in mind.

TABLE 3 | Levels of Evidence

Level	Research Design	Description
1A	Randomized Controlled Trial (RCT)	More than one RCT with PEDro score ≥6. Includes within subject comparisons, with randomized conditions and crossover designs
1B	RCT	One RCT with PEDro ≥6
2	RCT	One RCT with PEDro <6
	Prospective Controlled Trial (PCT)	Prospective controlled trial (not randomized)
	Cohort	Prospective longitudinal study using at least two similar groups with one exposed to a particular condition
3	Case Control	A retrospective study comparing conditions including historical controls
4	Pre-Post Trial	A prospective trial with a baseline measure, intervention, and a post-test using a single group of subjects
	Post-test	A prospective intervention study using a post intervention measure only (no pre-test or baseline measurement) with one or more groups
	Case Series	A retrospective study usually collecting variables from a chart review
5	Observational study	Using cross sectional analysis to interpret relations
	Clinical Consensus	Expert opinion without explicit critical appraisal, or based on physiology, biomechanics or "first principles"
	Case Reports	Pre-post or case series involving one subject

Strength of the Evidence

The methodological quality of each randomized controlled trial (RCT) was assessed using the Physiotherapy Evidence Database (PEDro) rating scale developed by the Centre for Evidence-Based Physiotherapy in Australia (Moseley et al., 2002). The PEDro is an 11-item scale; a point is awarded for ten satisfied criterion yielding a score out of ten. The first criterion relates to external validity, with the remaining ten items relating to the internal validity of the clinical trial. The first criterion, eligibility criteria, is not included in the final score. A higher score is representative of a study with higher methodological quality.

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SUMMARY OF THE EVIDENCE

Intervention	Key Point Level of Evidence
Non-Pharmacological Interventions	
Individual Interventions	Targeted hypnosis may improve memory, attention, and cognitive function in post TBI patients or stroke; however, only as long as the intervention is being administered. - *There is level 1b evidence that targeted hypnosis may transiently improve cognitive function in post TBI patients or stroke.* Attention training programs likely do not improve executive functioning. - *There is level 1b evidence that an attention remediation intervention may not be superior to TBI education alone and improving executive function in patients post TBI.* - *There is level 2 evidence that dual-task training may improve not general cognitive functioning compared to a non-specific cognitive program in patients post TBI.* General cognitive training programs which include problem-solving appear to be effective for improving executive functioning following an ABI. - *There is level 1b evidence that a comprehensive cognitive treatment strategy program (which include problem solving), compared to controls, are effective for improving metacognition and goal achievement post TBI.* - *There is level 4 evidence that cognitive rehabilitation may increase productivity in everyday functioning, and cerebral blood flow during treatment in patients post TBI.* - *There is level 1b evidence that the specific cognitive training program ProSolv, compared to standard therapy, does not improve measures of executive functioning following an ABI.* - *There is level 2 evidence that the Intensive NeuroRehabilitation programme, compared to no treatment, does not improve executive functioning following an ABI.* Virtual reality does not likely improve executive functioning following an ABI. - *There is level 1b evidence that virtual-reality training is not superior to conventional cognitive training at improving cognitive and executive function outcomes post TBI.* Computer or smartphone software programs (BrainHQ, Parrot Software, ProSolv app) may not be superior to common interventions at improving memory, attention, and problem-solving skills in patients post TBI. - *There is level 2 evidence that computer or smartphone software programs, such as BrainHQ, Parrot Software, ProSolv app, may not be superior to no intervention at improving problem-solving skills and general functioning in patients post TBI.* Goal management training may be superior to motor skills training at improving everyday skills (meal preparation), but not intelligence or neuropsychological outcomes in patients post TBI. - *There is level 2 evidence that goal management training may be superior (compared to motor skills training or no treatment controls) for improving goal attainment or measures of intelligence following an ABI.*

	Heart rate variability biofeedback may improve executive functions; however, more controlled studies are required to make further conclusions. - *There is level 4 evidence that heart rate biofeedback may improve executive functioning following an ABI, although higher level studies are required to fully determine this.*
Group-based Interventions	Group goal-oriented interventions are effective for the remediation of executive functions, including comprehension and problem solving. - *There is level 1b evidence that goal orientated group interventions are successful at improving cognitive and executive function in patients post ABI.* Emotional regulation interventions delivered in a group setting may improve executive function in patients post TBI; however, it is unclear if it is superior at doing so compared to conventional cognitive remediation. - *There is level 1b evidence that emotional regulation group interventions are effective at improving executive function in post TBI patients compared to standard therapy.* The SMART program appears to be effective for improving executive functioning following an ABI. - *There is level 1b evidence that the Strategic Memory and Reasoning Training program is more effective than a brain health workshop for improving executive function, metacognition, and comprehension following ABI.* Touch screen-based games which include components of metacognition may be effective for improving self-awareness. - *There is level 4 evidence that touch screen-based games (which include components of reasoning and problem-solving) may be effective for improving self-awareness and social skills following an ABI.* Metacognitive instruction does not appear to improve comprehension or abstract reasoning; however, more studies are needed to fully evaluate its effects. - *There is level 4 evidence that metacognitive strategy instruction may not be effective for improving executive functioning following an ABI.*
	General cognitive rehabilitation programs are effective for improving cognitive functioning following an ABI. - *There is level 1b evidence that cognitive therapies compared to standard therapy are more effective than no therapy for improving generalized cognitive functioning, as well as self-perception following an ABI* - *There is level 1b evidence that cognitive therapies compared to standard therapy are more effective than no therapy for improving generalized cognitive functioning, as well as self-perception following an ABI.* - *There is level 4 evidence that a low intensity outpatient cognitive rehabilitation program may improve goal attainment and cognitive impairment in patients post ABI.* - *There is level 2 evidence that the Trabajadora de Salud program may improve general cognitive functioning compared to standard therapy for those with an ABI.*

	There is limited evidence that mindfulness-based stress reduction is effective for improving cognitive functioning. - *There is level 4 evidence that mindfulness-based stress reduction may be effective for improving general cognitive functioning and psychological health for those with an ABI.* Corrective video feedback is more effective than verbal feedback alone for improving general cognitive function and self-awareness. - *There is level 1b evidence that corrective video feedback is more effective for improving generalized cognitive functioning and self awareness compared to verbal feedback only in those with an ABI.* Remedial and adaptive occupational therapy are equally effective for improving general cognitive functioning. - *There is level 1b evidence that remedial occupational therapy and adaptive occupational therapy may have equal effects on generalized cognitive function in those with an ABI.*
Pharmacological Interventions	
Donepezil	Donepezil might improve attention, learning and short-term memory following TBI; however, side effects may incur from its use. - *There is level 4 evidence that donepezil is effective in improving learning, memory, divided attention, and executive function in patients post TBI.*
Methylphenidate	The effectiveness of methylphenidate to improve cognitive impairment following brain injury is unclear. Further studies with larger populations are required. - *There is conflicting (level 1a) evidence regarding the effectiveness of the administration of methylphenidate, compared to placebo, following TBI for the improvement of general and executive functioning.*
Sertraline	Sertraline has not been shown to improve cognitive functioning within the first 12 months post TBI, and may be associated with side effects. - *There is level 1b evidence that sertraline does not improve cognitive functioning, compared to placebo, in individuals who have sustained a moderate to severe TBI.*
Amantadine	Amantadine is not effective for improving generalized cognition. Its impact o executive functioning should be studied further. - *There is level 1b evidence that Amantadine may not help to improve general functioning deficits in post TBI patients compared to placebo.*
Bromocriptine	Bromocriptine may improve other measures of cognition such as attention, but its effects on generalized cognition are conflicting. More research is required. - *There is conflicting level 2 (against) and level 4 (for) evidence as to whether or not bromocriptine may improve executive or general cognitive functioning following ABI.*
Growth Hormone Replacement Therapy	The administration of human growth hormones appears to have positive (although sometimes limited effects) on general and executive functioning in those with an ABI.

	- *There is level 1b evidence that recombinant human Growth Hormone (rhGH) is superior to placebo at improving processing speed (6 mo), executive function and learning in patients post TBI.* - *There is level 2 evidence that growth hormone (GH) therapy is effective for improving quality of life, instrumental activities of daily living (iADL), attention, memory, and visuospatial ability in patients post TBI.* - *There is level 2 evidence that recombinant human Growth Hormone (rhGH) administration improves intelligence and other cognitive subtests in TBI patients with growth hormone deficiency compared to TBI patients without; however, insulin-like growth factor-1 (IGF-1) levels may be the same between groups.*
Rivastigmine	Rivastigmine is not effective in treating general or executive dysfunction post ABI. - *There is level 1b evidence that rivastigmine is not effective for improving general or executive cognitive functioning, compared to placebo, following an ABI.*
Hyperbaric Oxygen Therapy	Hyperbaric oxygen therapy may be beneficial for improving general and executive functioning following an ABI; however, more research is needed. - *There is level 4 evidence that hyperbaric oxygen therapy may improve general and executive functioning following an ABI.*
Dextroamphetamine	There is moderate evidence to suggest that dextroamphetamine is not effective for the remediation of general functioning. - *There is level 1b evidence that dextroamphetamine is not effective for the remediation of general cognitive functioning following an ABI.*

INTRODUCTION

Executive functions refer to higher-level cognitive functions that are primarily mediated by the frontal lobes. These functions include insight, awareness, judgment, planning, organization, problem solving, multi-tasking and working memory (Lezak, 2004). Executive deficits are particularly relevant following traumatic brain injury from both a pathophysiologic as well as a psychosocial perspective. The frontal lobes tend to be one of the brain areas most likely to be injured following trauma (Greenwald et al., 2003). Frequently bilateral frontal lobe injury occurs following TBI which in contrast to typically unilateral insults following vascular injury. Direct contusion to the frontal and temporal lobes can occur but also diffuse axonal injury sustained as a result of TBI affects executive functioning. Patients with a TBI often present with cognitive and behavioral deficits in the presence of little physical impairment.

Cicerone et al. (2000) reviewed 14 studies examining executive functioning and problem-solving (Table 6.13). Only three of the identified studies included a control group and were classified as a randomized controlled trial or non-randomized cohort study.

In later reviews by Cicerone et al. (2005; 2011) 9 and 18 additional studies, respectively, were identified. Some of these studies were not included in our review as they did not meet our inclusion criteria. Based on the results of the studies in their review, Cicerone et al. (2000) recommended, "*training of formal problem-solving strategies and their application to everyday situations and functional activities".*

Executive function deficits are particularly relevant to brain injury survivors who tend to be younger (average age less than 40 years) and who often desire to re-integrate back into pre-injury life roles. Patients with executive function deficits may have the capacity to be independent for basic activities of daily living where actions tend to be more ingrained and one-dimensional. However, instrumental activities of daily living such as banking, scheduling and household activities require intact executive functions due to the increased cognitive complexity and variability of the tasks. Of particular importance are the advanced tasks such as return to driving and competitive employment which are of increased relevance to the younger age demographic associated with TBI (Miller et al., 2003).

Non-Pharmacological Interventions

Rehabilitation of Executive Functioning

Within the typical medical and rehabilitation settings, executive function deficits themselves are difficult to identify and evaluate since there is a tendency to focus on other cognitive functions such as memory and attention. It is vital to evaluate interventions for executive functioning as impairment can ultimately hinder successful community re-integration. Further to this, it is also important to address the issue of self-awareness which is particularly important in those who sustain moderate to severe TBI. If individuals are not aware they have a problem, they are less likely to work on compensating for it.

Individual Interventions

Although executive function deficits post TBI are a common there is little overall research directly addressing the impact of rehabilitation on executive function. Individual interventions aimed at improving executive and general cognitive function are reviewed below.

TABLE 4 | The Effect of Individual Therapies on Executive Function Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Siponkoski et al. (2020) Finland RCT-Crossover PEDro=8 N= 40	**Population:** TBI; Mean Age=41.3±13.3yr; Gender: Male=23, Female=16; Mean Time Post Injury= 8.9±6.4mo; Mean GCS= 11.8±4.2. **Intervention:** Participants were randomized to either neurological music therapy and standard care (n=20) or standard care only. Neurological music therapy (adapted from Functionally-Oriented Music Therapy and Music-Supported Training) was 20 sessions (2/wk, 1hr each) by a music therapist. Each session contained rhythmical training, structured cognitive-motor training, and assisted music playing. Assessments were conducted at baseline (T1), 3 months (crossover, T2) and 6 months (T3).	1. There was significant time X group interaction for executive function (FAB; p=0.045) with the music therapy block showing greater improvement in executive function than the control group. 2. No significant between group differences were found between T1 and T2 for reasoning, verbal memory or motor performance. 3. There was significant improvement for the NLT error rate for the music therapy block compared to the control block (p=0.032); however, no significant between group differences were found for the other computerized executive functioning/attention tests.

	Outcome Measures: Frontal Assessment Battery (FAB), Number-Letter Task (NLT), Auditory N-back Task, Simon Task, Sustained attention to response task (SART), Wechsler Adult Intelligence Scale IV (WAIS-IV).	
Elbogen et al., (2019) USA RCT PEDro=8 $N_{Initial}$=112, N_{Final}=89	**Population:** TBI=64; *Treatment Group (n=57):* Mean Age=36.77±8.60yr; Gender: Male=43, Female=4; Mean Time Post Injury= Not Reported; Severity: Mild=22, Moderate-to-Severe=35. *Control Group (n=55):* Mean Age=36.25±8.30yr; Gender: Male=50, Female=5; Mean Time Post Injury=Not Reported; Severity: Mild=, Moderate-to-Severe=29. **Intervention:** Participants were randomized to receive cognitive rehabilitation with a novel program - Cognitive Applications for Life Management (CALM; Treatment Group) or psychoeducation on TBI (Control Group). The program focuses on goal management and brain health training utilizing mobile technology and social support. Participants completed three 60-90min sessions at 0, 2 and 4mo. Outcome measures were assessed at baseline and 6mo post randomization. **Outcome Measures:** Delis-Kaplan Executive Dysfunction System (DKEFS), Barratt Impulsiveness Scale (BIS), Dimensions of Anger Reactions (DAR), Head Injury Behaviour Scale (HIBS), Clinician Administered Posttraumatic Stress Disorder Scale (CAPS).	1. No significant improvements were observed in measures of executive function (DKEFS; p>0.05) or impulsiveness (BIS; p>0.05) with the CALM intervention at 6mo. 2. Significant improvements in measures of emotion (DAR; p<0.05) and behavioural regulation (HIBS; p<0.05) were observed with the CALM intervention at 6mo. 3. Participants receiving calm reported a 25% decrease in anger compared to 8% in the control group at 6mo (p=0.008). 4. Family/friends of participants reported that participants receiving the CALM intervention had 26% fewer maladaptive interpersonal behaviours than 6% of those in the control group at 6mo (p=0.016). 5. Symptoms of PTSD significantly reduced in participants that were randomized to CALM (p<0.01).
Neville et al. (2019) Brazil RCT PEDro=9 $N_{Initial}$=36, N_{Final}=30	**Population:** TBI (Diffuse Axonal Injury). Experimental Group (n=17): Gender: Male=15, Female=2; Mean Age=32.62±12.8yr; Mean GCS=5.0±3.0. Control Group (n=13): Gender: Male=12, Female=1; Mean Age=29.0±10.4yr; Mean GCS=4.4±2.5. **Interventions:** Patients were randomized to receive 10 sessions of either repetitive transcranial magnetic stimulation (rTMS) or sham stimulation. Neuropsychological evaluations were performed at baseline, post treatment and at 90d post treatment. **Outcome Measure:** Trail Making Test (TMT) A & B, Controlled Oral Word Association Test, Stroop Test, Five-Point Test, Digit Span Test (Forwards & Backwards), Symbol Digit Test, Hopkins Verbal Learning Test, Brief Visuospatial Memory Test, Grooved Pegboard Test.	1. No significant group, time or group by time interactions were found for executive function, attention, memory, or motor function, with the exception of a significant effect due to time for executive function (p<0.001) 2. Between-group comparisons of performance on TMT Part B at baseline and after the 10th rTMS session did not differ between groups (p=0.680, p=0.341, respectively). 3. Within group comparisons showed a significant difference in only the sham group on the TMT-B, showing improvement in performance (p=0.023). 4. No significant differences were observed on any neuropsychological tests. 5. No serious adverse events were reported. There was a higher frequency of mild adverse events in the rTMS group than sham, but it was not significant.
Gracey et al. (2017) UK RCT PEDro=6	**Population:** CVA=23, Infection=3, TBI=33, Tumor=10, Missing=1. *Control First (n=34)*: Mean Age=50.18 yr; Gender: Male=23, Female=11; Mean Time Post Injury=8.62 yr.	1. Participants achieved a greater proportion of intentions during the AIM intervention relative to control (p=0.040).

$N_{Initial}$=74, N_{Final}=59	*Assisted Intention Monitoring (AIM, n=36)*: Mean Age=46.36 yr; Gender: males=23, females=13; Mean Time Post Injury=4.89 yr. **Intervention:** Participants were randomized to receive AIM or control first. In the AIM-first group, participants received goal management training followed by text messages for improving achievement of everyday intentions. Control-first group received brain injury information, Tetris game, and non-informational text messages. After 3 wk, participants were crossed over with AIM-first group receiving usual care and control-first group receiving AIM. **Outcome Measures:** Mean daily proportion of intentions achieved, Achievement of all goals excluding the phone call task, Profile of Mood States total mood disturbance (POMS MD), Hotel Task, Verbal Fluency.	2. Participants achieved a greater proportion of goal attainment (without the phone call task) during the AIM intervention relative to control (p=0.033). 3. No significant Group x Time interaction effect was found for the POMS MD or Hotel Test. 4. When only comparing group differences at post-intervention phase 1, intention to treat analysis showed no significant difference between groups for proportion of intentions achieved or achievement of goals excluding the phone task.
Lindelov et al. (2017) Denmark RCT PEDro=7 N=68	**Population:** TBI=34, Stroke=20, Other=12, NA=2. *Group A (n=27)*: Mean Age=45.2 yr; Gender: Male=12, Female=15; Mean Time Post Injury=5 yr. *Group B (N=22)*: Mean Age=47.0 yr; Gender: males=8, females=25; Mean Time Post Injury=6.5 yr. *Control Group (n=19)*: Mean Age=54.1 yr; Gender: males=8, females=11; Mean Time Post Injury=7 yr. **Treatment:** Participants were randomly assigned to Group A or Group B; Control group was recruited separately and received no intervention. In Phase 1, Group A received the first version of a targeted hypnosis procedure (improving brain injury or working memory-relating abilities) and Group B received a non-targeted hypnosis procedure (4 weekly 1 h sessions). After a 7 wk break, Phase 2 occurred, with Group A receiving a second version of a targeted hypnosis procedure and Group B receiving the first version of a targeted hypnosis procedure. **Outcome Measure:** Working Memory Index (WMI), B-A Trail Making Index (TMT).	1. In Phase 1, there was significantly more improvement in Group A compared to Group B for WMI (Bayes factor=342) and TMT (Bayes factor=37.5). 2. After the break, the WMI and MT showed no significant differences for either groups compared to before the break. 3. In Phase 2, Group B crossed over to the targeted intervention and showed significant improvements in WMI (Bayes factor=535) and TMT (Bayes factor=72813). Group A showed a small improvement for WMI (Bayes factor=1.5) and TMT (Bayes factor=30). 4. From baseline to last test, there were no significant difference in improvements between Group A and Group B for WMI and TMT.
Powell et al. (2017) USA RCT PEDro=4 N=23	**Population:** TBI=17, Stroke/aneurysm=4, Other=6, More than 1 brain injury=3; Mean Age=44 yr; Gender: Male=11, Female=12; Mean Time Post Injury=4 yr. **Treatment:** Coaches were randomly assigned to ProSolv intervention or usual care. Participants new to the outpatient rehabilitation programme were randomized to coaches and clients already working with coaches were offered the opportunity to participate in the study with that coach. In six 1 h sessions over 8wk, ProSolv group (n=14) received training on using ProSolv app and Usual Care group (n=9) received usual care	1. No significant differences between groups were found for knowledge test, PSQ clear thinking, PSQ emotional self-regulation, TBI-SE, or SWLS. 2. The average SUS score reported at post-test was 3.5 for the tutorial and 3.6 for the app, suggesting that on average, ProSolv participants were slightly higher than neutral on whether the programme components were usable.

	including training in goal planning/management, time pressure management, and problem-solving skills. ProSolv group had access to the ProSolv app outside of the sessions as a resource for remembering steps to effective problem solving and creating personalized problem-solution lists. **Outcome Measure:** Project-specific knowledge test, Problem Solving Questionnaire (PSQ clear thinking and emotional self-regulation subscales), Problem Solving Rating Scale (PSRS), TBI Self-Efficacy Questionnaire (TBI-SE), Satisfaction with Life Scale (SWLS), System Usability Scale (SUS).	
Jacoby et al. (2013) Israel RCT PEDro=7 N=12	**Population:** TBI; *Experimental group (EG; n=6)*: Mean Age=27.83 yr; Gender: Male=4, Female=2; Mean Time Post Injury=126 d; Mean GCS=8. *Control group (CG; n=6)*: Mean Age=30.67 yr; Gender: Male=4, Female=2; Mean Time Post Injury=100 d; Mean GCS=6.25. **Intervention:** Participants were randomly assigned to the EG group or the CG group. All participants in the EG received 10 sessions of virtual reality (VR) training (45 min/session, 3-4 x/wk). The CG received general cognitive re-training treatment identical in length and duration to the EG. **Outcome Measure:** Multiple Errands Test – Simplified Version (MET-SV), Executive Function Performance Test (EFPT).	1. Participants in the EG group improved more in their final scores on the MET-SV relative to their initial scores compared to the CG group (p=0.046). 2. Participants in the EG improved more in their final scores on the EFPT relative to their initial scores compared to the CG (p=0.046). 3. Between group differences showed no significant difference at baseline.
Man et al. (2013) Hong Kong RCT PEDro=4 N=40	**Population:** TBI. Age Range=18-55yr; Gender: Unspecified; Time Post Injury: Unspecified; Mean GCS=10. **Intervention:** Participants received twelve 20-25 minute sessions of a vocational problem-solving skill training program. Participants were randomized to either artificial intelligence virtual reality (treatment group, TG) or conventional psychoeducation (control group, CG). Outcomes were assessed before and after treatment, and at follow-up of 1, 3, and 6 months. **Outcome Measures:** Wisconsin Card Sorting Test (WCST); Tower of London Test (TLT); Vocational Cognitive Rating Scale (VCRS); Self efficacy (SE); Vocational outcomes.	1. Both groups showed significant improvements on WCST, TLT, VCRS, SE, and vocational outcomes after treatment compared to baseline ($p<0.050$). 2. On WCST, the TG performed better than the CG after treatment ($p\leq0.020$). No other significant between-group differences were found.
Couillet et al. (2010) France RCT PEDro=5 N=12	**Population:** severe TBI; Gender: Male=9, Female=3. *Group 1 (n=5)*: Mean Age=23.8 yr; Mean GCS=4.8; Mean Time Post Injury=6.3 mo. *Group 2 (n=7)*: Mean Age=26.7 yr; Mean GCS=4.8; Mean Time Post Injury=16.1 mo. **Intervention:** Randomized AB versus BA design, where "A" represents the control phase and	1. Following training, there was a significant improvement in the 2 tasks that targeted divided attention (TAP-divided attention, Go-no go and Digit Span: $p<0.0001$ for both). 2. The two groups differed significantly at 6 wk with those in the BA design doing better on TAP reaction times ($p<0.010$), the digit span

	"B" represents the treatment (dual-task training) phase. In the dual-task phase, patients were trained to conduct two concurrent tasks simultaneously. Group 1 started with the control phase (AB) and Group 2 (BA) with the treatment phase. Each phase lasted 6 wk (4, 1 hr sessions/wk). **Outcome Measure:** Test Battery for Attentional Performance (TAP: divided attention and flexibility subtests), Go-no go and Digit Span, Trail Making Test, Stroop Test, Brown-Peterson Paradigm, Rating Scale of Attentional Behaviour.	dual-task (p<0.001), and the Rating Scale of Attentional Behaviour (p<0.010). 3. There was a significant difference between groups at 6 wks on the Stroop test (p<0.001) and the flexibility subtest of the TAP (p<0.001), but not the Trail Making Test or the Brown-Peterson task. 4. Experimental training had no significant effects on non-target measures.
Spikman et al. (2010) Netherlands RCT PEDro=7 N=75	**Population:** Mean Age: 42.5 yr; Gender: male=50, female=25; Condition: TBI=33, Stroke=32, Other=10. **Intervention:** Individuals were randomly assigned to either the experimental group which comprised of multifaceted strategy training (n=38) or the control group (n=37). The primary goal of the treatment group was to improve 8 aspects of executive functioning. **Outcome Measure:** Role resumption list (RRL); treatment goal attainment (TGA) and Executive Secretarial Task (EST).	1. The experimental group improved significantly more over time than the controls on the RRL and attained significantly higher scores on the TGA and EST (p<0.010).
Levack et al. (2009) (Levack et al., 2009) New Zealand RCT PEDro=5 N=34	**Population:** *GMT (N=12):* Median age=29; Gender: Male=10, Female=2; Median time post-injury=5yr. *IOGT (N=10):* Median age=28yr; Gender: Male=9, Female; Median time post-injury=5yr. *Usual Care (N=12)*: Median age=40; Gender: Male=8, Female=4; Median time post-injury=7. **Intervention:** Individuals were assigned to either no treatment, goal management training, or identity oriented goal training. **Outcomes:** Goal Attainment Scale, behavioral observations.	1. All groups improved GAS scores over the course of treatment and at follow-up. The greatest improvement in scores was seen in the usual care group. Observationally both clinicians and participants reported feeling positively about the efficacy of GMT, and its ability to improve goal execution, multitasking, and time management.
Constantinidou et al. (2008) United States RCT PEDro=8 N=14	**Population:** *Experimental Group (N=21)*: Mean age=32.1yr; Mean time post-injury=9.74 mo. *Control Group (N=14)*: Mean age=27.57yr; Mean time post-injury=10.55 yr. **Intervention:** Individuals received either the Categorization Program intervention for 13 weeks averaging 4.5 hours of therapy per week, or 'regular therapy' (control group). **Outcomes:** CP Test 1 (object recognition/memory), CP Test 2 (executive functioning), CP Probe Tasks (executive functioning), Community Reintegration Questionnaire (CIQ), Mayo-Portland Adaptability Inventory (MPAI-3), California Verbal Learning Test (CVLT), Rey Complex Figure Test (RCF), Wechsler Memory Scale (WMS-III), Woodcock Johnson (WJ-III), Scales of	1. The experimental group significantly improved on CP Test 1 (object recognition) compared to the control group (p=0.039). 2. Individuals in the experimental group performed significantly better on the CP Test 2 (executive functioning) compared to the control group post-intervention (p=0.010). 3. Individuals in the experimental group performed significantly better on the probe tasks, compared to controls, post-treatment (p=0.008). 4. Individuals in both groups significantly improved performance on the CIQ and MPAI-3 (p<0.05). 5. The experimental group had greater improvement on the CVLT-R.

	Cognitive Ability for Traumatic Brain Injury (SCATBI).	6. There were no differences in scores between groups on the RCF, WMS-III, WJ-III, SCATBI.
Levine et al. (2000) Canada UK RCT PEDro=4 N=30	**Population:** TBI: *Goal Management Training (GMT) Group* (n=15): Mean Age=29.0 yr; Gender: Male=5, Female=10; Mean GCS=10.7; Mean Time Post Injury=3.7 yr. *Motor Skill Training (MST) Group* (n=15): Mean Age=30.8 yr; Gender: Male=9, Female=6; Mean GCS=10.8; Mean Time Post Injury=3.8 yr. **Intervention:** Patients were randomized into the GMT or MST group. The GMT was comprised of five steps: 1) orienting and alerting to task, 2) goal selection, 3) partitioning goals into sub-goals, 4) encoding and retention of sub-goals, and 5) monitoring. The MST was training that was unrelated to goal management: reading and tracing mirror-reversed text and designs. Participants were tested on everyday paper and pencil tasks that focused on holding goals in mind, sub-goal analysis and monitoring. **Outcome Measure:** Goal Neglect (Everyday paper and pencil tasks), Stroop Interference Procedure, Trail Making A and B, Wechsler Adult Intelligence Scale Revised (WAIS-R).	Everyday paper and pencil Task 1. The GMT group compared to the MST group had significantly greater accuracy on the everyday paper and pencil tasks post-training ($p<0.050$). 2. The MST group also had significantly more errors during the everyday paper and pencil tasks ($p<0.010$). 3. The GMT group significantly reduced their errors from pre-post training during the everyday paper and pencil tasks ($p<0.010$). 4. The GMT also devoted significantly more time to proofreading and the room-layout tasks than the MST group from pre to post-training ($p<0.050$). Neuropsychological Tasks 1. The GMT group was generally slower on timed neuropsychological tests: Stroop Interference Procedure, Trail Making Part A and B ($p<0.050$ and $p<0.060$, respectively). 2. No significant differences between groups for the WAIS-R ($p>0.050$).
Sohlberg et al. (2000) USA RCT PEDro=8 N=14	**Population:** TBI=11, ABI=1, Other=2. *Attention Process Training (APT) Group (n=7)*: Mean Age=33.1 yr; Mean Time Post Injury=7.5 yr; *Control Group (n=7)*: Mean Age=38.1 yr; Mean Time Post Injury=1.6 yr. **Intervention:** Patients were randomized to receive either the APT training (treatment) or the brain injury education and supportive listening (control), in a cross over design. APT was 24 hr over 10 wk and the control group received 10 hr over 10 wk. All subjects worked directly with a therapist and assessed pre and post intervention. **Outcome Measure:** Trail Making Test, Paced Auditory Serial Addition Task (PASAT), Gordon Diagnostic Vigilance and Distraction, Controlled Oral Word Association Task (COWAT), Stroop Task, Attention Questionnaire.	1. Those in the APT group reported significantly more changes than the control group (0.91 and 0.58 respectively, $p<0.050$). 2. The effect of type of change was significant ($p<0.0001$); a greater number of memory/ attention changes were reported for the APT group, whereas more psychological changes were reported for the control. 3. Changes in PASAT scores corresponded with perceived cognitive improvement in the interview; changes in PASAT scores were greater for those who reported >2 cognitive changes ($p<0.050$). 4. Results of the PASAT, Stroop Task, Trail Making Test B, and COWAT also found that those with higher levels of vigilance had improved scores ($p<0.01$). 5. For the aforementioned tasks, there were also specific improvements in performance associated with APT that were greater than those associated with brain injury education ($p<0.050$).
Webb & Glueckauf (Webb & Glueckauf, 1994) United States RCT PEDro=6 N=16	**Population:** Mean age=27.4yr; Mean time post-injury=8.7yr; Mean coma duration=88.9dy. **Intervention:** Participants were randomly assigned to a high involvement goals setting program or a low involvement program for 8 weeks meeting 1 hour per week. Individuals	1. There were no significant between group differences at baseline. 2. Both groups significantly improved on the GAS over time regardless of condition ($p<0.001$) post-treatment. 3. The high involvement group showed significant additional gains on the GAS compared to the

	were assessed pre-intervention, post-intervention, and at 2-month follow-up. **Outcomes:** Goal Attainment Scale (GAS).	low involvement group at 2-month follow-up ($p<0.05$).
Cizman et al., (2020) Slovenia Pre-Post $N_{Initial}=7$, $N_{Final}=7$	**Population:** TBI=6; Mean Age=34±18.6yr; Gender: Male=5, Female=2; Mean Time Post Injury=4±1.25mo; Severity: Mild=0, Moderate=2, Severe=4. **Intervention:** Participants completed a Goal-Orientated Attentional Self-Regulation (GOALS) training program consisting of ten 2h group sessions twice a wk, 3h of individual therapy with a psychologist and 20h of self-training at home. The program focused on cognitive and social skill training, as well as psychoeducation. Outcome measures were assessed at baseline and conclusion of the program. **Outcome Measures:** Alertness and Distractibility, Mobility Version of Test of Attentional Performance (TAP-M), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Letter Fluency Test, Tower of London Test, Stroop Interference Test, Clinical Assessment of Depression (CAD).	1. No significant differences in reaction times were observed on the Alertness and Distractibility task when compared to baseline ($p>0.05$). 2. No significant improvements were observed in measures of executive function (Tower of London, STROOP and Verbal Fluency; $p>0.05$). However, TAP-M performance significantly worsened when compared to baseline ($p<0.05$). 3. List learning and story delayed recall measures of the RBANS significantly improved from baseline ($p=0.028$, $p=0.043$), while the remainder of RBANS measures were not significant ($p>0.05$). 4. No significant differences in ratings of depression or anxiety were observed from baseline ($p>0.05$).
Holleman et al. (2018) Netherlands PCT N=75	**Population:** *Experimental Group (N=42):* Mean age=43.3yr; Gender: Male=27, Female=15; Mean time post-injury=7.9yr. *Control Group (N=33)*: Mean age=40.7yr; Gender: Male=20, Female=13; Mean time post-injury=6.9yr. **Intervention:** Participants were either assigned to the Intensive NeuroRehabilitation programme or the control group. The programme took place over the course of 16 weeks and consisted of 2 groups of 7 weeks of training with a 2-week break in between. Individuals had 5 hours of training 4 days a week in a group setting. **Outcomes:** Symptom checklist (SCL), Beck Depression Inventory-II (BDI-II), Hospital Anxiety and Depression Scale (HADS), Zelfbeeldenvragenlijst-trait (ZBV), Quality of Life in Brain Injury (QOLIBRI), Trail making test Part A, Stroop test, Wechsler Adult Intelligence Scale-III (WAIS-III), Rey Auditory Verbal Learning Test, Rivermead Behavioural Memory Test, Groninger Intelligentie Test 2, Trail making test Part B.	1. There were no significant between group differences pre-intervention on any measures. 2. Following the intervention, the experimental group had significantly lower SCL scores indicating a reduction in overall symptoms ($p=0.005$). 3. On measures of neuropsychological functioning, the experimental group reported significantly lower scores on the BDI-II ($p=0.001$), HADS ($p<0.01$), and ZBV-trait ($p=0.002$) showing improvement on these neuropsychological measures. 4. The experimental group reported significantly higher scores for quality of life on the QOLIBRI ($p<0.05$). 5. On measures of cognitive functioning no significant differences were seen for any outcome measures.
Kim et al. (2018) United States Pre-post N=13	**Population:** Median age=40yrs; Gender: Male=7, Female=6; Median time post-injury=23yr. **Intervention:** Heart rate variability biofeedback training was conducted for 10 1-hour sessions. After the fourth session individuals were given a portable biofeedback device to take home and self-monitor.	1. HRV biofeedback significantly improved CT scores ($p<0.05$), this effect was magnified by those experiencing positive affects during treatment as measured by the PANAS. 2. No other significant results were found.

	Outcomes: Category Test (CT), Heart rate variability index (HRV), Positive Affect and Negative Affect Schedule (PANAS).	
Dahdah et al. (2017) USA Pre-Post $N_{Initial}$=21 N_{Final}=15	**Population:** CVA=6, TBI=5, Tumor=2, Anoxia brain injury=2; Mean Age=40.3 yr; Gender: Male=12, Female=3. **Treatment:** Participants received the virtual reality (VR) intervention sessions (apartment and classroom) twice per week for a 4 wk period. Sessions 1 and 8 included all types of distractors, sessions 2 and 3 included no distracting stimuli, sessions 4 and 5 included only auditory distracting stimuli, and sessions 6 and 7 included only visual distracting stimuli. **Outcome Measure:** Woodcock-Johnson, 3rd edition (WJ-III pair cancellation subtest), Delis-Kaplan Executive Function System (D-KEFS Color-Word Interference subtest), Automated Neuropsychological Assessment Metrics (ANAM Go/No-Go and unimodal Stroop subtests), VR Stroop task (apartment and classroom).	1. No statistically significant performance differences were found from baseline to conclusion of the study for the VR apartment Stroop or D-KEFS Stroop test. 2. For the VR classroom, participants' shortest response time on the word-reading condition was significantly reduced by session 8 (p=0.0383). All other VR classroom Stroop variables did not show significant differences. 3. No significant differences from session 1 to session 8 were found for all pair cancellation subtest scores. 4. From session 1 to 8, the ANAM Stroop word-reading percentage of items with a correct response (p=0.0293), ANAM Stroop word-reading number of correct responses per minute (p=0.0321), and ANAM Go/No-Go number of impulsive/bad responses (p=0.0408) significantly increased. All other ANAM variables did not show significant differences.
O'Neil-Pirozzi and Hsu (2016) PCT $N_{Initial}$=14 N_{Final}=12	**Population:** TBI=4, CVA=2, Brain tumour=1; Severity: moderate/severe. *Experimental Group (n=7)*: Mean Age=51.3 yr; Gender: Male=5, Female=2; Mean Time Post Injury=20.9 yr; Etiology: TBI=5, CVA=2. *Control Group (n=7):* Mean Age=46.9 yr; Gender: Male=7; Mean Time Post Injury=25.0 yr. **Treatment:** Experimental group participants received BrainHQ, a commercially available online computerized cognitive exercise program (Attention, Brain Speed, Memory, People Skills, Intelligence, and Navigation) for 5 mo, 5 d/wk. Control group participants did not have a private computer and received no intervention. **Outcome Measure:** Number/Percentage of Sessions Completed, Number/Percentage of Sessions Initiated by Participants, Number/Percentage of Sessions Completed Independently by Participants, Mean Amount of External Cures Provided for Session Completion, Wisconsin Card Sorting Test (WCST), Hopkins Verbal Learning Test-Revised (HVLT-R immediate, delayed), Controlled Oral Word Association Test-FAS (COWAT), Trail Making Test (TMT A and B accuracy and speed), Satisfaction with Life Scale (SWLS), Semi-structured interview questions.	1. Of the five experimental group participants that completed the study, they completed an average 87% of sessions, initiated an average 25% of sessions, and independently completed an average 7% of sessions. Two participants needed minimum external cues, two participants needed moderate external cures, and one participant needed maximum external cues. 2. Comparing 3 mo prior to intervention with 1 wk prior to intervention, there were no significant differences within either group for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 3. There were no significant differences between groups at 1 wk prior to intervention (baseline) for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 4. Compared to baseline, experimental group showed significant improvement post-intervention for HVLT-immediate (p=0.0255) and SWLS (p=0.0075). There were no significant improvements for WCST, HVLT-delayed, or TMT A or B. 5. Compared to baseline, control group did not show significant differences post-intervention for WCST, HVLT, TMT A or B, or SWL. 6. Compared to control group, experimental group showed significantly higher post-intervention improvements on HVLT-immediate (p=0.0068) and COWAT (p=0.0310). No significant differences between groups

		were found for changes in WCST, HVLT-delayed, TMT A or B, or SWL. 7. Of the experimental group participants who completed the study, 60% reported improved everyday thinking abilities, 60% reported improved memory, and 20% reported improved attention, organization, and/or problem solving skills, but 60% reported they would not continue with exercise program post-study completion.
Li et al. (2015) USA Pre-Post $N_{Initial}$=13 N_{Final}=12	**Population:** Stroke=5, TBI=5, Brain tumor=2; Mean Age=61 yr; Gender: Male=10, Female=2. **Treatment:** Participants received the computer-based cognitive retraining program, Parrot Software. The following eight modules were each completed in separate 1 h sessions: Visual Instructions, Attention Perception and Discrimination, Concentration, and Visual Attention Training, Remembering Written Directions, Remembering Visual Patterns, Remembering Written Letters, and Remembering Written Numbers. **Outcome Measure:** Montreal Cognitive Assessment (MoCA overall, attention, memory), Medication-box sorting task.	1. Compared to baseline, there was a significant mean increase in overall MoCA of 3.25 (p=0.030) post-intervention. However, the attention and memory subscales did not show significant differences. 2. There were no significant differences before and after intervention for the medication-box sorting task. 3. Participants with previous computer-based cognitive retraining experience had significantly more MoCA improvement than those without (p<0.010). 4. Age, education level, or type of ABI diagnosis did not have any significant effects on MoCA or medication-box scores.
Fong & Howie (2009) China PCT N=33	**Population:** Mean age=33.4yr; Gender: Male=27, Female=6; Mean time post-injury=12.3 mo. **Intervention:** The experimental group received an enhanced cognitive training program in addition to the standard cognitive rehabilitation training program received by the control group. **Outcomes:** Key Search test, Social Problem-Solving Video Measure (SPSVM), Means-Ends Problem-Solving Measure (MEPSM), Raven's Progressive Matrices (RPM), Metacomponential Interview (MI).	1. No significant differences were found on the Key Search test, the SPSVM, RPM, or the MEPSM between groups following intervention. 2. There were significant between group differences on two of the categories for the MI; correctness of representation scores (p=0.041), and total average correct scores (p=0.009). No other significant differences were found.
Laatsch et al. (1999) USA Case Series N=5	**Population:** TBI; Age Range=18-65 yr; Time Post-Injury=2-48 months; **Intervention:** Cognitive rehabilitation therapy (CRT) programme in a longitudinal protocol involving a resting SPECT and neuropsychological evaluation are pre-treatment, post-treatment and post non-treatment intervals. **Outcome Measure:** Neuropsychological measures.	1. NP measures: WAIS-R, WMS-R, CVLT, RCFT, SCWT, WCST or ACT, SPECT image. 2. SPECT data revealed significant increases in cerebral blood flow during the treatment period (p<0.050). 3. CRT was found to be effective in improving both NP and everyday functioning. All patients were able to be more productive in their lives following treatment.
Chen et al. (1997) USA Case-Control N=40	**Population:** Age=18+ yr; Gender: male=27, female=13; Condition: TBI. **Intervention:** Divided retrospectively into computer-assisted rehabilitation (CACR) and tradition therapy groups **Outcome Measure:** Neurophysiological Test Scores (WAIS-R; WMS).	1. Both groups made significant post-treatment gains on the neurophysiological test scores (p<0.050), with the CACR group making significant gains on 15 measures (p<0.050) and the comparison group making significant gains on seven measures (p<0.005). 2. However, no significant difference was found

		between groups on their post-treatment gains.
Freeman et al. (1992) United States PCT N=12	**Population:** *Experimental Group (N=6):* Mean age=38.5yr; Mean time post-injury=33.33mo. *Control Group (N=6)*: Mean age=47.83yr; Mean time post-injury=11.83mo. **Intervention:** The intervention consisted of being enrolled in a 6-month cognitive rehabilitation programme which met 3x weekly, for 2 hours. The control group received no such treatment. **Outcomes:** Wechsler Adult Intelligence Scale for Children (WAIS-R)	1. Post-intervention the experimental group was seen to have significantly improved scores on the WAIS-R compared to the control group (p=0.02).

Discussion

The effects of hypnosis, as delivered in a targeted or non targeted manner, on memory, attention, and cognitive function in a mixed TBI and stroke population has been investigated (Lindelov et al. 2017). The researchers showed that working memory, attention, and cognitive function could be transiently increased during targeted hypnosis; however, the benefits of the treatment were not sustained when the treatment was discontinued. With respect to attention process training, it was shown that this intervention may have indirectly improved executive function as individuals with higher vigilance achieved higher executive function scores, but it was not explicitly demonstrated that training resulted in increased vigilance (Sohlberg et al., 2000).

Siponkoski et al. (2020) investigated the effects of 20 sessions of music therapy (rhythmical training, structured cognitive-motor training and assisted music playing) on measures of executive function. Compared to the control group, significant improvements on measures of executive function were observed for those receiving music therapy.

Dual-task training which is also used as a form of attention training was also evaluated in another RCT and although individuals were improved on measures of attention to a significantly greater extent than controls, no such relationship was found for measures of executive function (Couillet et al., 2010).

With the development of technology, the use of virtual-reality training and computer programs have gained traction as an intriguing tool used for improving executive function in patients post TBI. In terms of cognitive functioning, two RCTs found varying results for executive functioning outcomes after training in a virtual environment (Jacoby et al., 2013; Man et al., 2013). One RCT focusing on vocational problem-solving skills (Man et al., 2013) identified significant improvements in both VR intervention and conventional psychoeducation control groups; however, there were no significant between-group differences for cognitive or vocational outcomes except on WCST % errors and % conceptual level response (Man et al., 2013). Conversely, Jacoby et al (2013) found that patients receiving virtual reality training improved more on multi-tasking measures and executive function when compared to the control group who received general cognitive re-training treatment. In a pre-post study, Dadah et al.

(2017) investigated virtual reality interventions in a mixed ABI population. The researchers found that repetition of the Stroop test in different virtual reality environments showed limited improvement in performance on those specific tests (Dahdah et al., 2017). As a result of the mixed results reported on the efficacy of virtual reality training post ABI, it is difficult to make a conclusive decision on what aspects of executive functioning virtual reality benefits, and to what degree.

As previously mentioned, computer software programs have also been investigated for their efficacy in improving executive dysfunctions post TBI. Recently, BrainHQ, a commercially available online computerized cognitive exercise program, showed mixed results for improving executive function post ABI (O'Neil-Pirozzi & Hsu, 2016). Although individuals self-reported improvements in daily functioning, no significant results were seen on objective measures (O'Neil 2016). Parrot Software is another computer-based cognitive retraining program, and was investigated by a pre-post study assessing the efficacy of using eight modules focussed on attention and memory (Li et al., 2015; Li et al., 2013). While significant post-treatment improvements in attention and memory on the Cognistat assessment were found in a pilot study (Li et al., 2013), a subsequent study did not find significant improvements on the Montreal Cognitive Assessment (MoCA) or a medication-box sorting task despite significantly improved overall MoCA scores (Li et al., 2015). This lack of improvement compared to a control group was also reported by Powell et al. (2017) when the ProSolv smartphone application was used to improved pressure management and problem-solving skills. Finally, Chen et al. (1997) studied the effect of computer assisted cognitive rehabilitation versus traditional therapy methods. While measures of attention significantly improved in both groups after treatment, no significant differences were observed between groups on any measures related to executive function (Chen et al., 1997). Cumulatively, by observing studies from across a period of nearly 20 years, the literature reveals little support for the use of computer software programs for the improvement of executive function post TBI.

In an RCT, Spikman et al. (2010) randomly divided a group of individuals who had sustained a TBI to either a multifaceted strategy training group or a control group. Those in the treatment group were taught a comprehensive cognitive strategy which allowed them to tackle the issues and problems of daily living, compared to the control group which received a computerized training package that was aimed at improving general cognitive functioning. Overall, results indicate both groups improved on many aspects of executive functioning; however, those in the treatment group showed greater improvement in their ability to set and accomplish realistic goals and to plan and initiate real life tasks (Spikman et al., 2010). The findings of the previous experiment agree with the findings of the study by Laatsch et al. (1999) and Freeman et al. (1992), where cognitive rehabilitation therapy was found to increase productivity and everyday functioning. This older study (Laatsch et al., 1999) also had the benefit of reporting SPECT imaging results, which revealed increases in cerebral blood flow during the intervention. It should be noted that one study has found mixed results on measures of executive functioning after administering a cognitive training program, with individuals improving on some measures of executive functioning, such as metacognition, but not others (Fong & Howie, 2009). It should be noted that none of the above studies were completed by the same groups or had overlapping methodology and although

the results suggest cognitive training programs are effective for improving executive functioning following an ABI, programs themselves should be considered unique.

A specific cognitive program (Categorization Program) was evaluated in an RCT by Constantinidou et al. (2008). The authors found that after 13 weeks of therapy (mean 4.5 hr/day), individuals significantly improved on measures of executive functioning such as object recognition. Although the Categorization Program treatment group and standard therapy therapy group showed improvement on the community reintegration questionnaire and adaptability measures, there were greater executive function gains in the treatment group (Constantinidou et al., 2008). The Intensive NeuroRehabilitation Programme investigated by Holleman et al. (2018) resulted in significantly reduced depression and anxiety compared to the control group but did not improve measures of executive functioning. Similarly, a novel program – Cognitive Applications for Life Management, did not find significant improvements in measure of executive functioning (Elbogen et al., 2019). Although the program did improve measures of emotion and behavioural regulation (Elbogen et al., 2019).

Another unique study used heart rate variability biofeedback in an attempt to increase awareness and cognitive control (Kim et al., 2018). In this study it was noted that individuals who underwent heart rate biofeedback significantly improved scores of executive functioning on the Category Test. However, this study consisted of a pre-post design and lacked a control group for comparison, and as such results should be interpreted with caution. Only one study evaluated the effects of repetitive transcranial magnetic stimulation on executive function; however, no significant improvements were observed between groups (Neville et al., 2019).

Levine et al. (2000) completed an RCT comparing a group of patients using goal management training strategies to a control group who were received only motor skills training. The treatment group improved on paper and pencil everyday tasks as well as meal preparation-which the authors used as an example of a task heavily reliant on self-regulation in comparison to the motor treatment group. It is important to note, however, that the motor group performed superiorly on timed neuropsychological tests, and no differences were found between treatments in terms of intelligence. Two other studies evaluated goal management training and did not find any significant results suggesting that goal management training improves executive functioning following an ABI (Cizman Staba et al., 2020; Levack et al., 2009). A single older study reported positive affects of a goal setting program in its ability to help an individual achieve goals (Webb & Glueckauf, 1994). The execution of goals themselves requires executive functioning; however, no objective measures of executive function were directly evaluated in this study.

Conclusions

There is level 1b evidence that targeted hypnosis may transiently improve cognitive function in post TBI patients or stroke.

There is level 1b evidence that an attention remediation intervention may not be superior to TBI education alone and improving executive function in patients post TBI.

There is level 2 evidence that dual-task training may improve not general cognitive functioning compared to a non-specific cognitive program in patients post TBI.

There is level 1b evidence that a comprehensive cognitive treatment strategy program (which include problem solving), compared to controls, are effective for improving metacognition and goal achievement post TBI.

There is level 4 evidence that cognitive rehabilitation may increase productivity in everyday functioning, and cerebral blood flow during treatment in patients post TBI.

There is level 1b evidence that virtual-reality training is not superior to conventional cognitive training at improving cognitive and executive function outcomes post TBI.

There is level 1b evidence that the specific cognitive training program ProSolv, compared to standard therapy, does not improve measures of executive functioning following an ABI.

There is level 2 evidence that the Intensive NeuroRehabilitation programme, compared to no treatment, does not improve executive functioning following an ABI.

There is level 2 evidence that computer or smartphone software programs, such as BrainHQ, Parrot Software, ProSolv app, may not be superior to no intervention at improving problem-solving skills and general functioning in patients post TBI.

There is level 4 evidence that heart rate biofeedback may improve executive functioning following an ABI, although higher level studies are required to fully determine this.

There is level 2 evidence that goal management training may be superior (compared to motor skills training or no treatment controls) for improving goal attainment or measures of intelligence following an ABI.

KEY POINTS

- Targeted hypnosis may improve memory, attention, and cognitive function in post TBI patientsor stroke; however, only as long as the intervention is being administered.
- Attention training programs likely do not improve executive functioning.
- General cognitive training programs which include problem-solving appear to be effective for improving executive functioning following an ABI.
- Virtual reality does not likely improve executive functioning following an ABI.
- Computer or smartphone software programs (BrainHQ, Parrot Software, ProSolv app) may not be superior to common interventions at improving memory, attention, and problem-solving skills in patients post TBI.
- Goal management training may be superior to motor skills training at improving everyday skills (meal preparation), but not intelligence or neuropsychological outcomes in patients post TBI.
- Heart rate variability biofeedback may improve executive functions; however, more controlled studies are required to make further conclusions.

Group-based Interventions

Although executive function deficits are a common there is little overall research directly addressing the impact of rehabilitation on executive function. However, community integration and other similar group-based interventions are highly related to executive function and it is possible that programs and interventions presented in a group-based setting may in fact be focusing efforts on instrumental activities of daily living which may reflect (or are dependent on) executive functions. The efficacy of group-based interventions on cognitive and executive function are discussed below.

TABLE 5 | The Effects of Group therapy on Executive Function Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Tornas et al. (2016) Norway RCT PEDro=9 $N_{Initial}$=70, N_{Final}=67	**Population:** TBI=45, Stroke=15, Tumour=6, Anoxia=2, Other=2. Mean Age=42.89 yr; Gender: Male=38, Female=32; Mean Time Post Injury=97.47 mo. **Intervention:** Participants were randomized to receive Goal Management Training (TG) or Brain Health Workshop (CG) group sessions. GMT group (n=33) discussed distinctions between absentmindedness/presentmindedness, slip-ups in daily life, habitual responding, stopping and thinking, working memory, importance of goals, defining/splitting goals into subtasks, and	1. In the TG, significant improvements were found on BRIEF-A, DEX, and CFQ at T3 ($p<0.010$). 2. In the CG, significant improvements were found on only BRIEF-A at T2 ($p<0.050$). 3. The TG showed significant improvements on BRIEF-A and DEX ($p<0.010$), but not CFQ, compared to the CG over time 4. In the TG, significant improvements were found on CPT-II, CWI, TT, and HT at T2 and T3 ($p<0.050$), VFT at T3 ($p<0.050$), and UPSA at T2 ($p<0.001$).

	checking. BHW control group (n=37) discussed brain function/dysfunction, brain plasticity, memory, executive function, and attention. Treatment was received one day every second week, for a total of eight two-hour sessions distributed over four days. Outcomes were assessed at baseline (T1), after treatment (T2), and at six-month follow-up (T3). **Outcome Measures:** Behaviour Rating Inventory of Executive Function–Adult (BRIEF-A); Dysexecutive Questionnaire (DEX); Cognitive Failures Questionnaire (CFQ); Continuous Performance Test II (CPT-II); UCSD Performance-Based Skills Assessment (UPSA); Delis-Kaplan Executive Function System Battery–Colour-Word Interference Test (CWI), Verbal Fluency Test (VFT), and Tower Test (TT); Trail Making Test (TMT); Hotel Task (HT).	5. In the CG, significant improvements were found on CPT-II, TT, and HT at T2 and T3 ($p<0.050$), and VFT and UPSA at T2 ($p<0.050$). 6. The TG showed a significant improvement on CWI, VFT, and TT ($p<0.050$), but not CPT-II, UPSA, and HT, compared to the CG over time. 7. No significant differences were found on TMT within or between groups over time.
Tornas et al. (2019) Norway $N_{Initial}$=67, N_{Final}=50 **5yr Follow-up to:** Tornas et al. (2016) Norway RCT PEDro=9 NInitial=70, NFinal=67	**Population:** TBI=29, Stroke=13, Tumor=6, Anoxic/other=2. Mean Age=45.8±10.9yr; Gender: Male=27, Female=23; Mean Time Post Injury=104.9±128.1mo. **Intervention:** Participants were randomized to receive Goal Management Training (GMT) or Brain Health Workshop (BHW) group sessions. GMT group (n=33) discussed distinctions between absentmindedness/ present mindedness, slipups in daily life, habitual responding, stopping and thinking, working memory, importance of goals, defining/splitting goals into subtasks, and checking. BHW control group (n=37) discussed brain function/dysfunction, brain plasticity, memory, executive function, and attention. Treatment was received one day every second week, for a total of eight, two-hour sessions distributed over four days. Outcomes were assessed at baseline (T1), after treatment (T2), and at six-month follow-up (T3). This was a 5-year follow-up. **Outcome Measures:** Behavior Rating Inventory of Executive Function- Adult Version (BRIEF-A), the Quality of Life after Brain Injury (QOLIBRI).	1. A significant main effect of time was found for all BRIEF-A indexes between baseline and 6mo follow-up. 2. A significant time by group interaction for the Behavioural Regulation Index; the GMT-group showed a significant increase in behavioural regulation index symptoms that the BHW group did not 3. There was no significant difference found between baseline and 5yr follow-up in either group on the BRIEF-A or QOLIBRI.
Cantor et al. (2014) USA RCT PEDro=6 N=98	**Population:** TBI; Mean Age=45.3 yr; Gender: Male=37, Female=61; Mean Time Post Injury=12.6 yr; Severity: Mild=49, Moderate=19, Severe=30. **Intervention:** Participants were randomly assigned to either immediate start (IS; n=49) or waitlist control (WL; n=49) groups. Participants received group sessions of emotional regulation (2 sessions, 45 min) and an individual problem-solving session of attention training (1 session, 60 min) per day (3 days/wk for 12 weeks). Group sizes were generally 4-6 participants.	1. There was a significant treatment effect for the EF index favoring the IS group ($p=0.008$). 2. There was no significant difference between groups in the DERS of ARMS. 3. Secondary analysis revealed a significant treatment effects for the FeSBe scale ($p=0.049$) and the PSI ($p=0.016$). There were no other significant treatment effects. Variance of depression, age, severity and time since injury did not change treatment effects.

	Outcome Measure: Attention Rating and Monitoring Scale (ARMS), Behavioural Assessment of the Dysexecutive Syndrome, Difficulties in Emotion Regulation Scale (DERS), Executive Function Composite from Factor Analysis (EF index), Problem Solving Inventory (PSI), Frontal System Behavioural Scale (FrSBe).	
Vas et al. (2011) USA RCT PEDro=6 N=28	**Population:** TBI: *Strategic Memory and Reasoning Training (SMART) Group* (n=14): Mean Age=39 yr; Gender: Male=9, Female=5; Mean Time Post Injury=16.71 yr. *Brain Health Workshop Group* (n=14): Mean Age=47 yr; Gender: Male=7, Female=7; Mean Time Post Injury=16.35 yr. **Intervention:** Participants were randomly assigned to the SMART group or the BHW group. Participants received a total of 12 group sessions over an 8 wk period. The SMART group learned about strategies they could apply in their daily lives; homework was given at the end of each session. The BHW group sessions were designed to be information-based and reading assignments were given each week. Participants were assessed at baseline, post-training (3 weeks) and at a 6 month follow-up. **Outcome Measure:** Test of Strategic Learning (TOSL); Working memory listening span task; Community Integration Questionnaire (CIQ); Wechsler Adult Intelligence Scale III (WAIS III).	1. The SMART group had significantly greater TOSL scores compared to the control group post-training (SMART *Mean*=19.76, BHW *Mean*=13.69, p=0.030). 2. The SMART group had significant improvements in TOSL scores: post-training (*Mean*=19.76, p=0.007) and at 6-month follow-up (*Mean*=21.15, p=0.004) from baseline (*Mean*=14). 3. The SMART group had significantly greater improvements than the control group on the working memory listening span task post-training (SMART *Mean*=4.23, BHW *Mean*=2.59, p<0.001). 4. The SMART group had significant improvements post-training in the working memory listening span task (*Mean*=4.23, *p*=0.005) and at 6-month follow-up (*Mean*=4.96, P=0.0001) compared to baseline (*Mean*=2.76). 5. The SMART group had significantly greater improvements on CIQ compared to the BHW group (SMART *Mean*=18.73, BHW *Mean*=16.45, p=0.020). 6. The SMART group had significant improvements in the CIQ at the 6-month (*Mean*=19.88, p=0.010) follow-up from baseline (*Mean*=15.19). Those in the SMART group showed significant improvement on 3 executive functions following training (inhibition: p=0.010; nonverbal reasoning: p=0.001; and cognitive flexibility: p=0.010) on the WAIS-III.
Chen et al. (2011) USA RCT PEDro=5 N=12	**Population:** TBI=9, Other=3: Mean Age=48 yr; Gender: Male=5, Female=7; Time Post-Injury Range=6 mo-6 yr. **Intervention:** Participants were randomized to receive either the goals training intervention (n=7) or education intervention (n=5) for 5 wk, after which they switched to the other condition for another 5 wk. The goals training was spread over 5 wk and involved: group, individual and home-based training. The education program was a 5 wk didactic educational instruction regarding brain injury. **Outcome Measures:** Letter number sequencing, Wechsler Adult Intelligence Scale-	1. On the domain of attention and executive functions, all participants in the goal training intervention showed an increase from pre to post goals training; while only 7/12 in the education intervention showed an increase from pre to post education (p<0.0001). 2. For learning and memory performance scores increased an average of 0.70 units after participation in goals training than after participation in education intervention (p=0.020). 11/12 participants improved in the goals training group while 4/12 improved in the education group (p=0.009).

	III, Auditory consonant trigrams, Digit Vigilance Test, Design and Verbal Fluency Switching, Trails B, Stroop Inhibition, Hopkins Verbal Learning Test, Brief Visual Memory Test Revised, Trails A test, Visual Attention Task.	3. Tests of motor speed of processing showed no significant differences between the two interventions with a non-significant trend for greater improvements in goal-training compared to education (p=0.070).
Novakovic-Agopian et al. (2011) USA RCT Crossover PEDro=5 N=16	**Population:** TBI=11, Stroke=3, Other=2: Mean Age=50.4 yr; Gender: Male=7, Female=9; Time Post Injury Range=1-23 yr. **Intervention:** Participants were randomized to 5 wk interventions consisting of a goals training program (n=8) or an educational instruction group (n=8). Goal training focused on mindfulness-based attentional regulation and goal management strategies for participant-defined goals. Educational training was didactic instructional sessions about brain injury. At the end of 5 wk, participants were switched to the other intervention. All participants were assessed at baseline, Week 5 and again at Week 10. **Outcome Measure:** Auditory Consonant Trigrams, Letter Number Sequencing (working memory); Digit Vigilance Test (sustained attention); Stroop Inhibition Delis-Kaplan Executive Function System (Inhibition); Trails B, Design Fluency-switching (mental flexibility), Hopkins Verbal Learning Test-Revised, Brief Visual Memory Test-Revised.	1. At the end of wk 5 participants in the goals-edu group showed significant improvement on measures of attention and executive function from baseline (p<0.0001), while the edu-goals group showed no change or minimal change (p>0.050). 2. The goals-edu group had significantly greater improvements than the edu-goals group on the following at wk 5: working memory (M*ean* 1.12 vs -0.12, p<0.0001); mental flexibility (*Mean* 0.64 vs 0.04, p=0.009); inhibition (*Mean* 0.62 vs 0.04, p=0.005); sustained attention (*Mean* 0.96 vs 0.27, p=0.010); learning (*Mean*=0.51 vs 0.08, p=0.020); and delayed recall (*Mean* 0.39 vs -0.27, p=0.010). 3. At wk 10, the edu-goals group significantly improved compared to wk 5 on: attention and executive function (0.79 vs 0.03, p<0.0001); working memory (1.31 vs -0.12, p<0.0008); mental flexibility (0.66 vs 0.04, p<0.0008); inhibition (0.50 vs 0.04, p=0.010); sustained attention (0.44 vs 0.27, p=0.010); memory (0.609 vs -0.10, p=0.020); learning (0.66 vs 0.08, p=0.050); and delayed recall (0.55 vs -0.27, p=0.020). Those in the goals-edu group who had completed the training session were able to maintain their gains and there were significant improvements in attention and executive function (p<0.040) and working memory (p<0.020).
Ownsworth et al. (2008) Australia RCT PEDro=9 N=35	**Population:** TBI=21, Other=14; Mean Age=43.89yr; Gender: Male=19, Female=16; Mean Time Post Injury=5.29yr. **Treatment:** Participants were randomized to receive one of three 8wk intervention groups for goal attainment: individual (n=10), group (n=11), or combined (n=10). Individual treatment occurred in participant homes and community while also focusing on client-centered goals. Group-based treatment involved education, peer and facilitator feedback, and goal setting. The combined group received the equivalent amount of individual and group therapy. **Outcome Measure:** Canadian Occupational Performance Measure (COPM): performance self-rating, satisfaction self-ratings, relatives' performance ratings, and relatives' satisfaction ratings.	1. There were significant improvements on performance self-ratings between pre-post intervention for the individual (4.08 to 6.78, p<0.01) and combined interventions (5.04 to 6.98, p<0.01) but not the group intervention (4.68 to 6.10, p=0.029). At follow-up, all interventions had significant improvements from pre-intervention (p<0.01). 2. There were significant improvements on the satisfaction self-ratings between pre-postintervention for all three interventions: individual (3.75 to 7.22, p<0.001), group (4.51 to 5.95, p<0.025) and combined (4.35 to 7.47, p<0.01). 3. There were significant improvements for relatives' rating of performance between pre-post intervention for the individual (3.94 to 6.53, p<0.01) and combined interventions (4.37 to 5.32, p<0.025) but not the group intervention (4.78 to 5.93, p=0.028). At follow-

		up, all interventions had significant improvements ($p<0.01$).
Rath et al. (2003) USA RCT PEDro=2 N=46	**Population:** TBI: Mean Age=43.6 yr; Gender: Male=23, Female=37; Mean Time Post Injury=48.2 mo. **Intervention:** Patients were randomized into the innovative (n=32) or conventional (n=28) treatment groups. The innovative group received 24, 2 hr sessions focusing on emotional self-regulation and clear thinking. The conventional group received 24, 2-3 hr sessions focusing on cognitive remediation and psychosocial groups. **Outcome Measure:** Weinberg Visual Cancellation Test, Stroop Color–Word Task, FAS—Controlled Oral Word Association Test, Will-Temperament Scale, Visual Reproduction, Immediate and Delayed recall, Watson-Glaser Critical Thinking Appraisal, Wechsler Adult Intelligence Scale—III.	1. The innovative group showed significant improvements in visual memory immediate recall ($p<0.001$). 2. The conventional and the innovative group showed significant improvements: on logical memory recall ($p<0.001$), logical memory delayed recall ($p=0.010$), and visual memory delayed recall ($p=0.010$). 3. The conventional group had significant improvements in reasoning ($p<0.050$). 4. The innovative group had significant improvements in executive function ($p<0.050$); problem-solving self-appraisal ($p=0.005$); self-appraised clear thinking and emotional self-regulation ($p<0.010$); and observer ratings of roleplayed scenarios ($p<0.005$).
Copley et al. (2015) Australia Pre-Post N=8	**Population:** ABI; Mean Age=44.5 yr; Gender: Male=5, Female=3; Mean Time Post Injury=12 mo; Severity: Moderate-Severe. **Intervention:** All participants completed a treatment consisting of metacognitive strategy instruction (MSI) during 3 components. 1) Individualized sessions (IS) consisted of identifying language based goals and strategies to accomplish them (2 hr x2 sessions). 2) Group sessions (GS) where participants work on their goals in a group setting completing auditory and written comprehension tasks (1.5 hrs). 3) Daily home practice sessions (HS) involved transferring the skills learnt in the first 2 components into everyday life by teaching the significant other how to implement MSI. **Outcome Measure:** Measure of Cognitive-Linguistic Abilities Subtests: Paragraph Comprehension, Story Recall, Verbal Abstract Reasoning, Functional Reading, Factual Comprehension, Inferential Reasoning Skills (Low Level and High Level).	1. There was no significant difference in pre-post scores for paragraph comprehension ($p=0.340$). 2. There was no significant difference in pre-post scores for story recall ($p=0.028$). 3. There was no significant difference in pre-post scores for verbal abstract reasoning ($p=0.111$). 4. There was no significant difference in pre-post scores for functional reading ($p=0.204$). 5. There was no significant difference in pre-post scores for factual comprehension ($p=0.891$). 6. There was no significant difference in pre-post scores for inferential reasoning skills, both low level ($p=0.125$) and high level ($p=0.020$).
Gabbatore et al. (2015) Italy Pre-Post $N_{Initial}=20$, $N_{Final}=15$	**Population:** TBI; Mean Age=36.7 yr; Gender: Male=10, Female=5; Mean Time Post Injury=76.1 mo; Mean GCS=4.5. **Intervention:** Participants completed a cognitive group rehabilitation program focussed on mental representations underlying one's behaviours (2 x/week for 3 months). Each session consisted of comprehension activities (discussing specific communication modalities) and production activities (role-playing activities). Participants were assessed at T0 (3 months before intervention (regular activities	1. No significant improvements in ABaCo (production and comprehension) were observed from T0 to T1. 2. Participants showed significant improvements from T1 to T2 for ABaCo comprehension ($p<0.001$), production ($p<0.001$), linguistic ($p=0.005$), extralinguistic ($p=0.008$), paralinguistic ($p=0.02$), and context ($p=0.01$). 3. The improvements made during the treatment period were stable between T2 and T3 for both Comprehension ($p=0.86$) and Production

	during this time), T1 (before intervention), T2 (after intervention) and T3 (3 month follow-up – regular activities during this time). Total study duration was 9 months. **Outcome Measure:** : Assessment Battery for Communication (ABaCo-comprehension, production, linguistic, extralinguistic, paralinguistic, and context), Verbal Span Task (VST), Spatial Span Task (SST), Attentive Matrices Test (AMT), Trail Making Test (TMT), Tower of London Test (TOL), Colored Progressive Matrices Raven (CPM Raven), Aachener Aphasie Test-Denomination Scale (AAT), Sally-Ann Task, Strange Stories Task, Immediate and Deferred Recall Test (IDR), Wisconsin Card Sorting Test (WCST).	(p=0.32). At T3, AbaCo scores did not show significant differences from T2. 4. There was no significant difference between T1 and T2 on the VST (p=0.49), SST (p=0.74), AMT (p=0.35), TMT (p=0.45), TOL (p=0.50), CPM Raven (p=0.09), AAT (p=0.22), Sally-Ann (p=0.58), or strange stories task (p=1.00). 5. There was a significant improvement between T1 and T2 on the IDR (p=0.01) and WCST (p=0.003).
Llorens et al. (2012) Spain Pre-Post N=10	**Population:** ABI=10; Mean Age=41.1yr; Gender: Male=7, Female=3; Mean Time Post Injury=402.2d. **Intervention:** Participants underwent sessions (1hr/wk for 8mo) using an interactive touch screen based game asking questions related to knowledge, reasoning, action, and cohesion in groups of ≤4. Testing of participants occurred at baseline and post intervention. **Outcome Measure:** Self-Awareness Deficits Interview (SADI), Social Skills Scale (SSS).	1. On the SADI, after treatment all participants perceived their deficits properly compared to only 4 participants at baseline; 2 participants had difficulty perceiving their disability post treatment compared to 7 participants at baseline and 5 participants had difficulty establishing realistic goals post treatment compared to 7 at baseline. 2. On the SSS at baseline, 6 participants showed altered levels in social skills, compared to 2 following treatment.
Parente & Stapleton (1999) USA Case-Control N=33	**Population:** ABI. **Intervention:** A one year measure of group cognitive skills (CSG) training module. **Outcome Measure:** Return to work.	1. Ten of 13 CSG clients who completed the training program by the end of the year had maintained full employment for >60 days (76%) - versus 58% of the control group. Significance not calculated.

Discussion

Several studies have evaluated the effects of group goal management training. One study has compared the effect of group Goal Management Training (TG) to a group Brain Health workshop (CG) on cognitive outcomes post brain injury (Tornas et al. 2016). The study showed that individuals receiving goal management training improved significantly in cognitive and executive outcomes after treatment, and at 6-month follow-up. While this study showed promising results, it is important to remember that despite its rigorous methodology, the patient population was very heterogenous and it is unclear how different injuries impacted the outcomes. In a five-year follow-up to this study, Tornas et al. (2019) examined the long-term benefits to goal management training, and found no significant difference between groups on measures of executive function. Similar results of goal management training were found in an RCT by Novakovic-Agopian et al. (2011), where a goals training group showed significant improvement on attention and executive function assessments compared to the educational group. Despite switching interventions at the 5-week mark to the educational intervention, the goal training group continued to improve significantly. Interestingly, an RCT published in the same year also demonstrated that goal training is beneficial for executive functions (Chen et al., 2011). In this study

both groups significantly improved in attention directed goal completion. A final RCT evaluated group goal attainment interventions compared to educational interventions (Ownsworth et al., 2008). This study found that all individuals who received goal attainment interventions significantly improved over time on measures of executive functioning, regardless of group assignment at 3-month follow-up based on self-ratings, and relative's ratings (Ownsworth et al., 2008).

Emotional regulation was also examined as a potential intervention for the remediation of attention and executive dysfunction post ABI (Cantor et al., 2014; Rath et al., 2003). While this treatment was not found to be effective in the recovery of attention, significant improvements on executive function were noted (EF, FeSBe, PSI) (Cantor et al., 2014). Further support for emotional oriented intervention can be found in an earlier study by Rath et al. (2003). The group completed an RCT comparing two cognitive rehabilitation therapies: conventional (cognitive remediation and psychosocial components) versus an innovative rehabilitation approach focusing on emotional self-regulation and clear thinking. Outcomes were measured across multiple domains of cognition including attention, memory, reasoning, psychosocial functioning, and problem-solving measures. Significant changes comparing baseline to post intervention outcomes were seen for each group on problem-solving measures; however, the improvements were different for the interventions. No between-group comparisons were made.

A pre-post study by Copley et al. (2015) investigated the effects of a Metacognitive Strategy Instruction (MSI) intervention on verbal and cognitive outcomes post ABI. The program was delivered individually, in a group-setting, and at home. Despite the multi-step process, no improvements were observed in cognitive or verbal abilities from baseline after the intervention. Gabbatore et al. (2015) implemented a cognitive group rehabilitation program for patients post TBI, and discovered that compared to before the intervention, patient's recall (IDR), attention (WCST), and communication skills (ABaCo) all significantly improved. Specifically, the ABaCo was used to measure linguistic comprehension and context comprehension.

In addition to its use as a memory intervention the Strategic Memory and Reasoning Training (SMART) program is also an effective intervention for executive functioning. Vas et al. (2001) compared its use to that of a brain health workshop. The SMART group had significantly higher scores on the Test of Strategic Learning, and Wechsler Adult Intelligence Scale III for sections examining inhibition, non-verbal reasoning, and cognitive flexibility, demonstrating an overall improvement in metacognition and comprehension.

Only one study using a technology-based intervention met our inclusion criteria. Llorens et al. (2012) used an interactive touch screen game in an attempt to improve social skills and self-awareness following ABI. Although no formal statistical analysis took place, at the end of the treatment period all participants had an accurate perception of their deficits (compared to 4/10 at baseline), and six of ten participants showed alterations in their social skills (Llorens et al., 2012).

Parente and Stapleton (1999) compared brain injury survivors who completed a cognitive skills group to comparable controls. The cognitive skills group interventions included education regarding "thinking skills" such as problem solving, concentration/ attention, decision making, remembering names and faces, study skills, functional mnemonics, prosthetic memory devices, social cognition, organizational skills and goal setting. Other important aspects of the cognitive skills group included computer training, prosthetic aid training, interviewing skills training and focus on a model of clients teaching clients. There was no statistical analysis completed; however, the return to work rate for 13 of 33 participants assigned to the cognitive skills group training was 76% as compared to 58% for the control group. Competitive employment for the intervention group was maintained at 6-month follow up.

Conclusions

There is level 1b evidence that goal orientated group interventions are successful at improving cognitive and executive function in patients post ABI.

There is level 1b evidence that emotional regulation group interventions are effective at improving executive function in post TBI patients compared to standard therapy.

There is level 1b evidence that the Strategic Memory and Reasoning Training program is more effective than a brain health workshop for improving executive function, metacognition, and comprehension following ABI.

There is level 4 evidence that metacognitive strategy instruction may not be effective for improving executive functioning following an ABI.

There is level 4 evidence that touch screen-based games (which include components of reasoning and problem-solving) may be effective for improving self-awareness and social skills following an ABI.

KEY POINT

- Group goal-oriented interventions are effective for the remediation of executive functions, including comprehension and problem solving.
- Emotional regulation interventions delivered in a group setting may improve executive function in patients post TBI; however, it is unclear if it is superior at doing so compared to conventional cognitive remediation.
- The SMART program appears to be effective for improving executive functioning following an ABI.
- Touch screen-based games which include components of metacognition may be effective for improving self-awareness.
- Metacognitive instruction does not appear to improve comprehension or abstract reasoning; however, more studies are needed to fully evaluate its effects.

Rehabilitation of General Cognitive Functioning

Interventions for the treatment of cognitive deficits post TBI tend to be diverse with variability between the interventions themselves and the outcome measures used to document results.

Gordon et al. (2006) conducted an extensive review of the TBI rehabilitation literature and identified 13 studies examining treatments for cognitive deficits. Studies included in that review had a multitude of inclusion criteria. Additionally, the studies identified were of limited methodological quality, but suggested that compensatory strategy training improved attention deficits and mild memory impairments (Gordon et al., 2006). Several researchers have noted that training-based therapies that target executive control, such as "*attention, problem solving, and the use of metacognitive strategies*" (Novakovic-Agopian et al., 2011) may improve functioning in those who sustain an ABI (Cicerone, 2002; Kennedy et al., 2008; Sohlberg et al., 2003b). Studies included in this section have examined the effects of cognitive rehabilitation strategies.

TABLE 6 | The Effect of Cognitive Rehabilitation Strategies on General Cognitive Function Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Linton & Kim (Linton & Kim, 2018) (2018) United States RCT PEDro=5 N=8	**Population:** Mean age=36.5yr; Gender: Male=4, Female=4. **Intervention:** Participants were either assigned to the 3-month, in home, Trabajadora de Salud group or the control group. The control group received the same intervention only via telephone. **Outcomes:** Neurobehavioral Functioning Inventory, Physical FIM, Cognitive FIM.	1. Both the experimental and control groups saw a decrease in their depressive symptoms on the Neurobehavioral Functioning Inventory. 2. Both groups saw an increase in physical FIM scores, although the experimental groups was slightly higher. 3. Only the experimental group saw an increase in Cognitive FIM scores. 4. No between-subjects' analyses were performed.
Schmidt et al. (2013)(Schmidt et al., 2013) Australia RCT PEDro=8 N=54	**Population:** *Video Feedback (N=18)*: Mean age=42.7yr; Gender: Male=14, Female=4; Mean time post-injury=1.5yr; Mean GCS=8.1. *Verbal Feedback (N=18):* Mean age=41.6yr; Gender: Male=14, Female=4; Mean time post-injury=4.7yr; Mean GCS=7.1. *Experimental Feedback (N=18):* Mean age=37.5yr; Gender: Male=18; Mean time post-injury=5.8yr; Mean GCS=7.0. **Intervention:** Participants received instructions for meal preparation on 4 occasions in one of three formats. The video feedback group watched their recorded meal preparation sessions, the verbal feedback group received feedback on task completion without the video,	1. There were significant differences between groups at baseline on measures of functional independence ($p<0.01$), and logical memory ($p<0.05$). 2. The video feedback group significantly improved online awareness more than either of the other two groups ($p<0.001$), and also had significantly fewer errors than either group ($p<0.05$). 3. The video feedback group had significantly higher intellectual awareness on the AQ ($p<0.05$). 4. There were no significant differences between groups on the DASS-21 or the SPIRQ.

	and the experimental group received no therapist feedback on task completion. **Outcomes:** Error rate, Awareness Questionnaire (AQ), Depression Anxiety Stress Scales (DASS-21), Self-perceptions in Rehabilitation Questionnaire (SPIRQ).	
Goverover et al. (2007) United States RCT PEDro=6 N=20	**Population:** *Experimental Group (N=10)*: Mean age=39.5yr; Gender: Male=8, Female=2; Mean time post-injury=12.9mo; Mean GCS=4.6. *Control Group (N=10)*: Mean age=39.2yr; Gender: Male=8, Female=2; Mean time post-injury=8.6mo; Mean GCS=3.6. **Intervention:** Six individualized cognitive treatment task sessions were administered over three weeks, with one session per day 2-3 days a week. Tasks included everyday activities such as making lunch, or a telephone call. **Outcomes:** Assessment of awareness of disability (AAD), Assessment of Motor and Process Skills (AMPS), Activities of Daily Living (ADL), Relf-Regulation Skills Interview (SRSI), Satisfaction with quality of care, Awareness Questionnaire (AQ), Community Integration Questionnaire (CIQ).	1. Groups were not statistically different at baseline. 2. There were no significant differences between groups following treatment on AAD. 3. There was a significant improvement in the experimental group on SRSI scores compared to the control group ($p<0.05$). 4. There was a significant improvement in AMPS and ADLs for the experimental group, compared to the control group ($p<0.05$, $p<0.05$), only on measures of processing and cognition. There were no significant differences on measures of motor AMPS or motor ADLs. There were no significant differences between groups on AQ or CIQ.
Neistadt et al. (1992) USA RCT PEDro=6 N=45	**Population:** TBI: Mean Age=33.2 yr; Gender=Male; Time since injury=7.9 yr. **Intervention:** Participants were randomly assigned to an adaptive (n=23) or a remedial (n=22) approaches for their occupational therapy. **Outcome Measure:** The Parquetry Block test; Block design subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R).	1. After treatment, the remedial group improved significantly more than the adaptive group on the Parquetry Block test ($p=0.019$), but there were no significant differences on the WAIS-R Block Design subtest. 1. There was a non-significant tendency in the expected direction to support that the adaptive group would perform better than the remedial group on the RKE-R after treatment.
Combs et al. (Combs et al., 2018) United States Pre-Post N=19	**Population:** Mean age=32.8yr; Gender: Male=89.5%, Female=10.5%; TBI injury severity: mild=15.8%, severe=63.2%, Other=21.1%. **Intervention:** All individuals experienced weekly group meetings around topics in mindfulness-based stress reduction. Each group session lasted 60 mins and group sessions were completed over the course of 32 weeks. **Outcomes:** Participants were asked dichotomous questions, or on a Likert-scale about their psychological wellbeing, cognitive functioning, and physical health and their beliefs of the efficacy of the intervention related to those topics.	1. Overall, the majority of participants reported a significant improvement in their overall health ($p<0.001$) in relation to the number of sessions they attended. 2. Participants also reported their beliefs in the ability of the number of sessions to improve physical health symptoms ($p<0.05$), focus and attention ($p<0.05$), self-awareness ($p<0.05$), and mood and anxiety ($p<0.001$). 2. No similar significant relationship was found for measures on sleep benefits, or pain.
Rasquin et al. (2010) Netherlands Cohort N=52	**Population:** Mean Age: 49.5 yr; Gender: male=14, female=13; Mean Time Post-Injury:1.9 yr; Condition: CVA=9, TBI=5, Other ABI=13. Controls who were relatives of the patients=25. **Intervention:** Participants were asked to formulate individual strategies to address	1. Results from the Goal Attainment Scaling, the Stroke Adapted Impact Scale and the Cognitive Failure Questionnaire all indicate there was significant improvement from baseline (T0) to immediately after treatment (T1) ($p<0.05$). 2. Patients improved on significantly on individual goals ($p<0.05$) between T0 to T1.

	specific cognitive issues (attention memory or problem solving) and to develop methods to ask for help with problems resulting from the head injury. Caregivers were asked to attend sessions. Sessions lasted approximately 2.5 hours and ran for approximately 15 weeks. Assessment was conducted at baseline, 21 weeks after treatment, 6 months after treatment. **Outcome Measure:** Goal Attainment Scaling; Stroke Adapted Impact Scale; Cognitive Failure Questionnaire	3. No further changes were noted on the primary outcomes 6 months post intervention (T2).
Laatsch et al. (1999) USA Case series N=5	**Population:** TBI; Age Range=18-65yr; Time Post-Injury=2-48 months; **Intervention:** Cognitive rehabilitation therapy (CRT) programme in a longitudinal protocol involving a resting SPECT and neuropsychological evaluation are pre-treatment, post-treatment and post non-treatment intervals. **Outcome Measure:** Neuropsychological measures.	1. NP measures: WAIS-R, WMS-R, CVLT, RCFT, SCWT, WCST or ACT, SPECT image. 2. SPECT data revealed significant increases in cerebral blood flow during the treatment period ($p<0.05$). 4. CRT was found to be effective in improving both NP and everyday functioning. All patients were able to be more productive in their lives following treatment.

Discussion

Seven studies investigating the remediation of general cognitive functioning were found meeting our inclusion criteria. Neistadt (1992) divided 45 patients into one of two groups: a remedial group who received individual training with parquetry block assembly, and an adaptive group who received functional skills training over a six-week period. Outcomes for the effect of treatment for constructional test performance revealed that the remedial group improved significantly more than the adaptive group on the Parquetry Block test. However, there were no significant differences on the WAIS-R Block Design subtest after treatment. Training-specific learning appears to be an effective approach to rehabilitation as demonstrated by the treatment effect.

Goverover et al. (2007) used an RCT to study individualized cognitive treatments (such as making lunch or a telephone call) on the ability to remediate self-awareness and generalized processing skills. Groups did not significantly differ at baseline; however, following treatment individuals in the treatment group experienced a significant increase in their self-regulation, and processing skills (Goverover et al., 2007). In a study, Rasquin and colleagues (2010) they investigated the effectiveness of a low intensity outpatient cognitive rehab program on those (n=27) who had sustained an ABI. All participants were in the chronic phase of recovery and all were asked to invite a caregiver to attend sessions with them (n=25). Sessions lasted 2.5 hours each week for a total of 15 weeks. All were assessed prior to the session beginning, immediately afterward and again 6 months later. Participants worked on developing strategies to assist them with their attention, memory and problem-solving difficulties. Social skills training sessions were also held. Changes were noted immediately after the cognitive rehab program

ended and this improvement in goal attainment, and cognitive improvement was maintained at the 6-month follow-up. Laatsch et al. (1999) found similar results where cognitive rehabilitation therapy helped individuals increase productivity in their daily lives and found improvements on neuropsychological measures.

Two other RCTs have evaluated specific training programs attempting to improve generalized cognitive functioning (Linton & Kim, 2018) (Schmidt et al., 2013). The more recent RCT had individuals participate in the in-home program (Trabajadora de Salud) and found that although both groups improved on physical measures over time, only the experimental group saw a significant increase in cognitive FIM scores. The second study involved individuals receiving task completion instructions in a variety of formats to determine how feedback might influence general cognition (Schmidt et al., 2013). Those in the video feedback group (compared to verbal feedback) saw significant improvements in self-perception, and general awareness. The video feedback condition showed a recording of the individual performing the meal preparation task required with corrective feedback, compared to the verbal feedback group which only received verbal corrective feedback (Schmidt et al., 2013).

Mindfulness-based stress reduction was evaluated in an attempt to improve self-awareness and overall cognitive health (Combs et al., 2018). Individuals participated in weekly mindfulness sessions for 60 minutes and were asked to self-report on their general cognitive functioning. Individuals reported a significant reduction in cognitive symptoms which was positively correlated to the number of sessions they attended. This was true for both general cognitive functioning as well psychological wellbeing. Although this single pre-post study offers insight into the benefits of mindfulness-based stress reduction, more research is needed.

Conclusions

There is level 1b evidence that cognitive therapies compared to standard therapy are more effective than no therapy for improving generalized cognitive functioning, as well as self-perception following an ABI.

There is level 4 evidence that a low intensity outpatient cognitive rehabilitation program may improve goal attainment and cognitive impairment in patients post ABI.

There is level 2 evidence that the Trabajadora de Salud program may improve general cognitive functioning compared to standard therapy for those with an ABI.

There is level 1b evidence that corrective video feedback is more effective for improving generalized cognitive functioning and self awareness compared to verbal feedback only in those with an ABI.

There is level 1b evidence that remedial occupational therapy and adaptive occupational therapy may have equal effects on generalized cognitive function in those with an ABI.

There is level 4 evidence that mindfulness-based stress reduction may be effective for improving general cognitive functioning and psychological health for those with an ABI.

KEY POINTS

- General cognitive rehabilitation programs are effective for improving cognitive functioning following an ABI.
- There is limited evidence that mindfulness-based stress reduction is effective for improving cognitive functioning.
- Corrective video feedback is more effective than verbal feedback alone for improving general cognitive function and self-awareness.
- Remedial and adaptive occupational therapy are equally effective for improving general cognitive functioning.

Pharmacological Interventions

Donepezil

The effectiveness of donepezil, a cholinesterase inhibitor, in improving cognitive and memory functions following brain injury was assessed. Cognitive impairments negatively impact patient autonomy, affecting one's ability to return to work or school, and live alone (Masanic et al., 2001). When tested in individuals diagnosed with Alzheimer's disease, donepezil has been found to be useful in treating memory problems (Morey et al., 2003; Walker et al., 2004). The impact of Donepezil impact on cognitive function and memory in a TBI population is explored in the table below.

TABLE 7 | The Effect of Donepezil on Executive and General Cognitive Functioning Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Khateb et al. (2005) Switzerland Pre-Post $N_{initial}$=15, N_{final}=10	**Population:** TBI; Mean age=43 yr; Gender: Male=8, Female=7; Mean Time Post Injury=4 2mo. **Intervention:** Patients were administered donepezil 5 mg/day for 1 mo, followed by 10 mg/day for 2 mos. **Outcome Measure:** Stroop test, Trail Making Test (TMT), Rey Auditory Verbal Memory Test (RAVMT), Test for Attentional Performance (TAP).	1. Four of 15 participants stopped due to side effects within the first week (e.g., nausea, sleep disorders, anxiety, dizziness, etc.). 2. Changes on the neuropsychological evaluation show modest improvement. However, the comparison of the global score of all questionnaires before and after therapy was not significant (p=0.058). A significant improvement in executive function was only found for the Stroop Colour naming test (87.3±22.9 to 79.5±19.1, p=0.030); the RAVMT-learning for learning and memory

		(47.7±6.9 to 53.5±5.0, p=0.050); and the errors subsection of divided attention for attention, (5.8±3.3 to 2.9±2.7, p=0.030).

Discussion

Khateb et al. (2005) found only modest improvement on the various neuropsychological tests used to measure executive function, attention, and learning and memory. Of note, results from the learning phase of the Rey Auditory Verbal Memory Test (RAVMT) showed significant improvement ($p<0.050$). The Donepezil intervention also demonstrated improvement in executive function, as the results from the Stroop-colour naming test showed significant improvements ($p<0.030$). On the test for Attentional Performance a significant change was noted on the divided attention (errors) subsection of the test. Overall, donepezil was found to be effective in improving learning, memory, divided attention, and executive function. However, possible benefits of donepezil administration must be balanced against the observed side effects in 27% of the population. Further randomized control trials are required to better explore the efficacy of donepezil post TBI.

Conclusions

There is level 4 evidence that donepezil is effective in improving learning, memory, divided attention, and executive function in patients post TBI.

KEY POINT

- Donepezil might improve attention, learning and short-term memory following TBI; however, side effects may incur from its use.

Methylphenidate

Methylphenidate is a stimulant which inhibits the reuptake of dopamine and norepinephrine and increases activity in the prefrontal cortex. In the past, methylphenidate has been extensively used as a treatment for attention deficit disorder, as well as narcolepsy (Glenn, 1998). A total of three RCTs examined the efficacy of methylphenidate as a treatment for the recovery of executive and general cognitive deficits post ABI.

TABLE 8 | The Effect of Methylphenidate on Executive and General Cognitive Functioning Post ABI

	Methods	Outcome
Jenkins et al., (2019) UK RCT Crossover	**Population:** TBI=40; *Treatment Group (Intervention First; n=20):* Mean Age= 40±12yr; Gender: Male=18,	1. No significant differences ($p>0.05$) were observed between groups on several measures: • TMT

	Methods	Outcome
PEDro=9 $N_{Initial}$=46, N_{Final}=40	Female=2; Mean Time Post Injury=67±85mo; Severity: Mean GCS=8.3±5.2. *Control Group (Placebo First; n=20):* Mean Age=39±12yr; Gender: Male=16, Female=4; Mean Time Post Injury=67±85mo; Severity: Mean GCS=8.3±5.4. **Intervention:** Participants were randomized to receive 0.3mg/kg of methylphenidate (treatment group) twice a day for 2wk with crossover to placebo (control group) twice a day for 2wk and vice versa. Outcome measures were assessed at baseline, 2 and 4wk. **Outcome Measures:** Choice Reaction Time (CRT) Task, Single-Photon Emission Computed Tomography (SPECT), Trail Making Test (TMT), Stroop Test, People Test, Wechsler Abbreviated Scale for Intelligence (WASI), Lille Apathy Rating Scale (LARS), Visual Analogue Scale for Fatigue (VAS-F), Glasgow Outcome Scale-Extended (GOSE), Hospital Anxiety and Depression Scale (HADS), Frontal Systems Behaviour Scale (FrSBe), Cognitive Failures Questionnaire, Rating Scale of Attentional Behaviour.	• Stroop • People Test • WASI • FrSBe • GOSE • HADS • Cognitive Failures Questionnaire • Rating Scale of Attentional Behaviour 2. Using SPECT imaging, participants were divided into groups with low and normal dopamine transporter levels for analysis. 3. Participants with low dopamine transporter levels receiving methylphenidate significantly improved on several measures when compared to controls: • CRT (p=0.02) • LARS self-reported (p=0.03) and caregiver (p=0.02) • VAS-F (p=0.007) 4. Participants with normal dopamine transporter levels receiving methylphenidate reported significantly less fatigue when compared to controls (VAS-F, p=0.03).
Dymowski et al. (Dymowski et al., 2017) Australia RCT PEDro=9 $N_{Initial}$=11, N_{Final}=10	**Population:** TBI. *Methylphenidate Group (n=6)*: Mean Age=35 yr; Gender: Male=4, Female=2; Mean Time Post Injury=366 d; Mean Worst GCS=4.83. *Placebo Group (n=4)*: Mean Age=32.5 yr; Gender: Male=2, Female=2; Mean Time Post Injury=183.5 d; Mean Worst GCS=4.50. **Treatment:** Participants were randomly assigned to receive either methylphenidate (0.6 mg/kg/d rounded to the nearest 5mg with maximum daily dose of 60 mg) or placebo (lactose). Outcomes relating to processing speed, complex attentional functioning, and everyday attentional behaviour were assessed at baseline, 7 wk (on-drug), 8 wk (off-drug), and 9 mo follow-up. **Outcome Measures:** Symbol Digit Modalities Test (SDMT), Trail Making Test (TMT) A and B; Hayling (A, B, error), Digit Span (DS-Forward, Backward, Sequencing, Total), Ruff 2&7 Selective Attention Test Automatic Speed Raw Score (2&7 ASRS), Ruff 2&7 Selective Attention Test Controlled Speed Raw Score (2&7 CSRS), Simple Selective Attention Task Reaction Time (SSAT RT), Complex Selective Attention Task Reaction Time (CSAT RT), N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, Rating Scale of Attentional Behaviour Significant Other (RSAB SO).	1. After applying Bonferroni corrections, no significant differences between groups from baseline to 7 wk, baseline to 8 wk, or baseline to 9 mo were observed for SDMT, TMT A, TMT B, Hayling A, Hayling B, Hayling error, DS Forward, DS Backward, DS Sequencing, DS Total, 2&7 ASRS, 2&7 CSRS, SSAT RT, CSAT RT, N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, or RSAB SO.

	Methods	Outcome
Zhang and Wang (Zhang & Wang, 2017) China RCT PEDro=10 $N_{Initial}$=36, N_{Final}=33	**Population:** TBI; Severity: mild to moderate. *Methylphenidate Group (n=18)*: Mean Age=36.3 yr; Gender: Male=13, Female=5. *Placebo Group (n=18)*: Mean Age=34.9 yr; Gender: Male=14, Female=4. **Treatment:** Participants were randomly assigned to receive methylphenidate (flexibly titrated from 5 mg/d at the beginning, then gradually increased by 2.5 mg/d until reaching 20 mg/d) or placebo for 30 wk. **Outcome Measures:** Mental Fatigue Scale (MFS), Choice Reaction Time (CRT), Compensatory Tracking Task (CTT), Mental Arithmetic Test (MAT), Digit Symbol Substitution Test (DSST), Mini-Mental State Examination (MMSE), Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HAMD).	1. At baseline, there were no significant differences between groups in terms of demographics, MFS, CRT, CTT, MAT, DSST, MMSE, BDI, or HAMD. 2. Post-intervention, the experimental group had significantly lower scores compared to control group for MFS ($p=0.005$), CRT ($p<0.001$), CTT ($p<0.001$), BDI ($p=0.040$), and HAMD ($p=0.005$). 3. Post-intervention, the experimental group had significantly higher scores compared to control group for MAT ($p=0.020$), DSST ($p<0.001$), MMSE ($p<0.001$).
Speech et al. (1993) USA RCT PEDro=7 N=12	**Population:** TBI; Mean Age=27.6 yr; Gender: Male=5, Female=7; Mean Time Post Injury=48.5 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 0.3 mg/kg methylphenidate, 2×/d, for 1 wk, followed by 1wk of placebo, or receive the treatment in a reverse order. **Outcome Measures:** Gordon Diagnostic System, Digit Symbol and Digit Span subtests of the Wechsler Adult Intelligence Scale-Revised, Stroop Interference Task, Sternberg High Speed Scanning Task, Selective Reminding Test, Serial Digit Test, and Katz Adjustment Scale.	1. No significant differences were found between methylphenidate and placebo condition in any of the outcome measures studied.
Al-Adawi et al., (2020) Oman Pre-Post $N_{Initial}$=32, N_{Final}=24	**Population:** TBI=32; Age Range 18-25yr=17, Age Range 26-35yr=7; Gender: Male=13, Female=11; Time Post Injury: Acute(<2mo)=9, Chronic (≥2mo)=15; Severity: Mild=5, Moderate=15, Severe=1. **Intervention:** Participants received methylphenidate starting at a dose of 5mg/d, increasing to a dose of 10mg/d for 30 days. Outcome measures were assessed at baseline, 15d prior to the initiation of methylphenidate, 30d and follow-up at 15 and 30d. **Outcome Measures:** Digit Span, Verbal Fluency, Hospital Anxiety and Depression Scale (HADS).	1. Methylphenidate significantly improved measures of executive functioning (Digit Span and Verbal Fluency) from baseline to 30 days ($p<0.001$) and post withdrawal (Digit Span, $p<0.001$; Verbal Fluency, $p=0.008$). 2. Affective measures did not significantly improve from baseline to 30 days or post-withdrawal from methylphenidate (HADS, $p>0.05$). 3. No significant differences were observed between genders on executive functioning or affective measures with methylphenidate ($p>0.05$).

Discussion

Dymowski et al. (2017) investigated the effects of short-term, 7-week, methylphenidate administration in post TBI patients compared to a placebo control group. There was no significant improvement, or difference between groups for various measures and tests of attention and cognition. Speech et al. (1993) conducted a double blind placebo controlled trial evaluating the effects of methylphenidate

following closed head injury and arrived at similar conclusions, as the treatment and placebo group did not vary in any measurements of memory, intelligence, or attention. Conversely, Zhang and Wang (2017) used a larger sample size to investigate the effects of long-term (30 wk) methylphenidate use in patients post TBI. While there was no difference between the groups at baseline, the treatment group had improved reaction time, cognitive ability, attention capacity, and depression when compared to the placebo group. This is similar to the findings of Al-Adawi et al. (2020), where they found short term use of methylphenidate significantly improved measures of executive functioning. The controversy on methylphenidate use post TBI creates an interesting conflict, as all studies were conducted with high methodological quality and proper controls. Zhang and Wang (2017) used a fraction of the dose of methylphenidate compared to the Dymowski et al. (2017) study. Although methylphenidate has been found to be effective for the management of specific cognitive functions, such as attention, its effects on general and executive function remains inconclusive.

Conclusions

There is conflicting (level 1a) evidence regarding the effectiveness of the administration of methylphenidate, compared to placebo, following TBI for the improvement of general and executive functioning.

KEY POINTS

- The effectiveness of methylphenidate to improve cognitive impairment following brain injury is unclear. Further studies with larger populations are required.

Sertraline

Sertraline, better known under its trade name Zoloft (Pfizer), is a selective serotonin reuptake inhibitor (SSRI) used for the treatment of depression and mood (Khouzam et al., 2003; Jorge et al., 2016). The majority of sertraline TBI research focuses on the prevention or treatment of major depressive symptoms post brain injury. However, recent studies have shifted focus and begun to evaluate the benefits of sertraline at improving cognitive disorders (Banos et al., 2010). The study reviewed below investigated the effect of sertraline on cognitive outcomes post TBI.

TABLE 12 | The Effect of Sertraline on Executive and General Cognitive Functioning Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Banos et al. (2010) USA RCT PEDro=9 N=99	**Population:** TBI. *Treatment group (n=49)*: Gender: Male=39, Female=10; Mean Age=35.3 yr; Mean Time Post Injury=21.5 d; Mean GCS=5.8. *Placebo group (n=50):* Gender: Male=33, Female=17; Mean Age=34.5 yr; Mean Time Post Injury=19.2 d; Mean GCS=5.8. **Intervention:** Participants were randomized to either the treatment group which took sertraline daily (50 mg) or placebo. Patients were assessed at 3, 6 and 12 months. **Outcome Measure:** Wechsler Memory Index (Wechsler Adult Intelligence Scale III), Symbol-Digit Modalities Test, Logical Memory, Trial Making Test and 64-item Wisconsin Card Sorting Test.	1. More subjects in the treatment group dropped out at each time point. 2. Those in the placebo groups at the 6th and 12th month assessment period were older than the control group and had higher GCS. 3. Overall, there were no significant differences between the two groups on any of the cognitive measures.

Discussion

The effect of early administration of sertraline on cognitive functioning was evaluated by Banos et al. (2010) in an RCT. When comparing the sertraline group, who received 50 mg per day, to a control group (placebo), there were no significant between group differences on any of the neuropsychological tests. The assessments examined attention and concentration, speed of processing, memory and executive function at 3, 6 and 12 months. Cognitive functioning was not found to improve following the administration of sertraline. Of note, more patients in the sertraline group dropped out of the study compared to the control group when this was quantified at all assessment points indicating the potential side effects associated with the treatment. Combined with the lack of apparent benefit to using the drug, use of sertraline is not currently recommended.

Conclusions

There is level 1b evidence that sertraline does not improve cognitive functioning, compared to placebo, in individuals who have sustained a moderate to severe TBI.

KEY POINT

- Sertraline has not been shown to improve cognitive functioning within the first 12 months post TBI, and may be associated with side effects.

Amantadine

Amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist and has been used as an antiviral agent, prophylaxis for influenza A, treatment of neurological diseases such as Parkinson's Disease, and the treatment of neuroleptic side-effects such as dystonia, akinthesia and neuroleptic malignant syndrome (Schneider et al., 1999). Amantadine is also thought to work pre- and post-synaptically by increasing the amount of dopamine in the synapse (Napolitano et al., 2005). Three studies have been identified that investigate the effectiveness of amantadine as a treatment for the remediation of learning and memory deficits and cognitive functioning following TBI.

TABLE 13 | The Effect of Amantadine on Executive and General Cognitive Functioning Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Ghalaenovi et al. (2018) Iran RCT PEDro=10 N=40	**Population:** *Amantadine Group (N=19)*: Mean age=32.16yr; Gender: Males=19, Female=0; Mean GCS=7.1; Mean time post-injury=3.21days. *Control Group (N=21)*: Mean age=40.95yr; Gender: Male=18, Female=3; Mean GCS=6.95; Mean time post-injury=3.42days. **Intervention:** Participants either received a placebo or 100mg of amantadine twice a day for 6 weeks. Assessments were conducted at baseline, day 3 of treatment, day 7 of treatment, at 6-weeks completion of the intervention, and 6 months post initial start time. **Outcomes:** Mini-Mental State exam (MMSE), Glasgow Outcome Scale (GOS), FOUR score, Disability Rating Scale (DRS), Karnofsky Performance Scale (KPS), mean hospitalization time.	1. There were no significant differences observed on the MMSE, GOS, DRS, or KPS. It should be noted that these measures were only taken at baseline and 6-month follow-up. 2. On day 7 the amantadine group had significantly better rising GCS scores than the control group (p=0.044). No other significant differences were observed between groups.
Schneider et al. (1999) USA RCT PEDro=5 N=10	**Population:** TBI; Mean Age=31 yr; Gender: Male=7, Female=3; GCS Score Range=3-11. **Intervention:** Patients randomized to either amantadine (50-150 mg 2 x/d) or placebo for 2 wk in a crossover design with a 2 wk washout period. **Outcome Measure:** Battery of Neuropsychological tests, Neurobehavioural Rating Scale.	1. There was a general trend towards improvement in the study sample over the 6 wk. There were no significant between group differences in terms of orientation (p=0.062), attention (p=0.325), memory (p=0.341), executive flexibility (p=0.732) or behaviour (p=0.737).
Kraus et al. (2005) USA Pre-Post N=22	**Population:** TBI; Mean Age=36 yr; Gender: Male=17, Female=5; Severity of Injury: Mild=6, Moderate=6, Severe=10; Mean Time Post Injury=63.2 mo. **Intervention:** Positron emission tomography (PET) scan was done and participants received amantadine (10 0mg titrated to up to 400 mg/d over 3 wk). Amantadine was administered 3×/d (200 mg at 8AM, 100 mg at 12PM, and 100mg at 4PM) for 12 wk. **Outcome Measure:** Trail Making Test Part A and B	1. Measures of executive function, as indicated by TMT B and COWAT, were significantly improved in patients following treatment with amantadine (t=-2.47; p<0.020). 2. No significant differences were found for attention (TMT A and Digit Span) or memory (CVLT, Rey Im, and Rey De). 3. Correlational analyses with PET scan results suggest that there may be a strong

Author Year Country Study Design Sample Size	Methods	Outcome
	(TMT A, TMT B), Controlled Oral Word Association Test (COWAT), Digit Span, California Verbal Learning Test (CVLT), Rey Osterreith Complex Figure-Immediate (Rey Im) and Delayed (Rey De) recall.	relationship between executive domain improvement and changes in left pre-frontal metabolism (r=0.92; p=0.010) and left medial temporal metabolism (r=0.91; p=0.010).

Discussion

In a small sample RCT by Schneider et al. (1999) the effects of Amantadine on cognition and behaviours were assessed. In this six-week cross-over study, patients received both placebo and amantadine for 2 weeks each, with a 2-week washout period in between. No significant differences were found between groups on measures of executive or general cognitive functioning. A recent RCT reinforces these findings after finding no significant differences on measures of cognition following 6-weeks of amantadine treatment (Ghalaenovi et al, 2018). Similarly, Kraus et al. (2005) demonstrated that the administration of amantadine over a 12-week treatment period does not improve memory deficits or attention; however, significant improvements in executive functioning were observed. Given the quality and sample size of the current studies, future studies exploring the efficacy of amantadine for learning and memory are warranted.

Conclusions

There is level 1b evidence that Amantadine may not help to improve general functioning deficits in post TBI patients compared to placebo.

KEY POINT

- Amantadine is not effective for improving generalized cognition. Its impact o executive functioning should be studied further.

Bromocriptine

Bromocriptine is a dopaminergic agonist which primarily exerts its actions through binding and activating D_2 receptors (Whyte et al., 2008). It has been suggested that dopamine is an important neurotransmitter for prefrontal function, an important area of the brain that contributes to cognitive function, memory, intelligence, language, and visual interpretation (McDowell et al., 1998; Siddiqui et al., 2008). In a study looking at the effects of bromocriptine on rats, Kline et al. (2002) noted that the animals showed improvement in working memory and spatial learning; however, this improvement was not seen in

motor abilities. Two studies have been identified investigating the use of bromocriptine as an adequate treatment for the recovery of cognitive impairments following TBI.

TABLE 14 | The Effect of Bromocriptine on Executive and General Cognitive Functioning Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
McDowell et al. (1998) USA RCT PEDro=4 N=24	**Population:** TBI; Median Age=32.5 yr; Gender: Male=20, Female=4; GCS Range=3-8; Time Post injury Range=27 d-300 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive bromocriptine (2.5 mg) then placebo or receive treatment in the reverse order. **Outcome Measure:** Dual-task Paradigm (counting and digit span), Stroop Test, Spatial Delayed-response Task, Wisconsin Card Sorting Test (WCST), Reading Span Test, Trail Making Test (TMT), Controlled Oral Word Association Test (COWAT), and Control Tasks.	1. Following bromocriptine treatment there were significant improvements on the dual-task counting (p=0.028), dual-task digit span (p=0.016), TMT (p=0.013), Stroop Test (p=0.050), COWAT (p=0.020), and WCST (p=0.041). 2. Bromocriptine had no significant effects on working memory (e.g. spatial delayed-response task and reading span test; p=0.978), or on control tasks (p=0.095).
Powell et al. (1996) UK Case Series N=11	**Population:** TBI=8, SAH=3; Mean Age=36 yr; Gender: Male=6, Female=5; Time Post Injury Range=2mo-5 yr. **Intervention:** Patients received bromocriptine (a maximum dose of 5-10 mg/d). Patient assessments included two baseline evaluations (BL1 and BL2), evaluation when stabilized at maximum bromocriptine dose (MAXBROMO), and two post withdrawal evaluations (POST1 and POST2). **Outcome Measure:** Percentage Participation index (PPI), Spontaneity, Motivation, Card Arranging Reward Responsivity Objective Test (CARROT), Digit Span, Buschke Selective Reminding Test (BSRT), Verbal Fluency, Hospital Anxiety and Depression Scale.	1. Reported PPI (p<0.0001), motivation, and spontaneity (both p<0.005) increased significantly from BL2 to MAXBROMO. Improvements were seen in CARROT as well (p<0.0001). 2. Significant improvements were observed from BL2 to MAXBROMO on the digit span (p<0.001), BSRT (p<0.01), and verbal fluency (p<0.001). Scores on all three tests decreased (non-significant) from MAXBROMO to POST1, scores recovered to near MAXBROMO levels by POST2. **3.** Bromocriptine was not associated with improvements in mood state.

Discussion

The effect of bromocriptine on cognitive function in patients with ABI was explored in one RCT (McDowell et al., 1998), and one case series (Powell et al. 1996). Low-dose bromocriptine (2.5 mg daily) improved functioning on tests of executive control including a dual task, Trail Making Test, the Stroop test, the Wisconsin Card Sorting Test and the controlled oral word association test (McDowell et al., 1998). However, bromocriptine did not significantly influence working memory tasks. Although McDowell et al. (1998) demonstrated some benefits following administration of bromocriptine, there was only a single administration of bromocriptine and the dose was considerably lower than that given by other studies that did not meet our criteria. Spontaneous recovery may have been a factor leading to the improved abilities in individuals receiving a single dose (2.5 mg daily) of the medication; however, study results did not answer this question. Powell et al. (1996) conducted a multiple baseline design on 11 patients with TBI or subarachnoid hemorrhage who received bromocriptine. Improvements were

found on all measures assessed (memory, attention, motivation spontaneity) except mood, creating conflicting results between these two studies. The last RCT investigating the effects of bromocriptine was conducted 20 years ago; newer studies are required to fully determine the potential of bromocriptine as a treatment for general and executive cognitive functions.

Conclusions

There is conflicting level 2 (against) and level 4 (for) evidence as to whether or not bromocriptine may improve executive or general cognitive functioning following ABI.

KEY POINT

- Bromocriptine may improve other measures of cognition such as attention, but its effects on generalized cognition are conflicting. More research is required.

Growth Hormone Replacement Therapy

Following an ABI, it is not uncommon for individuals to be diagnosed with hypopituitarism. It is estimated that as many as 25 to 40% of individuals with a moderate to severe ABI demonstrate chronic hypopituitarism (Bondanelli et al., 2007; Kelly et al., 2006; Schneiderman et al., 2008). Despite this, few patients are screened for GH deficiencies; thus, the link between cognitive impairment and growth hormone deficiencies has not yet been definitively established (High et al., 2010). The benefits of GH replacement therapy on patient's executive and general cognitive function post TBI is investigated below.

TABLE 15 | The Effect of Growth Hormone Replacement Therapy on Executive and Cognitive Functioning Post ABI.

Author Year Country Study Design Sample Size	Methods	Outcome
High Jr et al. (2010) USA PEDro=8 N=23	**Population:** TBI. *Placebo* (n=11): Mean Age=39.1 yr; Time Post Injury=5.1 yr. *Active rhGH* (n=12): Mean Age=36.1 yr; Time Post Injury=11 yr. **Intervention:** Participants were randomized to either a growth hormone replacement injection (rhGH) group or a placebo injection. Initially the drug was administered at 200 *ug*, followed by a 200 *ug* increase every month until the dosage reached 600 *ug*. Both groups received these injections for one year.	1. Overall study results did not show great improvements on the majority of assessments between groups. 2. There was a significant improvement on the Finger tapping demonstrated in the treatment group. 3. Processing Speed Index: the treatment group improved significantly over the one-year period ($p<0.050$). The control group showed improvement at the end of the first 6 mo ($p<0.010$) but this was not seen at the end of the 1 yr.

Author Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measure: Wechsler Adult Intelligence Scale-III, Delis-Kaplan Executive Function System.	4. Significant improvement was also noted on the Wisconsin Card Sorting Test (executive functioning) for the treatment group (p<0.010). 5. On the California Verbal learning Test-II improvement was noted for the treatment group on learning and memory.
Moreau et al. (2013) France PCT N=50	**Population**: TBI. Treatment Group (TG, n=23): Mean Age=37.9 yr; Gender: Male=19, Female=4; Mean Time Post Injury=7.8 yr; Mean GCS=8.1. Control Group (CG, n=27): Mean Age=37.1 yr; Gender: Male=24, Female=3; Mean Time Post Injury=5.5 yr; Mean GCS=9.4. **Intervention**: Participants were allocated to receive GH therapy (TG, 0.2-0.6mg/d) or no treatment (CG) for 1yr. Outcomes were assessed before (T1) and after (T2) treatment. **Outcome Measures**: Activities of Daily Living (ADL); Quality of Life Brain Injury (QOLBI); Verbal Memory (VM); Rey Complex Figure (RCF); Reaction Time (RT).	1. Both groups showed significant improvement in instrumental ADL (iADL, p=0.001) at T2, but not personal ADL (pADL). 2. Both groups showed significant improvement in QOLBI total scores (p=0.019) and intellectual (p=0.001), functional (p=0.023), and personal (p=0.044) subscores at T2, but not physical, psychological, and social subscores. 3. Both groups showed significant improvement (p<0.050) in aspects of attention (RT), memory (VM), and visuospatial (RCF) abilities at T2. 4. The TG showed significantly greater improvement in QOLBI functional (p=0.023) and personal (p=0.019) subscores, as well as RCF (p=0.037), but no significant difference was found for other outcome measures. 5. There was a significant correlation (p<0.050) between QOLBI total and pADL (r=0.49). 6. There was a significant negative correlation (p<0.01) between attention (RT) and pADL (r=-0.59) and iADL (r=-0.56).
Reimunde et al. (2011) Spain Cohort N=19	**Population:** TBI; Gender: Male=19, Female=0. With Growth Hormone Deficiency (GHD) Group (n=11): Mean Age=53.36 yr; Mean Time Post Injury=44.55 mo. Without GHD group (n=8): Mean Age=47.12 yr; Mean Time Post Injury=46.6 mo. **Intervention:** Those with GHD received recombinant human GH (rhGH), subcutaneously (0.5 mg/d for 20d then 1 mg/d for 5 d). Those without GHD were given a placebo. Cognitive rehabilitation was given to everyone (1 hr/d, 5d for 3 mo). **Outcome Measure:** Weschler Adult Intelligence Scale (WAIS).	1. Results of the WAIS indicated that the control group improved significantly on the digits and manipulative intelligence quotient (p<0.050). 2. For those in the treatment groups improvement was noted in cognitive parameters: understanding digits, numbers and incomplete figures (p<0.050) and similarities vocabulary, verbal IQ, Manipulative IQ, and total IQ (p<0.010).

Discussion

A 2010 RCT compared the long term (6 months and 1 year) effects of rhGH administration to placebo in a TBI population (High Jr et al. 2010). Significant improvements were noted in processing speed,

executive functioning (Wisconsin Card Sorting Test), and learning (California Verbal learning test II) for both he rhGH and placebo groups. It is important to note while processing speed also improved in both groups at 6 mo, the improvement was only sustained in the treatment group at 1 year. Further positive results were reported in a more recent PCT by Moreau et al. (2013). Patient quality of life, instrumental activities of daily living, attention, memory and visuospatial ability improved over the treatment period in both the treatment and control group. However, the treatment group improved significantly more in the functional and personal subscales of quality-of-life assessments. Reimunde et al. (2011) also examined the use of recombinant human growth hormone in a cohort study. Results of the study indicate that those receiving the rhGH improved significantly on the various cognitive subtests such as: understanding, digits, numbers and incomplete figures ($p<0.05$), verbal IQ, Manipulative IQ, and Total IQ ($p<0.01$). The control group also showed significant improvement but only in digits and manipulative intelligence quotient ($p<0.05$). Of note IGF-I levels were similar between both groups at the end of the study.

Conclusions

There is level 1b evidence that recombinant human Growth Hormone (rhGH) is superior to placebo at improving processing speed (6 mo), executive function and learning in patients post TBI.

There is level 2 evidence that growth hormone (GH) therapy is effective for improving quality of life, instrumental activities of daily living (iADL), attention, memory, and visuospatial ability in patients post TBI.

There is level 2 evidence that recombinant human Growth Hormone (rhGH) administration improves intelligence and other cognitive subtests in TBI patients with growth hormone deficiency compared to TBI patients without; however, insulin-like growth factor-1 (IGF-1) levels may be the same between groups.

KEY POINT

- The administration of human growth hormones appears to have positive (although sometimes limited effects) on general and executive functioning in those with an ABI.

Rivastigmine

Rivastigmine is an acetylcholinesterase inhibitor which prevents the enzyme acetylcholinesterase from breaking down acetylcholine. This increases the concentration of acetylcholine in synapses. Acetylcholine has been most strongly linked with the hippocampus and memory deficits; however, it is also implicated in attentional processing.

TABLE 16 | The Effect of Rivastigmine on Executive and General Cognitive Functioning Post ABI.

Author Year Country Study Design Sample Size	Methods	Outcome
Silver et al. (2006) USA RCT PEDro=9 N=123	**Population:** TBI. *Rivastigmine* (n=80): Mean Age=37 yr; Gender: Male=53, Female=27. *Placebo* (n=77): Mean Age=37.1 yr; Gender: Male=53, Female=24. **Intervention:** Participants were randomized to receive either rivastigmine (3-6 mg/d) or placebo. At the end of the first 4 wk, rivastigmine doses were increased to 3.0 mg, 2x/d. If necessary, doses were decreased to 1.5 mg or 4.5 mg 2x/d. **Outcome Measure:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	1. Results of the CANTAB RVIP A' and HVLT found no significant differences between the placebo group and the treatment group. 2. Rivastigmine was found to be well tolerated and safe.
Silver et al. (2009) USA RCT PEDro=9 N=127	**Population:** TBI. *Ex-Rivastigmine* (n=65): Mean Age=36.9 yr; Gender: Male=43, Female=22; Time Post Injury=73.5 mo. *Ex-placebo* (n=62): Mean Age=38 yr; Gender: Male=42, Female=20; Time Post Injury=100.1 mo. **Intervention:** Participants were randomized to receive rivastigmine injections (1.5 mg 2x/d to a max of 12 mg/d) or placebo injection. **Outcome Measure:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	1. The mean final dose of rivastigmine was 7.9 mg/day. 2. Forty percent of patients were responders on CANTAB RVIP A' or HVLT score at week 38. 3. At the end of the study period all (n=98) were seen to improve of the CANTAB RVIP A' ($p<0.001$), the HVLT ($P<0.001$), and the Trails A and B ($p<0.001$). 4. Sub-analysis controlling for order effects revealed there were no significant differences between groups.

Discussion

In two studies rivastigmine was administered to patients who had sustained a moderate to severe TBI (Silver et al., 2006; Silver et al., 2009). Neither RCT found significant effects of rivastigmine on measures of general or executive function. However, after controlling for order-effects, there were no significant effects of treatment.

Conclusions

There is level 1b evidence that rivastigmine is not effective for improving general or executive cognitive functioning, compared to placebo, following an ABI.

KEY POINT

- Rivastigmine is not effective in treating general or executive dysfunction post ABI.

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy involves the inhalation of pure oxygen under pressure allowing the lungs to absorb more oxygen per breath. Currently hyperbaric oxygen therapy is used to treat decompression sickness, serious infections, and delayed wound healing as a result of a comorbid illness such as diabetes (The Mayo Clinic, 2019).

TABLE 17 | The Effect of Hyperbaric Oxygen Therapy on General and Executive Functioning Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Hadanny et al. (2018) Israel Case Series N=154	**Population:** Mean age=42.7yr; Gender: Male=58.4%, Female=43.6%; Mean time post-injury=4.6yr; Injury severity: mild=44.8%, moderate=15.6%, severe=39.6%. **Intervention:** All individuals received hyperbaric oxygen therapy (HBOT). Sessions consisted of 60-90 mins of 100% oxygen at 1.5/2 ATA exposure 5 days a week. **Outcomes:** NeuroTrax software subsets: general, memory, executive functions, attention, information processing speed, visual spatial processing, motor skills.	1. On measures of general cognitive functioning there was a significant increase in scores after HBOT treatment ($p<0.0001$). 2. Memory scores significantly increased following HBOT treatment ($p<0.0001$). 3. Executive function scores significantly increased following HBOT treatment ($p<0.0001$). 4. Attentional scores significantly improved following HBOT treatment ($p<0.0001$). 5. Information processes speed significantly increased following HBOT treatment ($p<0.0001$). 6. Visual spatial processing significantly improved following HBOT treatment ($p=0.005$). 7. Motor skills significantly improved following HBOT treatment ($p<0.0001$).

Discussion

One recent case series has evaluated the potential benefits of hyperbaric oxygen therapy on general and executive functioning (Hadanny et al., 2018). This study used NeuroTrax to evaluate all neurocognitive measures. Both measures of general and executive functioning saw a significant improvement over the treatment period. However, it should be noted that this study did not contain a control group and therefore it is difficult to separate the effects of the treatment from spontaneous recovery.

Conclusions

There is level 4 evidence that hyperbaric oxygen therapy may improve general and executive functioning following an ABI.

KEY POINT

- Hyperbaric oxygen therapy may be beneficial for improving general and executive functioning following an ABI; however, more research is needed.

Dextroamphetamine

Dextroamphetamine is another central nervous stimulant, and similar to methylphenidate it is used to treat narcolepsy and attention deficit hyperactivity disorder. Dextroamphetamine is a non-catecholamine and sympathomimetic amine that acts as a stimulant, unfortunately more direct mechanisms of action are not currently known.

TABLE 18 | The Effect of Dextroamphetamine on General and Executive Functioning Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Hart et al. (2018) United States RCT PEDro=10 N=32	**Population:** *DEX Group (N=17)*: Mean age=39.6yr; Gender: Male=11, Female=6; Mean GCS=8.2; Mean time post-injury=53.6dy. *Control Group (N=15):* Mean age=38.7yr; Gender: Male=15, Female=0; Mean GCS=7.5; Mean time post-injury=60.2dy. **Intervention:** Participants either received the placebo or 10 mg of dextroamphetamine (DEX). Each treatment was administered once a day, in the morning, for 3 weeks. **Outcomes:** Moss Attention Rating Scale (MARS), Hopkins Rehabilitation Engagement Rating Scale (HRER), Cognitive Failures Questionnaire (CFQ), Rating Scale of Attentional Behavior (RSAB), Finger Taping Test (FT), the Symbol Digit Modalities Test (SDMT), Disability Rating Scale (DRS), Agitated Behavior Scale (ABS), Profile of Mood States (POMS),	1. There was a significant difference between groups on the ABS (p=0.04), with the DEX group demonstrating more agitation over time. 2. No other significant differences were found.

Discussion

One RCT has recently evaluated the effects of dextroamphetamine on general and executive functioning using a variety of outcomes (Hart et al., 2018). Although dextroamphetamine was seen to significantly reduce agitation compared to the placebo group, no significant effects were seen on measures of cognition. Given the use of dextroamphetamine in other attentional disorders such as attention deficit hyperactivity disorder, the lack of results on any cognitive measures between these two studies is unexpected.

Conclusions

There is level 1b evidence that dextroamphetamine is not effective for the remediation of general cognitive functioning following an ABI.

KEY POINT

- There is moderate evidence to suggest that dextroamphetamine is not effective for the remediation of general functioning.

CONCLUSION

Cognitive interventions target a large variety of cognitive functions and deficits. The rehabilitation of these functions is complicated by the lack of consensus on the definition of general and executive functioning. Comparing the efficacy of various remediation efforts is also complicated by cross-study variability in treatment duration (e.g., from 30 minutes once a day for 5 days to 5 hours, every day for 6 weeks). Severity of injury and time since injury may also fluctuate from study to study.

Frequency of intervention has an impact on general and executive cognitive functioning, although the exact parameters of this are unclear at the present time. The optimal duration of a program is also open for speculation. No studies reviewed examined the number of sessions required to be effective and only one study evaluated a difference in effectiveness between mild and severely impaired individuals after sessions.

REFERENCES

Al-Adawi, S., Al-Naamani, A., Jaju, S., Al-Farsi, Y. M., Dorvlo, A. S. S., Al-Maashani, A., Al-Adawi, S. S. H., Moustafa, A. A., Al-Sibani, N., Essa, M. M., Burke, D. T., & Qoronfleh, M. W. (2020, Mar 19). Methylphenidate improves executive functions in patients with traumatic brain injuries: a feasibility trial via the idiographic approach. *BMC Neurol, 20*(1), 103. https://doi.org/10.1186/s12883-020-01663-x

Banos, J. H., Novack, T. A., Brunner, R., Renfroe, S., Lin, H. Y., & Meythaler, J. (2010, Sep-Oct). Impact of early administration of sertraline on cognitive and behavioral recovery in the first year after moderate to severe traumatic brain injury. *J Head Trauma Rehabil, 25*(5), 357-361. https://doi.org/10.1097/HTR.0b013e3181d6c715

Bondanelli, M., Ambrosio, M. R., Cavazzini, L., Bertocchi, A., Zatelli, M. C., Carli, A., Valle, D., Basaglia, N., & Uberti, E. C. (2007, Nov). Anterior pituitary function may predict functional and cognitive outcome in patients with traumatic brain injury undergoing rehabilitation. *J Neurotrauma, 24*(11), 1687-1697. https://doi.org/10.1089/neu.2007.0343

Campbell, M. (2000). *Rehabilitation for traumatic brain injury: physical therapy practice in context* (2 ed.). Churchill Livingstone

Cantor, J., Ashman, T., Dams-O'Connor, K., Dijkers, M. P., Gordon, W., Spielman, L., Tsaousides, T., Allen, H., Nguyen, M., & Oswald, J. (2014, Jan). Evaluation of the short-term executive plus intervention for executive dysfunction after traumatic brain injury: a randomized controlled trial with minimization. *Arch Phys Med Rehabil, 95*(1), 1-9.e3. https://doi.org/10.1016/j.apmr.2013.08.005

Chen, A. J., Novakovic-Agopian, T., Nycum, T. J., Song, S., Turner, G. R., Hills, N. K., Rome, S., Abrams, G. M., & D'Esposito, M. (2011, May). Training of goal-directed attention regulation enhances control over neural processing for individuals with brain injury. *Brain, 134*(Pt 5), 1541-1554. https://doi.org/10.1093/brain/awr067

Chen, S. H., Thomas, J. D., Glueckauf, R. L., & Bracy, O. L. (1997, Mar). The effectiveness of computer-assisted cognitive rehabilitation for persons with traumatic brain injury. *Brain Inj, 11*(3), 197-209. http://www.ingentaconnect.com/content/apl/tbin/1997/00000011/00000003/art00004?token=005219c73f7f0c5a8405847447b496e2f5f73446f554779663e33757e6f4f2858592f3f3b57d640982

Cicerone, K. D. (2002, Mar). Remediation of "working attention" in mild traumatic brain injury. *Brain Inj, 16*(3), 185-195. https://doi.org/10.1080/02699050110103959

Cicerone, K. D., Dahlberg, C., Kalmar, K., Langenbahn, D. M., Malec, J. F., Bergquist, T. F., Felicetti, T., Giacino, J. T., Harley, J. P., Harrington, D. E., Herzog, J., Kneipp, S., Laatsch, L., & Morse, P. A. (2000, Dec). Evidence-based cognitive rehabilitation: recommendations for clinical practice. *Arch Phys Med Rehabil, 81*(12), 1596-1615. https://doi.org/10.1053/apmr.2000.19240

Cicerone, K. D., Dahlberg, C., Malec, J. F., Langenbahn, D. M., Felicetti, T., Kneipp, S., Ellmo, W., Kalmar, K., Giacino, J. T., Harley, J. P., Laatsch, L., Morse, P. A., & Catanese, J. (2005, Aug). Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002. *Arch Phys Med Rehabil, 86*(8), 1681-1692. https://doi.org/10.1016/j.apmr.2005.03.024

Cicerone, K. D., Langenbahn, D. M., Braden, C., Malec, J. F., Kalmar, K., Fraas, M., Felicetti, T., Laatsch, L., Harley, J. P., Bergquist, T., Azulay, J., Cantor, J., & Ashman, T. (2011, Apr). Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. *Arch Phys Med Rehabil, 92*(4), 519-530. https://doi.org/10.1016/j.apmr.2010.11.015

Cizman Staba, U., Vrhovac, S., Mlinaric Lesnik, V., & Novakovic-Agopian, T. (2020, 01 Mar). Goal-oriented attentional self-regulation training in individuals with acquired brain injury in a subacute phase: a pilot feasibility study. *International journal of rehabilitation research, Internationale Zeitschrift fur Rehabilitationsforschung. Revue internationale de recherches de readaptation. 43*(1), 28-36. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emexb&AN=629766267

Combs, M. A., Critchfield, E. A., & Soble, J. R. (2018, May). Relax while you rehabilitate: A pilot study integrating a novel, yoga-based mindfulness group intervention into a residential military brain injury rehabilitation program. *Rehabil Psychol, 63*(2), 182-193. https://doi.org/10.1037/rep0000179

Copley, A., Smith, K., Savill, K., & Finch, E. (2015). Does metacognitive strategy instruction improve impaired receptive cognitive-communication skills following acquired brain injury? *Brain Inj, 29*(11), 1309-1316. https://doi.org/10.3109/02699052.2015.1043343

Couillet, J., Soury, S., Lebornec, G., Asloun, S., Joseph, P. A., Mazaux, J. M., & Azouvi, P. (2010, Jun). Rehabilitation of divided attention after severe traumatic brain injury: a randomised trial. *Neuropsychol Rehabil, 20*(3), 321-339. https://doi.org/10.1080/09602010903467746

Dahdah, M. N., Bennett, M., Prajapati, P., Parsons, T. D., Sullivan, E., & Driver, S. (2017). Application of virtual environments in a multi-disciplinary day neurorehabilitation program to improve executive functioning using the Stroop task. *NeuroRehabilitation, 41*(4), 721-734. https://doi.org/10.3233/nre-172183

Dymowski, A. R., Ponsford, J. L., Owens, J. A., Olver, J. H., Ponsford, M., & Willmott, C. (2017, Jun). The efficacy and safety of extended-release methylphenidate following traumatic brain injury: a randomised controlled pilot study. *Clin Rehabil, 31*(6), 733-741. https://doi.org/10.1177/0269215516655590

Elbogen, E. B., Dennis, P. A., Van Voorhees, E. E., Blakey, S. M., Johnson, J. L., Johnson, S. C., Wagner, H. R., Hamer, R. M., Beckham, J. C., Manly, T., & Beiger, A. (2019). Cognitive Rehabilitation With Mobile Technology and Social Support for Veterans With TBI and PTSD: A Randomized Clinical Trial. *Journal of Head Trauma Rehabilitation, 34*(1), 1-10. https://doi.org/10.1097/HTR.0000000000000435

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Gabbatore, I., Sacco, K., Angeleri, R., Zettin, M., Bara, B. G., & Bosco, F. M. (2015, Sep-Oct). Cognitive Pragmatic Treatment: A Rehabilitative Program for Traumatic Brain Injury Individuals. *J Head Trauma Rehabil, 30*(5), E14-28. https://doi.org/10.1097/htr.0000000000000087

Glenn, M. B. (1998, Oct). Methylphenidate for cognitive and behavioral dysfunction after traumatic brain injury. *J Head Trauma Rehabil, 13*(5), 87-90.

Gordon, W. A., Zafonte, R., Cicerone, K., Cantor, J., Brown, M., Lombard, L., Goldsmith, R., & Chandna, T. (2006, Apr). Traumatic brain injury rehabilitation: state of the science. *Am J Phys Med Rehabil, 85*(4), 343-382. https://doi.org/10.1097/01.phm.0000202106.01654.61

Greenwald, B. D., Burnett, D. M., & Miller, M. A. (2003, Mar). Congenital and acquired brain injury. 1. Brain injury: epidemiology and pathophysiology. *Arch Phys Med Rehabil, 84*(3 Suppl 1), S3-7.

High, W. M., Jr., Briones-Galang, M., Clark, J. A., Gilkison, C., Mossberg, K. A., Zgaljardic, D. J., Masel, B. E., & Urban, R. J. (2010, Sep). Effect of growth hormone replacement therapy on cognition after traumatic brain injury. *J Neurotrauma, 27*(9), 1565-1575. https://doi.org/10.1089/neu.2009.1253

Jacoby, M., Averbuch, S., Sacher, Y., Katz, N., Weiss, P. L., & Kizony, R. (2013, Mar). Effectiveness of executive functions training within a virtual supermarket for adults with traumatic brain injury: a pilot study. *IEEE Trans Neural Syst Rehabil Eng, 21*(2), 182-190. https://doi.org/10.1109/tnsre.2012.2235184

Jenkins, P. O., De Simoni, S., Bourke, N. J., Fleminger, J., Scott, G., Towey, D. J., Svensson, W., Khan, S., Patel, M. C., Greenwood, R., Friedland, D., Hampshire, A., Cole, J. H., & Sharp, D. J. (2019, Aug 2019

2020-01-30). Stratifying drug treatment of cognitive impairments after traumatic brain injury using neuroimaging. *Brain: A Journal of Neurology, 142*(8), 2367-2379. https://doi.org/http://dx.doi.org/10.1093/brain/awz149

Kelly, D. F., McArthur, D. L., Levin, H., Swimmer, S., Dusick, J. R., Cohan, P., Wang, C., & Swerdloff, R. (2006). Neurobehavioral and quality of life changes associated with growth hormone insufficiency after complicated mild, moderate, or severe traumatic brain injury. *J Neurotrauma, 23*(6), 928-942.

http://www.scopus.com/inward/record.url?eid=2-s2.0-33745483268&partnerID=40&md5=7eb755dbc986d8d040c7cde8e6266ef4

http://online.liebertpub.com/doi/abs/10.1089/neu.2006.23.928?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

Kennedy, M. R., Coelho, C., Turkstra, L., Ylvisaker, M., Moore Sohlberg, M., Yorkston, K., Chiou, H. H., & Kan, P. F. (2008, Jun). Intervention for executive functions after traumatic brain injury: a systematic review, meta-analysis and clinical recommendations. *Neuropsychol Rehabil, 18*(3), 257-299. https://doi.org/10.1080/09602010701748644

Khateb, A., Ammann, J., Annoni, J. M., & Diserens, K. (2005). Cognition-enhancing effects of donepezil in traumatic brain injury. *Eur Neurol, 54*(1), 39-45. https://doi.org/10.1159/000087718

Kline, A. E., Massucci, J. L., Marion, D. W., & Dixon, C. E. (2002, Apr). Attenuation of working memory and spatial acquisition deficits after a delayed and chronic bromocriptine treatment regimen in rats subjected to traumatic brain injury by controlled cortical impact. *J Neurotrauma, 19*(4), 415-425. https://doi.org/10.1089/08977150252932370

Kraus, M. F., Smith, G. S., Butters, M., Donnell, A. J., Dixon, E., Yilong, C., & Marion, D. (2005, Jul). Effects of the dopaminergic agent and NMDA receptor antagonist amantadine on cognitive function, cerebral glucose metabolism and D2 receptor availability in chronic traumatic brain injury: a study using positron emission tomography (PET). *Brain Inj, 19*(7), 471-479.

Laatsch, L., Pavel, D., Jobe, T., Lin, Q., & Quintana, J. C. (1999, Aug). Incorporation of SPECT imaging in a longitudinal cognitive rehabilitation therapy programme. *Brain Inj, 13*(8), 555-570. http://www.ingentaconnect.com/content/apl/tbin/1999/00000013/00000008/art00001?token=00521b85b522afa72297b76504c48664625453a566c787a6a2d356a332b25757d5c4f6d4e227a9e757

Levack, W. M., Siegert, R. J., Dean, S. G., & McPherson, K. M. (2009, Mar). Goal planning for adults with acquired brain injury: how clinicians talk about involving family. *Brain Inj, 23*(3), 192-202. https://doi.org/10.1080/02699050802695582

Levine, B., Robertson, I. H., Clare, L., Carter, G., Hong, J., Wilson, B. A., Duncan, J., & Stuss, D. T. (2000, Mar). Rehabilitation of executive functioning: an experimental-clinical validation of goal management training. *J Int Neuropsychol Soc, 6*(3), 299-312.

Lezak, M. D. (2004). *Neuropsychological assessment*. Oxford university press.

Li, K., Alonso, J., Chadha, N., & Pulido, J. (2015). Does Generalization Occur Following Computer-Based Cognitive Retraining?-An Exploratory Study. *Occup Ther Health Care, 29*(3), 283-296. https://doi.org/10.3109/07380577.2015.1010246

Li, K., Robertson, J., Ramos, J., & Gella, S. (2013, Oct). Computer-based cognitive retraining for adults with chronic acquired brain injury: a pilot study. *Occup Ther Health Care, 27*(4), 333-344. https://doi.org/10.3109/07380577.2013.844877

Linton, K. F., & Kim, B. J. (2018, Jan). A pilot study of Trabajadora de salud, a lay health worker intervention for Latinas/os with traumatic brain injuries and their caregivers. *Disabil Health J, 11*(1), 161-164. https://doi.org/10.1016/j.dhjo.2017.04.009

Llorens, R., Navarro, M. D., Alcaniz, M., & Noe, E. (2012). Therapeutic effectiveness of a virtual reality game in self-awareness after acquired brain injury. *Stud Health Technol Inform, 181*, 297-301.

Man, D. W., Poon, W. S., & Lam, C. (2013). The effectiveness of artificial intelligent 3-D virtual reality vocational problem-solving training in enhancing employment opportunities for people with traumatic brain injury. *Brain Inj, 27*(9), 1016-1025. https://doi.org/10.3109/02699052.2013.794969

Masanic, C. A., Bayley, M. T., VanReekum, R., & Simard, M. (2001, Jul). Open-label study of donepezil in traumatic brain injury. *Arch Phys Med Rehabil, 82*(7), 896-901. https://doi.org/10.1053/apmr.2001.23833

McDowell, S., Whyte, J., & D'Esposito, M. (1998, Jun). Differential effect of a dopaminergic agonist on prefrontal function in traumatic brain injury patients. *Brain, 121 (Pt 6)*, 1155-1164.

Miller, M. A., Burnett, D. M., & McElligott, J. M. (2003, Mar). Congenital and acquired brain injury. 3. Rehabilitation interventions: cognitive, behavioral, and community reentry. *Arch Phys Med Rehabil, 84*(3 Suppl 1), S12-17.

Moreau, O. K., Cortet-Rudelli, C., Yollin, E., Merlen, E., Daveluy, W., & Rousseaux, M. (2013, Jun 01). Growth hormone replacement therapy in patients with traumatic brain injury. *J Neurotrauma, 30*(11), 998-1006. https://doi.org/10.1089/neu.2012.2705

Morey, C. E., Cilo, M., Berry, J., & Cusick, C. (2003, Sep). The effect of Aricept in persons with persistent memory disorder following traumatic brain injury: a pilot study. *Brain Inj, 17*(9), 809-815. https://doi.org/10.1080/0269905031000088586

Napolitano, E., Elovic, E. P., & Qureshi, A. I. (2005, Jun). Pharmacological stimulant treatment of neurocognitive and functional deficits after traumatic and non-traumatic brain injury. *Med Sci Monit, 11*(6), Ra212-220.

Neistadt, M. E. (1992, Feb). Occupational therapy treatments for constructional deficits. *Am J Occup Ther, 46*(2), 141-148. http://ajot.aotapress.net/content/46/2/141.full.pdf

Neville, I. S., Zaninotto, A. L., Hayashi, C. Y., Rodrigues, P. A., Galhardoni, R., Ciampi de Andrade, D., Brunoni, A. R., Amorim, R. L. O., Teixeira, M. J., & Paiva, W. S. (2019). Repetitive TMS does not improve cognition in patients with TBI: A randomized double-blind trial. *Neurology, 93*(2), e190-e199. https://doi.org/10.1212/WNL.0000000000007748

Novakovic-Agopian, T., Chen, A. J., Rome, S., Abrams, G., Castelli, H., Rossi, A., McKim, R., Hills, N., & D'Esposito, M. (2011, Sep-Oct). Rehabilitation of executive functioning with training in attention regulation applied to individually defined goals: a pilot study bridging theory, assessment, and treatment. *J Head Trauma Rehabil, 26*(5), 325-338. https://doi.org/10.1097/HTR.0b013e3181f1ead2

O'Neil-Pirozzi, T. M., & Hsu, H. (2016). Feasibility and benefits of computerized cognitive exercise to adults with chronic moderate-to-severe cognitive impairments following an acquired brain injury: A pilot study. *Brain Inj, 30*(13-14), 1617-1625. https://doi.org/10.1080/02699052.2016.1199906

Ownsworth, T., Fleming, J., Shum, D., Kuipers, P., & Strong, J. (2008). Comparison of individual, group and combined intervention formats in a randomized controlled trial for facilitating goal attainment and improving psychosocial function following acquired brain injury. *Journal of Rehabilitation Medicine, 40*(2), 81-88. http://www.scopus.com/inward/record.url?eid=2-s2.0-40949118113&partnerID=40&md5=29dcf661b63298ef1fb26a49a33dbad6

http://www.ingentaconnect.com/content/mjl/sreh/2008/00000040/00000002/art00001?token=004f1c21a33ea9a1e378437a63736a6f7c47635d7a666744443a5b6f644a467b4d616d3f4e4b34d

Parente, R., & Stapleton, M. (1999, 01/01/). Development of a Cognitive strategies group for vocational training after traumatic brain injury. *NeuroRehabilitation, 13*(1), 13-20. http://iospress.metapress.com/content/R3H1TDTHKNR8LQF0

Powell, J. H., al-Adawi, S., Morgan, J., & Greenwood, R. J. (1996, Apr). Motivational deficits after brain injury: effects of bromocriptine in 11 patients. *J Neurol Neurosurg Psychiatry, 60*(4), 416-421. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1073895/pdf/jnnpsyc00016-0058.pdf

Rasquin, S. M., Bouwens, S. F., Dijcks, B., Winkens, I., Bakx, W. G., & van Heugten, C. M. (2010, Oct). Effectiveness of a low intensity outpatient cognitive rehabilitation programme for patients in the chronic phase after acquired brain injury. *Neuropsychol Rehabil, 20*(5), 760-777. https://doi.org/10.1080/09602011.2010.484645

Rath, J. F., Simon, D., Langenbahn, D. M., Sherr, R. L., & Diller, L. (2003, 2003/09/01). Group treatment of problem-solving deficits in outpatients with traumatic brain injury: A randomised outcome study. *Neuropsychol Rehabil, 13*(4), 461-488. https://doi.org/10.1080/09602010343000039

Reimunde, P., Quintana, A., Castanon, B., Casteleiro, N., Vilarnovo, Z., Otero, A., Devesa, A., Otero-Cepeda, X. L., & Devesa, J. (2011). Effects of growth hormone (GH) replacement and cognitive rehabilitation in patients with cognitive disorders after traumatic brain injury. *Brain Inj, 25*(1), 65-73. https://doi.org/10.3109/02699052.2010.536196

Sackett DL, S. S., Richardson WS, Rosenberg W, Hayes RB. (2000). *Evidence-based medicine: how to practice and teach EBM* (2nd ed. ed.).

Schmidt, J., Fleming, J., Ownsworth, T., & Lannin, N. A. (2013, May). Video feedback on functional task performance improves self-awareness after traumatic brain injury: a randomized controlled trial. *Neurorehabil Neural Repair, 27*(4), 316-324. https://doi.org/10.1177/1545968312469838

Schneider, W. N., Drew-Cates, J., Wong, T. M., & Dombovy, M. L. (1999, Nov). Cognitive and behavioural efficacy of amantadine in acute traumatic brain injury: an initial double-blind placebo-controlled study. *Brain Inj, 13*(11), 863-872. http://www.ingentaconnect.com/content/apl/tbin/1999/00000013/00000011/art00003?token=00541cb6c8bd293d898d383a4b3b2570747b465f41385e572b67732a726e2d2954496f642f466fa656bd

Schneiderman, A. I., Braver, E. R., & Kang, H. K. (2008, Jun 15). Understanding sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: persistent postconcussive symptoms and posttraumatic stress disorder. *Am J Epidemiol, 167*(12), 1446-1452. https://doi.org/10.1093/aje/kwn068

Siddiqui, S. V., Chatterjee, U., Kumar, D., Siddiqui, A., & Goyal, N. (2008). Neuropsychology of prefrontal cortex. *Indian journal of psychiatry, 50*(3), 202. https://doi.org/10.4103/0019-5545.43634

Silver, J. M., Koumaras, B., Chen, M., Mirski, D., Potkin, S. G., Reyes, P., Warden, D., Harvey, P. D., Arciniegas, D., Katz, D. I., & Gunay, I. (2006). Effects of rivastigmine on cognitive function in patients with traumatic brain injury. *Neurology, 67*(5), 748-755. https://doi.org/10.1212/01.wnl.0000234062.98062.e9

Silver, J. M., Koumaras, B., Meng, X., Potkin, S. G., Reyes, P. F., Harvey, P. D., Katz, D. I., Gunay, I., & Arciniegas, D. B. (2009, Feb). Long-term effects of rivastigmine capsules in patients with traumatic brain injury. *Brain Inj, 23*(2), 123-132. https://doi.org/10.1080/02699050802649696

Siponkoski, S.-T., Martínez-Molina, N., Kuusela, L., Laitinen, S., Holma, M., Ahlfors, M., Jordan-Kilkki, P., Ala-Kauhaluoma, K., Melkas, S., Pekkola, J., Rodriguez-Fornells, A., Laine, M., Ylinen, A., Rantanen, P., Koskinen, S., Lipsanen, J., & Särkämö, T. (2020, 2020 Feb 15

2020-02-27). Music therapy enhances executive functions and prefrontal structural neuroplasticity after traumatic brain injury: Evidence from a randomized controlled trial. *Journal of Neurotrauma, 37*(4), 618-634. https://doi.org/http://dx.doi.org/10.1089/neu.2019.6413

Sohlberg, M. M., Avery, J., Kennedy, M., Ylvisaker, M., Coelho, C., Turkstra, L., & Yorkston, K. (2003b). Practice guidelines for direct attention training. *Journal of Medical Speech-Language Pathology, 11*(3), xix-xxxix. http://www.scopus.com/inward/record.url?eid=2-s2.0-0141478707&partnerID=40&md5=154ee5f86521f8e4217df7799c31334b

Sohlberg, M. M., McLaughlin, K. A., Pavese, A., Heidrich, A., & Posner, M. I. (2000, Oct). Evaluation of attention process training and brain injury education in persons with acquired brain injury. *J Clin Exp Neuropsychol, 22*(5), 656-676. https://doi.org/10.1076/1380-3395(200010)22:5;1-9;ft656

Speech, T. J., Rao, S. M., Osmon, D. C., & Sperry, L. T. (1993, Jul-Aug). A double-blind controlled study of methylphenidate treatment in closed head injury. *Brain Inj, 7*(4), 333-338.

Spikman, J. M., Boelen, D. H., Lamberts, K. F., Brouwer, W. H., & Fasotti, L. (2010, Jan). Effects of a multifaceted treatment program for executive dysfunction after acquired brain injury on indications of executive functioning in daily life. *J Int Neuropsychol Soc, 16*(1), 118-129. https://doi.org/10.1017/s1355617709991020

The Mayo Clinic. (2019). *Hyperbaric Oxygen Therapy*. The Mayo Clinic Retrieved August 8 from https://www.mayoclinic.org/tests-procedures/hyperbaric-oxygen-therapy/about/pac-20394380

Tornas, S., Lovstad, M., Solbakk, A. K., Evans, J., Endestad, T., Hol, P. K., Schanke, A. K., & Stubberud, J. (2016, Apr). Rehabilitation of Executive Functions in Patients with Chronic Acquired Brain Injury with Goal Management Training, External Cuing, and Emotional Regulation: A Randomized Controlled Trial. *J Int Neuropsychol Soc, 22*(4), 436-452. https://doi.org/10.1017/s1355617715001344

Tornas, S., Lovstad, M., Solbakk, A. K., Schanke, A. K., & Stubberud, J. (2019, Nov). Use It or Lose It? A 5-Year Follow-up Study of Goal Management Training in Patients with Acquired Brain Injury. *J Int Neuropsychol Soc, 25*(10), 1082-1087. https://doi.org/10.1017/s1355617719000626

Vas, A. K., Chapman, S. B., Cook, L. G., Elliott, A. C., & Keebler, M. (2011, May-Jun). Higher-order reasoning training years after traumatic brain injury in adults. *J Head Trauma Rehabil, 26*(3), 224-239. https://doi.org/10.1097/HTR.0b013e318218dd3d

Walker, W., Seel, R., Gibellato, M., Lew, H., Cornis-Pop, M., Jena, T., & Silver, T. (2004, Aug). The effects of Donepezil on traumatic brain injury acute rehabilitation outcomes. *Brain Inj, 18*(8), 739-750. https://doi.org/10.1080/02699050310001646224

Webb, P. M., & Glueckauf, R. L. (1994). The effects of direct involvement in goal setting on rehabilitation outcome for persons with traumatic brain injuries. *Rehabil Psychol, 39*(3), 179-188. https://doi.org/10.1037/h0080321

Whyte, J., Vaccaro, M., Grieb-Neff, P., Hart, T., Polansky, M., & Coslett, H. B. (2008, Feb). The effects of bromocriptine on attention deficits after traumatic brain injury: a placebo-controlled pilot study. *Am J Phys Med Rehabil, 87*(2), 85-99. https://doi.org/10.1097/PHM.0b013e3181619609

Zhang, W. T., & Wang, Y. F. (2017, Jun). Efficacy of methylphenidate for the treatment of mental sequelae after traumatic brain injury. *Medicine (Baltimore), 96*(25), e6960. https://doi.org/10.1097/md.0000000000006960