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

ATTENTION, CONCENTRATION & INFORMATION PROCESSING

POST ACQUIRED BRAIN INJURY

Shawn Marshall MD FRCPC, Amber Harnett MSc,

Penny Welch-West M.Cl.Sc. SLP, Connie Ferri MSc SLP,
Shannon Janzen MSc, Leanne Togher PhD,

Robert Teasell MD FRCPC

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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.

Contact Information

Evidence-Based Review of Moderate to Severe Acquired Brain Injury

550 Wellington Rd South, London, Ontario, Canada N6C 0A7

Website: www.ERABI.ca

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) *Attention, Concentration & Information Processing 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, BScN (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	
Drill & Practice	Drill and practice training may not be effective for the remediation of attention following an ABI. - *There is level 2 evidence that drill, and practice training may not be effective for the remediation of attention compared to spontaneous recovery, regardless of the level of structure in the program for those with an ABI.*
Dual-Task Training	Dual-task training has been shown to improve measures of attention to the extent that the population with ABI does not significantly differ from healthy controls; however, it is undetermined if the strength of these effects compared to non-dual-task training, are greater. - *There is level 2 and level 3 evidence that dual task training may be effective in improving attention task performance in ABI populations compared to non-specific training.*
Technological Interventions	Computer-based interventions are no more effective than no intervention in improving measures of attention and concentration post ABI. - *There is level 2 evidence that neither general nor name brand computer-based rehabilitation intervention may improve attention outcomes compared to usual care in ABI populations.* Repetitive virtual reality tasks which include repetition are effective in improving attention and concentration in ABI populations. - *There is level 4 evidence that attention performance can be improved in ABI populations through repetition of tasks, either through computer-based or virtual reality environments.*
Attention Training Programs	Goal management training is effective in assisting those who sustain an ABI in learning to manage life goals through improved attention. - *There is level 2 evidence to suggest goal management training, when compared to education, may be effective at improving attention in individuals post ABI.* - *There is level 2 evidence that goal management training is more effective in remediating task completion times than motor skill training, however it is not more effective in treating attention deficits, in individuals post ABI.* In general, a variety of non-specific attentional training programs appear to be effective for improving attentional scores following an ABI. - *There is level 4 evidence that summation tasks may be effective at improving attention in individuals post ABI.*

	- *There is level 4 evidence that a working memory training program may remediate attention in individuals post ABI.* - *There is level 4 evidence that cognitive rehabilitation therapy may not be effective for improving attention post ABI.* - *There is level 2 evidence that adaptive training is no more effective than non-adaptive training in remediating attention in ABI populations.* - *There is conflicting (level 2) evidence that attentional control or processing training may not significantly improve attention in post ABI individuals compared to control training.* The addition of a therapy animal to an attentional training program may enhance concentration gains. - *There is level 1b evidence that the addition of a therapy animal to attention training programs may enhance gains in concentration in those with an ABI.* Therapies which focus on emotional regulation do not appear to be effective at improving attention post ABI, while mindfulness may improve some areas. - *There is level 1b evidence that emotional regulation therapy is not effective in treating attentional disorders compared to waitlist controls in ABI populations.* In order to determine if attentional training is effective in improving attention post-ABI, standardized protocols must be developed to allow between study comparisons. Tasks that involve mathematical skills may be effective at improving attention post ABI.
Brain Stimulation Techniques	Transcranial direct current stimulation may be effective in remediating attentional deficits when combined with computer assisted training in ABI populations. - *There is level 2 evidence that transcranial direct current stimulation when combined with an attention training program (compared to sham stimulation) may improve divided attention in individuals post ABI.* Repeated magnetic transcranial stimulation may not be effective in remediating attentional deficits following an ABI. - *There is conflicting level 1b evidence that repeated transcranial magnetic stimulation compared to sham stimulation may not improve attention following an ABI.*
Pharmacological Interventions	
Donepezil	It is unclear as to whether donepezil may improve attention in individuals with moderate to severe ABI. - *There is conflicting level 1b (positive) and level 2 (negative) evidence that donepezil may improve attention compared to placebo post ABI.*

Methylphenidate	The effectiveness of methylphenidate treatment to improve cognitive function following brain injury is unclear: - Methylphenidate may be effective in improving reaction time for working memory. - Response to methylphenidate may depend on the presence of the Met genotype and/or dopamine transporter levels. - *There is conflicting level 1a evidence regarding the effectiveness of methylphenidate following brain injury for the improvement of attention and concentration in individuals post ABI.* - *There is level 1a evidence that methylphenidate improves reaction time of working memory compared to placebo in individuals post ABI.* - *There is level 1b evidence that individuals carrying the Met allele may be more responsive to methylphenidate than those without the Met allele when it comes to the ABI population.*
Bromocriptine	Bromocriptine does not appear to improve attention in those with an ABI. - *There is conflicting evidence as to whether bromocriptine improves performance on attention tasks compared to placebo in patients post TBI.*
Cerebrolysin	Cerebrolysin may be beneficial for improving clinical outcomes and cognitive functioning following brain injury; however, controlled trials are needed to further evaluate its efficacy - *There is conflicting evidence as to whether bromocriptine improves performance on attention tasks compared to placebo in patients post TBI.*
Rivastigmine	Rivastigmine may not be effective in treating attention deficits post ABI. - *There is level 1b evidence that Rivastigmine compared to placebo is not effective for improving concentration or processing speed in post ABI individuals but may increase vigilance.*
Amantadine	Amantadine may not be effective in treating attention deficits following an ABI. - *There is level 1b evidence that amantadine is not effective for improving attention compared to placebo following an ABI.*
Hyperbaric Oxygen Therapy	Hyperbaric oxygen therapy may improve attention and processing speed following an ABI; however, more prospective data is required. - *There is level 4 evidence that hyperbaric oxygen therapy may improve both attention and processing speed following an ABI.*
Dextroamphetamine	Dextroamphetamine may not be an effective treatment for attentional deficits following an ABI and may actually increase agitation. - *There is level 1b evidence that dextroamphetamine does not improve attention following an ABI.*

INTRODUCTION

Although there is no specific agreement on the definition of attention, it is usually measured using externally directed tests, such as instructing participants to focus their attention on a sequence of stimuli or attenuating to a particular stimulus.

In general, TBI populations demonstrate significant deficits compared to control populations. Dymowski et al. (2015) showed that mild to severe TBI participants performed significantly worse on speed of information processing tasks compared to a healthy control group. Dockree et al. (2006) and Hasegawa and Hoshiyama (2009) found that TBI patients made significantly more errors than their non-TBI counterparts on dual task experiments for sustained attention. However, a case series by Foley et al. (2010) found that level of injury severity as measured by the Glasgow Coma Scale or PTA did not play a role in who performed poorly on the dual task assignment given to participants. They found that only 27% of TBI study participants performed below the cut-off for normal performance.

Two studies assessing the reaction times of individuals demonstrated that those with a TBI were found to have slower reaction times than individuals who had not sustained a TBI (Azouvi et al., 2004; Stuss et al., 1989). Results of the visual analogue scale also indicated that mental effort was higher for those with a TBI than for the controls. The results of this study confirmed what previous studies had found: those with a TBI have greater difficulty when dealing with two simultaneous tasks (Azouvi et al., 2004).

To better understand the mechanism by which cognitive interventions can improve attention, concentration, and information processing, there needs to be a consensus as to the definition of specific cognitive processes, including attention.

Non-Pharmacological Interventions

Drill & Practice

The following studies examined the influence of “drill & practice” exercises (either computerized and/or paper-and-pencil) on attentional functioning. Drill and practice training targets attention skills through repetitive training of specific tasks involving attention.

TABLE 4 | The Effect of Drill and Practice on Attention Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome

Novack et al. (1996) USA RCT PEDro=5 N=44	**Population:** Severe TBI; *Focused Stimulation Group (n=22)*: Mean Age=28.7yr; Mean Time Post Injury=5.9wk. *Unstructured Stimulation Group (n=22)*: Mean Age=26.4yr; Mean Time Post Injury=6.4wk **Intervention:** Participants were randomly placed into a focused or unstructured stimulation group. Patients in the focused group received hierarchical attentional learning training (30min, 5x/wk). Skills were not taught in a hierarchical or sequential fashion in the unstructured group. **Outcome Measures:** Digit Span and Mental Control subtests of Wechsler Memory Scale-Revised (WMS-R), computer-based simple and choice reaction time tests. *Secondary outcome measures*: Logical Memory I & II, Sentence Repetition, Judgment of Line Orientation, Trail Making A & B, Arithmetic subtest Wide Range Achievement Test-Revised, Visual imperceptions.	1. Analysis of primary outcome measures revealed no significant differences between the focused and unstructured stimulation groups, both at baseline and discharge. 2. There was a significant time effect with participants performing significantly better at the time of discharge than on admission ($p<0.0001$). 3. There were no significant differences between the groups with respect to any secondary outcome measures studied.
Lindelov et al. (2016) Denmark PCT $N_{Initial}$=78 N_{Final}=35	**Population:** ABI Group (n=17): Mean Age=56.1yr; Gender: Male=13, Female=4; Mean Time Post Injury=57d. Healthy Group (n=18): Mean Age=56.1yr; Gender: Male=8, Female=10. **Intervention:** ABI and healthy participants were randomized and analyzed separately. Experimental group participants received 20 sessions of N-back training (N-back), where participants press a key when presented stimulus is identical to the stimulus N back in the sequence. Control group participants received 20 sessions of visual search training (VS), where participants press a key if a target symbol is present in an NxN array of symbols. **Outcome Measures:** Raven's Advanced Progressive Matrices (RAPM), Wechsler Adult Intelligence Scale-IV (WAIS-IV), Working Memory Index (WMI Index, digit span, arithmetic, letter-number sequencing), Operation Span Test (OSPAN), WAIS-IV Processing Speed Index (PSI index, search, coding), Stroop Test.	1. Both ABI and healthy groups showed significant improvement post-intervention on the assigned training tasks (Bayes factor >> 1000). The standardized mean difference was 0.45 for ABI N-back, 6.11 for healthy N-back, 1.06 for ABI VS, and 3.34 for Healthy VS. The healthy group showed greater improvement than the ABI group (Bayes factor >> 1000). 2. No significant differences in improvements between N-back and VS treatments (time x treatment interaction) were found in ABI or healthy groups for WMI-digit span, WMI-arithmetic, WMI-letter-number sequencing, WMI index, PSI-search, PSI-coding, PSI index, RAPM, OSPAN, or Stroop. 3. No significant differences in improvement between healthy and ABI groups (group x time x test interaction) were found for WMI-digit span, WMI-arithmetic, WMI-letter-number sequencing, WMI index, PSI-search, PSI-coding, PSI index, RAPM, OSPAN, or Stroop.

Discussion

The two studies demonstrated no significant differences between groups for attentional, functional, and/or cognitive skills assessed (Lindelov et al., 2016; Novack et al., 1996). Novack et al. (1996) compared focused hierarchical attentional learning with an unstructured non-sequential, non-hierarchical intervention, while Lindelov et al. (2016) compared N-back training with visual search training. Novack et al. (1996) found that there were no significant differences between groups at either time points;

however, both groups significantly improved over time. Although the study by Lindelov et al. (2016) also found no significant treatment effects over time, in contrast to the previous study, no spontaneous recovery effects were found either. Overall, there is weak evidence in support of training programs as an effective rehabilitation intervention for attention.

Conclusions

There is level 2 evidence that drill, and practice training may not be effective for the remediation of attention compared to spontaneous recovery, regardless of the level of structure in the program for those with an ABI.

KEY POINT

- Drill and practice training may not be effective for the remediation of attention following an ABI.

Dual-Task Training

The following studies examined the effect of "dual-task" training on speed of processing. Dual-task training involves dividing attention between two stimuli in order to complete two tasks concurrently and successfully, such as walking while speaking.

TABLE 5 | The Effect of Dual-Task Training on Speed of Processing Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Couillet et al. (2010) France RCT PEDro=5 N=12	**Population:** severe TBI; Gender: Male=9, Female=3. *Group 1 (n=5)*: Mean Age=23.8yr; Mean GCS=4.8; Mean Time Post Injury=6.3mo. *Group 2 (n=7)*: Mean Age=26.7yr; Mean GCS=4.8; Mean Time Post Injury=16.1mo. **Intervention:** Randomized AB versus BA design, where "A" represents the control phase and "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 Measures:** Test Battery for Attentional Performance (TAP: divided attention and flexibility subtests), Go-no go 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<0.01), the digit span dual-task (p<0.001), and the Rating Scale of Attentional Behaviour (p<0.01). 3. There were significant differences 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.

	Digit Span, Trail Making Test, Stroop Test, Brown-Peterson Paradigm, Rating Scale of Attentional Behaviour.	
Stablum et al. (2000) Italy Case-Control N=38	**Population:** Condition: Chronic Head Injury (CHI)=10 [mean age:25.6 yr, time since injury: 27.8 months]. Anterior Communicating Artery Aneurysm (ACoA)=9 [mean age: 43.22 yr, time since injury=3.66 months]. Controls=19 (CHI study n=10, ACoA study n=9; Age Range: 14-68yr). **Intervention:** *CHI study:* Neuropsychological assessments (i.e., Wisconsin Card Sorting Task (WCST), Paced Auditory Serial Addition Task (PASAT)) were conducted. As well as a Dual-Task Paradigm: Participant had to indicate the position (right or left) of the stimuli and saying aloud if stimuli were congruent. Participants were evaluated at baseline, retest after treatment, and at 3 months follow-up. *ACoA study:* Neurological Assessments and Dual-task paradigm were conducted similar to the CHI study, but participants also performed a Continuous Performance Task (CPT) measuring inhibition responses in executive functioning. Participants were evaluated at baseline, retest after treatment, and at 3 months and 12 months follow-up. **Outcome Measures:** WCST, PASAT, CPT, dual-task cost.	*CHI study:* 1. Significant difference between patients and controls on number of preservative errors ($p<0.017$) and categories ($p<0.020$) achieved in WCST, and PASAT mean time ($p=0.031$). 2. Reaction time was slower for CHI patients than controls in dual-task ($p<0.005$); dual task cost significantly greater for CHI patients than controls ($p<0.028$). 3. At retest and at 3-months follow-up reaction time was slower for CHI patients than controls ($p<0.0001$); but patients demonstrated a greater reduction in dual-task cost after treatment (54 vs 22 ms). *ACoA Study:* 4. ACoA patients had slower reaction times than controls on CPT ($p<0.001$). 5. Reaction time for closed head injury ($p<0.0001$) and aneurysm ($p<0.007$) group significantly slower than control. 6. Inhibiting a habitual response took ACoA patients significantly longer than controls on the CPT ($p<0.011$). 7. The dual-task cost was greater for the ACoA group compared to the control group ($p<0.0001$). The dual-task cost was significantly greater at assessment than at retest, 3, and 12-month followup ($p<0.0001$); after treatment ACoA patients could co-ordinate two responses as efficiently as controls at 6-month re-assessment.

Discussion

One RCT in a population with TBI demonstrated that attention and information processing outcomes could be improved within the dual task paradigm (Couillet et al., 2010). Couillet et al. (2010) found that dual-task training significantly improved attentional behaviour and reaction time compared to a non-specific cognitive program. Stablum et al. (2000) found that initially individuals with a closed head injury (CHI) performed poorly on dual-task measures; however, with additional training their completion time of dual-task measures significantly increased compared to the control group.

Conclusions

There is level 2 evidence and level 3 evidence that dual task training may be effective in improving attention task performance in ABI populations compared to non-specific training.

KEY POINT

- Dual-task training has been shown to improve measures of attention to the extent that the population with ABI does not significantly differ from healthy controls; however, it is undetermined if the strength of these effects compared to non-dual-task training, are greater.

Technological Interventions

A surge in technology has allowed for the development of more computer-based intervention solutions designed to improve attention, concentration, and information processing. Current treatment modalities include computer cognitive training programs and virtual reality sessions. Virtual reality is discussed in further detail later on, where its effects on learning and memory are presented.

TABLE 6 | The Effect of Computer-Based Interventions of Reaction Time Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Dirette et al. (1999) USA RCT PEDro=4 N=30	**Population:** TBI: Mean age=38yr; Gender: male-22, female-8; Time since injury range=2-12 months. **Intervention:** Randomly assigned to remedial (without instruction, n=15) and compensatory strategy (verbalization, chunking and pacing) intervention (n=15) groups receiving a 45-minute session once a week for 4 weeks. **Outcome Measures:** Pre and Post-test on the Paced Auditory Serial Addition Task (PASAT).	1. Pre/post and weekly tasks significantly improved in both groups ($p<0.01$). 2. No significant improvement due to intervention ($p>0.05$).
Grealy et al. (1999) Scotland RCT PEDro=1 N=13	**Population:** TBI patients: Age Range: 19-64; Gender: male=8, female=5. **Intervention:** Crossover design: patients were allocated to 4-week interventions of receiving a single bout of Virtual reality (VR) exercise or a no-exercise control condition. **Outcome Measures:** Tests measuring attention, information processing, learning, memory, and reaction and movement times.	1. Intervention group (n=13) performed significantly better than control group (n=320) on digit symbol ($p<0.01$), verbal ($p>0.01$) and visual ($p<0.05$) learning tasks. 2. Reaction ($p<0.01$) and movement ($p<0.05$) times improved significantly after a single VR session.
Ruff et al. (1994) USA RCT PEDro=3 N=15	**Population:** Severe head injury; Mean Age=26.9yr; Time Post Injury≥6mo. **Intervention:** Participants were randomized to one of two treatment conditions: attention training followed by memory training (Group A; n=7) or vice versa (Group B; n=8). Training was provided from THINKable, a computer-based multi-media program. Training was terminated after either 20 hr (2hr/d) were completed, or 90% scores were achieved on the most advanced program. Patients were assessed before, during and after training. **Outcome Measures:** 2 + 7 Selective Attention Test, WAIS-R Digit Symbol, Continuous	1. Computer-based attention training resulted in significant improvements for attention ($p=0.003$). 2. Significant improvement in Memory II ($p=0.021$) but not Memory I or III. Gains were significant for Rey Verbal ($p=0.004$) and Corsi Block Learning ($p=0.03$) total correct as well. 3. Significant improvements in digital symbol scores ($p<0.001$) were noted as well, but no significant changes were found with CPT or 2+7 test scores.

	Performance Test (CPT); Rey Auditory Verbal Learning Test, Corsi Block Learning Test.	
Gray et al. (1992) UK RCT PEDro=5 N=31	**Population:** Close Head Injury=17; Others=14. *Experimental Group (n=17)*: Mean Age=26.18yr; Gender: Male=12, Female=5; Mean Time Post Injury=79wk. *Control Group (n=14)*: Mean Age=34.14yr; Gender: Male=10, Female=4; Mean Time Post Injury=84wk. **Intervention:** Participants in the experimental group received micro-computerized attentional training (1-1.5hr sessions for 3-9wk). The training covered reaction time training, rapid number comparison, digit symbol transfer, and divided attention tasks. The control group received recreational computing for a similar time period. **Outcome Measures:** Digit Span, Backward Digit Span, Paced Auditory Serial Addition task (PASAT), Information Processing Rate (IRP), Longest string, Wisconsin Card Sorting Test, Wechsler Adult Intelligence Scale-Revised (WAIS-R) Arithmetic.	1. At post-test assessment, the experimental group showed significant improvement on the WAIS-R picture completing (p=0.031) and the PASAT information processing rate (p=0.023). 2. At the 6 mo follow-up, differences between the groups indicated significant improvement on the Backward Digit Span (p=0.007), the WAIS-R Arithmetic (p=0.014), information processing rate and the PASAT (p=0.011), longest string (p=0.009), IPR (p=0.019). 3. For the experimental group, improvements from the intervention were found for IPR (p=0.004). 4. In general, course improvement was seen in the experimental group during the intervention phase and was continued into follow-up.
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=40.3yr; Gender: Male=12, Female=3. **Intervention:** Participants received the virtual reality (VR) intervention sessions (apartment and classroom) twice per week for a 4wk 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 Measures:** 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=51.3yr; Gender: Male=5, Female=2; Mean Time Post Injury=20.9yr; Etiology: TBI=5, CVA=2. *Control Group (n=7):* Mean Age=46.9yr; Gender: Male=7; Mean Time Post Injury=25.0yr. **Intervention:** Experimental group participants received BrainHQ, a commercially available online computerized cognitive exercise program (Attention, Brain Speed, Memory, People Skills, Intelligence, and Navigation) for 5	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 3mo prior to intervention with 1wk prior to intervention, there were no significant

	mo, 5d/wk. Control group participants did not have a private computer and received no intervention. **Outcome Measures:** 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.	differences within either group for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 3. There were no significant differences between groups at 1wk 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=61yr; Gender: Male=10, Female=2. **Intervention:** Participants received the computer-based cognitive retraining program, Parrot Software. The following eight modules were each completed in separate 1h 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 Measures:** 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=0.03) 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<0.01). 4. Age, education level, or type of ABI diagnosis did not have any significant effects on MoCA or medication-box scores.
Gerber et al. (2014) USA Pre-Post N=19	**Population:** TBI; Mean Age=50.4yr; Gender: Male=11, Female=8; Mean Time Post Injury=10yr; GCS=4-14; Severity: Severe=9, Moderate=1, Mild=7. **Intervention:** Participants completed a series of virtual reality tasks in a standardized order utilizing a hepatic stylus; 1) Participants were asked to clear a workbench and mount tools on an upright pegboard (TOOL), then 2) spell as	1. All the participants reported a high level of engagement during the interactions. 2. Thirty percent of participants reported a high level of frustration but were able to complete the tasks with short breaks. 3. From baseline to final, TOOL mean time decreased by 60s, TUSE mean time decreased by 68s, SAND mean time decreased by 72s and SPELL means increased by 2.7 words.

	many 3-letter words as possible from a set of letter tiles (SPELL), then 3) prepare a virtual peanut butter and jelly sandwich (SAND), and finally 4) hammer in two nails and tighten two screws through tool use (TUSE). TOOL, SAND and TUSE tasks had a time limit of 5 minutes while SPELL task had a time limit of 2 minutes. Participants had 3 chances to perform each task (Baseline, 2nd, Final). **Outcome Measures:** Self-reported measures (engagement and frustration), Boredom Propensity Scale (BPS), Purdue Pegboard Test (PPT), and Neurobehavioural Symptom Inventory (NSI).	4. PPT correlated with TOOL (p=0.016) and TUSE (p=0.014) time during the final trial. 5. SPELL correlated with the BPS (p=0.08) during the baseline and NSI (p=0.05) during the final trial.
Dvorkin et al. (2013) USA Pre-Post N=21	**Population:** TBI; Mean Age=37.8yr; Gender: Male=17, Female=4; Mean Time Post Injury=10.3wk. **Intervention:** Participants completed a virtual reality task and were instructed to hold the handle of a robot, moving the handle towards targets that appeared in the virtual environment. Patients reached to as many targets as they could within 4 minutes (1 block). Participants completed 6 blocks per day for 2 consecutive days. On each day, each pair of blocks included one haptic condition that affected the robotic handle and was either; 1) no haptic feedback (no force condition), 2) a break-through force, similar to popping a balloon (break-through condition) or 3) a gentle pulse of force (nudge condition). **Outcome Measures:** Tolerance, attention (pauses, pause duration), number of targets reached, and Agitated Behaviour Scale (ABS).	1. The interactive virtual environment was well tolerated by 18 of the 21 patients, 3 participants could not complete the 6 blocks in each visit due to fatigue or frustration. 2. In 15 participants ABS was reduced on the second visit. 3. Attention loss was reported before and during arm movements, however on the second visit patients exhibited significantly less pauses (p<0.0001) and shorter pause duration (p=0.007). 4. Patients were able to reach more targets on the second visit compared to the first visit (p<0.0001). 5. During the first visit, participants reached significantly less targets in the break-through and no force conditions compared to the nudge condition (p<0.02); the break-through and no force conditions were not significantly different. 6. During the second visit, participants reached significantly more targets in the nudge and no force conditions compared to the break-through condition (p<0.002); the nudge and no force conditions were not significantly different. 7. Break-through trials were significantly longer then the no force and nudge conditions on both the first and second day (p<0.0001). 8. Participants acquired more targets during the second visit compared to the first (p=0.0003) and acquired more targets with each block (p<0.0001).
Li et al. (2013) USA Pre-Post N=11	**Population:** ABI; Mean Age=49.45yr; Mean Time Post Injury=21.27yr. **Intervention:** All participants completed eight 60-min sessions using the attention and memory sub programs of the computer-based cognitive retraining Parrot Software. The participants focused on one of the eight subprograms during each session with each subprogram containing 10 lessons with	1. There was a significant improvement in attention cognitive assessment scores from pre to post intervention (mean change=2.091; p<0.005). 2. There was a significant improvement in memory cognitive assessment score from pre to post intervention (mean change=1.73; p<0.05).

	increasing difficulty. Assessments were conducted before and after intervention. **Outcome Measure:** The cognitive assessment (attention & memory).	
Zickefoose et al. (2013) USA Pre-Post N=4	**Population:** TBI; Mean Age=42.75yr; Gender: Male=4, Female=0; Mean Time Post Injury=17.5yr; Severity: Severe=4, Moderate=0. **Intervention:** Participants engaged in computer-based brain games over the course of two 1-month treatment phases. Participants received Attention Process Training-3 (APT-3) or Lumosity™ in phase 1, and then received the alternate treatment in phase 2. Both phases consisted of twenty 30-minute sessions. Outcomes were assessed at baseline and after each phase. **Outcome Measures:** Test of Everyday Attention (TEA); Neurological Assessment Battery (NAB)–Numbers and Letters Test Parts B, C, and D; Perceptual rating scale (PRS).	1. All four participants demonstrated significant progress in reaching new levels of difficulty on all tasks over the course of both treatments ($p<0.01$). 2. NAB analysis showed that one participant demonstrated significant improvement on one sub-test, while two participants demonstrated non-significant improvement on one or more sub-tests. Improvements occurred during phase 1, regardless of treatment. 3. TEA analysis showed that one participant demonstrated improvement on several sub-tests during both treatments, while the scores of the other three participants were inconsistent for either treatment. 4. On the PRS, two participants showed strong enjoyment and willingness to continue APT-3, while the other two participants showed an equally strong rejection of ATP-3. 5. On the PRS, all four participants showed strong enjoyment of Lumosity™, while only two participants showed a strong willingness to continue.
Chen et al. (1997) USA Case-Control N=40	**Population:** Age=18+years; Gender: male=27, female=13; Condition: TBI. **Intervention:** Divided retrospectively into computer-assisted rehabilitation (CACR) and tradition therapy groups **Outcome Measures:** Neurophysiological test scores (WAIS-R; WMS).	1. Both groups made significant post-treatment gains on the neurophysiological test scores ($p<0.05$), with the CACR group making significant gains on 15 measures ($p<0.05$) 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.
Malec et al. (1984) United States RCT Crossover PEDro=8 N=10	**Population:** Mean age=30yr; Gender: Male=8, Female=2; Mean time post injury=80dys. **Intervention:** Individuals played two types of first-person shooter video games, one with no interfering targets and one with them present. Individuals were randomly assigned to treatment order. Video game conditions were 1 week-long and included twice daily sessions of video game play. **Outcome Measures:** Stroop Test, Letter Cancellation task, Symbol Cancellation task, reaction time (RT).	1. No significant differences were found between conditions at any time points.

Discussion

An RCT by Dirette et al. (1999) found no significant differences in improvements between participants taught specific compensatory strategies and those that simply completed the computer tasks without

instruction of compensatory strategies. However, both groups significantly improved over time, with those that used the compensatory strategies (whether taught or spontaneously acquired) performing better than those that did not (Dirette et al., 1999). Similarly, 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 (Chen et al., 1997). Other studies with brand name computer-assisted cognitive rehabilitation have also shown limited effects. A small pre-post study examining the program Luminosity™ showed improvements in attention for a minority of participants; however, this improvement did not significantly differ from those who received Attention Process Training-III (Zickefoose et al., 2013). Parrot software showed mixed results with a pilot study reporting significant improvement in attention post-intervention (Li et al., 2013), but a subsequent study reported no significant changes on measures related to attention (Li et al., 2015). BrainHQ did not significantly improve attention outcomes over time or compared to no intervention (O'Neil-Pirozzi & Hsu, 2016). The lack of evidence supporting the efficacy of computer-based cognitive rehabilitation may be due to different programs and strategies used to train participants.

Repetition of tasks in virtual reality improved performance, both in terms of speed and accuracy (Dvorkin et al., 2013; Gerber et al., 2014). Gentle nudges corrected behaviour better than break-through or no feedback (Dvorkin et al., 2013). However, repetition of the Stroop test in different virtual reality environments showed limited improvement in performance on those specific tests (Dahdah et al., 2017). A virtual reality exercise program demonstrated significant benefits in reaction times but not attention after intervention; more high quality research is needed to confirm the efficacy of virtual reality exercise (Grealy et al., 1999).

Conclusions

There is level 2 evidence that neither general nor name brand computer-based rehabilitation intervention may improve attention outcomes compared to usual care in ABI populations.

There is level 4 evidence that attention performance can be improved in ABI populations through repetition of tasks, either through computer-based or virtual reality environments.

KEY POINTS

- Computer-based interventions are no more effective than no intervention in improving measures of attention and concentration post ABI.
- Repetitive virtual reality tasks which include repetition are effective in improving attention and concentration in ABI populations.

Attention Training Programs

With regard to cognitive rehabilitation, therapy is typically patient-directed and driven by both long- and short-term goals (Carswell et al., 2004). The ability to self-direct towards goals is emphasized as a component of brain injury community reintegration programs and is integral in the completion of instrumental activities of daily living. The execution of these goals relies on an individual having the ability to focus attention on a given task.

Cicerone et al. (2005) recommended strategy training for persons with TBI for improving deficits of attention. It should be noted, however, that there was insufficient evidence to distinguish the effectiveness of specific attention training during acute stage rehabilitation from improvements made from spontaneous recovery or from more general cognitive interventions (Cicerone et al., 2005).

TABLE 7 | The Effect of Attention Training Programs on Attention and Concentration Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Gocheva et al. (2018) Switzerland RCT Crossover PEDro=7 N=19	**Population:** Non-traumatic etiology (N=13), traumatic etiology (N=9). **Intervention:** All participants received both conditions in randomized order, each condition consisted of 12 sessions. The experimental condition consisted of speech, occupational or physical therapy sessions accompanied by a therapeutic animal, while the control condition consisted of the same rehabilitation interventions and did not include a therapeutic animal. All conditions were completed within 6 weeks. **Outcome Measures:** Attention span, alertness, instances of distraction, and concentration (all outcomes were measured through behavioral analysis).	1. Attention span did not differ significantly between experimental and control sessions. 2. When in the animal therapy sessions individuals displayed significantly more instances of distraction compared to control sessions ($p=0.001$). Physiotherapy sessions were significantly more effected by distractions when animals were present ($p=0.016$). Further analysis demonstrated that those with higher initial FIM scores had significantly decreased instances of distraction in animal therapy sessions ($p=0.003$). 3. During animal therapy sessions self-assessed alertness was significantly higher ($p<0.001$). There was also a significant main effect of therapy, with higher alertness in speech therapy sessions overall ($p=0.012$). Alertness was also significantly higher in the animal therapy session when individuals had higher initial FIM scores, than those that did not in animal sessions ($p<0.001$). Individuals had significantly higher rates of self-reported concentration during animal therapy sessions ($p=0.014$). Concentration was also seen to be significantly higher in speech therapy sessions regardless of animal presence ($p=0.027$), with therapy type overall having a significant effect ($p<0.001$), but no significant interaction effect. Individuals with higher initial FIM scores demonstrated higher concentration

		scores in sessions when animals were present compared to those who had lower initial FIM scores (p<0.001).
Dundon et al. (2015) Ireland RCT PEDro=3 N=26	**Population:** TBI; Mean Age=38.96yr; Gender: Male=19, Female=7. **Intervention:** Participants were assessed during a dichotic listening task (DLT) presented at 6 levels of distraction difficulty, and randomly received either adaptive training (AT, n=9), non-adaptive training (NAT, n=8), or no training (NT, n=9) between sessions (Study 2). Outcomes were assessed before and after training. **Outcome Measures:** DLT performance; Test of Everyday Attention (TEA).	1. For the DLT, there was a significant main effect of group (F=3.99, p=0.035), such that the AT group showed poorer performance than the NAT group (p=0.019) and the NT group (p=0.031). 2. For the DLT, there was a significant interaction between group and time (F=4.38, p=0.026), such that improved performance was seen in the AT (p=0.036) and NAT (p=0.0025) groups over time, but not in the NT group (p=0.34). 3. On the TEA, there was a significant main effect of group (F=2.45, p=0.13), such that the NT group showed better performance than the AT group (p<0.001) and the NAT group (p=0.036). 4. On the TEA, there was a significant main effect of time (p=0.022), such that performance improved in all groups.
Cantor et al. (2014) USA RCT PEDro=7 N=98	**Population:** TBI; Mean Age=45.3yr; Gender: Male=37, Female=61; Mean Time Post Injury=12.6yr; 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, 45min) and an individual problem-solving session of attention training (1 session, 60min) per day (3 days/wk for 12 weeks). Group sizes were generally 4-6 participants. **Outcome Measures:** 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), and Frontal System Behavioural Scale (FrSBe).	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 FrSBe scale (p=0.049) and the PSI (p=0.016). 4. There were no other significant treatment effects. Variance of depression, age, severity and time since injury did not change treatment effects.
McHugh and Wood (2013) Ireland RCT PEDro=5 N=24	**Population:** TBI. *Mindfulness Group (N=12)*: Mean Age=28.45yr; Mean Time Post Injury=785.5d; Mean GCS=8.5. *Control group (N=12)*: Mean Age=30.5yr; Mean Time Post Injury=664.7d; Mean GCS=7.42. **Intervention:** Patients were randomly assigned to the control group or mindfulness group (focused attention). The mindfulness group received instructions (mindfulness induction) prior to completing experimental tasks. Participants then completed a memory load task (remembering the location of symbols) and an over-selectivity task and test.	1. There was a significant decrease in stimulus over-selectivity after the mindfulness training compared to the control group (p<0.05, t (22) =1.74).

	Outcome Measures: Minimal Attention Awareness Scale (MAAS), Trail making test A and B (test of visual attention and task switching) and the Wechsler Test of Adult Intelligence.	
Chen et al. (2011) USA RCT PEDro=5 N=12	**Population:** TBI=9, Other=3: Mean Age=48yr; Gender: Male=5, Female=7; Time Post-Injury Range=6mo-6yr. **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-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.	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=0.02). 11/12 participants improved in the goals training group while 4/12 improved in the education group (p=0.009). 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=0.07).
Novakovic-Agopian et al. (2011) USA RCT Crossover PEDro=5 N=16	**Population:** TBI=11, Stroke=3, Other=2: Mean Age=50.4yr; Gender: Male=7, Female=9; Time Post Injury Range=1-23yr. **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 5wk, participants were switched to the other intervention. All participants were assessed at baseline, Week 5 and again at Week 10. **Outcome Measures:** 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>0.05). 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=0.01); learning (*Mean*=0.51 vs 0.08, p=0.02); and delayed recall (*Mean* 0.39 vs -0.27, p=0.01). 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=0.01); sustained attention (0.44 vs 0.27, p=0.01); memory (0.609 vs -0.10, p=0.02); learning (0.66 vs 0.08, p=0.05); and delayed recall (0.55 vs -0.27, p=0.02). 4. 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<0.04) and working memory (p<0.02).
McMillan et al. (2002) UK RCT PEDro=5 N=130	**Population:** TBI*; Attentional Control Training (ACT; n=44):* Mean Age=34.6yr; Gender: Male=35, Female=9; Median GCS=9. *Physical Exercise (PE) Group (n=38)*: Mean Age=31.4yr; Gender: Male=30, Female=8; Median GCS=10. *Control Group (n=48)*: Mean Age=36.2yr; Gender: Male=36, Female=12; Median GCS=9 **Intervention:** Patients were assigned to 1 of 3 groups. The ACT group received supervised practice (5, 45min session over 4wk) and were given an ACT audiotape to practice daily with. The PE group had the same amount of therapist contact, but the audiotape was based on physical training. The control group had no therapist contact. Assessments were done pre- and post-training, and 6 and 12mo. **Outcome Measures:** Test of Everyday Attention, Adult Memory and Information Processing Battery, Paced Auditory Serial Addition Test, Trail Making Test, Sunderland Memory Questionnaire, Cognitive Failures Questionnaire.	1. Results showed no significant differences in outcome measures among the 3 training groups at any of the assessment points. 2. The exception to the above finding was the results of the Cognitive Failure Questionnaire where patients in both treatment groups (ACT and PE) had significantly greater reduction in self-reported cognitive failures compared to the control group at 12 mo follow-up (p<0.05).
Amos (2002) Australia RCT PEDro=4 N=32	**Population:** TBI=16, CVA=6, Other=2, Healthy Controls=8. *Experimental Group (n=24)*: Mean Age=35.71yr; Gender: Male=17, Female=7; Mean Time Post Injury=5.96yr. *Control Group (n=8)*: Mean Age=31.25yr; Gender: Male=2, Female=6. **Intervention:** Patients with ABI were randomized into three treatment groups: unaided (n=8), external inhibition (n=8), and increased stimulus salience (n=8). All treatment groups were compared to the non-ABI controls (n=8). **Outcome Measures:** Wisconsin Card Sorting Test (WCST).	1. There were no significant differences in total errors between groups (p=0.138), but groups differed significantly in total number of trials (p=0.025), perseveration (p=0.033) and categories achieved (p=0.001). 2. The unaided ABI group compared to the aided ABI group (inhibition and salience) had significantly more trials (p<0.001), preservative errors (p<0.006) and lower categories score (p<0.001). 3. Comparisons between the inhibition and salience aid group revealed significance difference only for perseverative errors (p<0.045); the external inhibition group displayed much less.
Levine et al. (2000) Canada UK RCT PEDro=4 N=30	**Population:** TBI: *Goal Management Training (GMT) Group* (n=15): Mean Age=29.0yr; Gender: Male=5, Female=10; Mean GCS=10.7; Mean Time Post Injury=3.7yr. *Motor Skill Training (MST) Group* (n=15): Mean Age=30.8yr; Gender: Male=9, Female=6; Mean GCS=10.8; Mean Time Post Injury=3.8yr. **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-	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<0.05). 2. The MST group also had significantly more errors during the everyday paper and pencil tasks (p<0.01). 3. The GMT group significantly reduced their errors from pre-post training during the everyday paper and pencil tasks (p<0.01). 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<0.05).

	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 Measures:** Goal Neglect (Everyday paper and pencil tasks), Stroop Interference Procedure, Trail Making A and B, Wechsler Adult Intelligence Scale Revised (WAIS-R).	Neuropsychological Tasks 1. The GMT group was generally slower on timed neuropsychological tests: Stroop Interference Procedure, Trail Making Part A and B ($p<0.05$ and $p<0.06$, respectively). 2. No significant differences between groups for the WAIS-R ($p>0.05$).
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=33.1yr; Mean Time Post Injury=7.5yr; *Control Group (n=7)*: Mean Age=38.1yr; Mean Time Post Injury=1.6yr. **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 24hr over 10wk and the control group received 10hr over 10wk. All subjects worked directly with a therapist and assessed pre and post intervention. **Outcome Measures:** 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, $p<0.05$). 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 ($p<0.05$). 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 ($p<0.05$).
Fasotti et al. (2000) Netherlands RCT PEDro=5 N=22	**Population:** TBI; *Experimental Group (n=12)*: Mean Age=26.1yr; Gender: Male=8, Female=4; Mean Time Post Injury=9.8mo. *Control group (n=10)*: Mean Age=30.1yr; Gender: Male=7, Female=3; Mean Time Post Injury=8.3mo. **Intervention:** Patients in the experimental group received Time Pressure Management (TPM) training (1hr, 2-3x/wk, 2-3wk). TPM training used videotaped short stories. The program was designed to increase awareness of errors and deficits, encourage the acceptance and acquisition of the TPM strategy, and emphasize strategy application and maintenance. The control group received concentration training (30min, 2-5hr/wk, 3-4hr). Mean training was 7.4hr and 6.9hr for the TPM and control groups, respectively. Patients were assessed 2wk prior to training, post-training, and at 6mo follow-up. **Outcome Measures:** Waterbed (WB) and Harvard Graphics (HG) tasks, Rey's 15-word test, Rivermead Behavioural Memory Test, Auditory Concentration Test, Paced Auditory Serial Addition Task, Visual Choice Reaction	1. Training improved performances in both HG and WB tasks, but differences were not significant relative to control. 2. Scores on 2 of 3 standardized memory variables and all 3 attention variables increased significantly in the TPM group ($p<0.05$), whereas no memory variables and 1 of 3 attention variables increased significantly for the control group. 3. Follow-up (6 mo) data for 10 from the TPM group and 9 from the control group indicated that there was a significant time effect ($p<0.05$) but no significant group time interaction ($p=0.23$); this suggests that there still was a significant improvement after 6 mo but that this improvement could not be attributed specifically to the treatment or control training.

	Time Task.	
Niemann et al. (Niemann et al., 1990) (1990) United States RCT PEDro=7 N=29	**Population:** *Attention Group (N=13)*: Mean age=28.9yr; Mean time post-injury=41mo. *Memory Group (N=13):* Mean age=34.3yr; Mean time post-injury=37.1mo. **Intervention:** Individuals were randomly assigned to either an attention training program or a memory training program. Both programs lasted 9 weeks and had two 2-hour sessions each week. **Outcomes:** Attention Test d2, Paced Auditory Serial-Addition Task (PASAT), Divided Attention test (DAT), Trail Making Test-B (TMT-B), Rey Auditory Verbal Learning Test (RAVLT), Block Span Learning Test (BSLT), Ruff 2 & 7 Test, Logical Memory Subtest (Wechsler Memory Scale) (WMS-LM), Ruff-Light Trail Learning Test (RLTLT).	1. There were no significant within-group differences on the Test d2, PASAT, DAT, RAVLTBSLT, Ruff 2 & 7 Tests, WMS-LM, or the RLTLT. 2. Significant within group differences were seen on the TMT-B for both the attentional ($p<0.01$), and memory ($p<0.01$) groups. 3. The attention group improved significantly more on the TMT-B compared to the memory group ($p=0.05$). 4. The attention group improved significantly more than the memory group on the Attention Test d2 ($p=0.02$). 5. No other significant differences were found.
Lesniak et al. (2019) Poland PCT N= 15	**Population:** TBI; Mean Age= 26.2±7.6yr; Gender: Male=11, Female=4; Mean time post injury= 11.6±6.6mo; Severity: Severe=10, Moderate=5. **Intervention:** Cognitive rehabilitation therapy program focused on memory and attention. The individual therapy program was cognitive training conducted with computer software (RehaCom) and supervised by a psychologist. Group sessions were run by a neuropsychologist and focused on internal memory strategies and external aids. Participants had 15 group session (45 min, 5d/wk) and 15 individual therapy sessions (45min, 5 d/wk). Assessments were conducted at baseline (3wk prior to start), pretreatment, posttreatment and at 4mo follow-up. **Outcome Measures:** Cambridge Neuropsychological Test Automated Battery (CANTAB), Pattern Recognition Memory Test, Rey's Auditory Verbal Learning Test (RAVLT), Spatial Span Test (SSP), Paced Auditory Serial Addition Test (PASAT), Rapid Visual Information Processing, European Brain Injury Questionnaire (EBIQ).	1. From baseline to preintervention only the PASAT changed significantly ($p=0.047$). 2. From baseline to post-intervention there were no significant changes in short-term verbal memory (RAVLT; $p=0.242$), short-term visual memory (PRM; $p=0.172$) or visuospatial working memory (SSP; $p=0.24$). 3. From baseline to post-intervention RVP attention test ($p=0.002$) and PASAT ($p=0.005$) showed significant improvement. 4. Pre to Post intervention significant improvements were found for PRM ($p=0.022$), RVP ($p=0.002$) and PASAT ($p=0.012$). 5. Post-intervention, patients reported less everyday cognitive problem than at baseline (EBIQ). No significant differences were found between post-intervention and follow-up.
Bosco et al. (2018) Italy Pre-post N=19	**Population:** *Severe TBI:* Mean age=38.5yr; Gender: Male=16, Female=3; Mean time post-injury=99.4 months; GCS<8. **Intervention:** Groups of 5-6 participants met twice a week for 12 weeks for a total of 24 Cognitive Pragmatic Treatment (CPT) sessions. Participants were assessed at four time points, 3-months pretreatment, immediately before treatment, immediately following treatment, and 3-months post-treatment. **Outcome Measures:** Assessment Battery for	1. There was a significant difference in scores on the ABaCO between pretreatment and posttreatment scores ($p<0.001$). There were no significant differences between the two initial time points or the two posttreatment timepoints. 2. Similar results were seen for the CADL, with individuals showing a significant improvement in their functional communication skills following treatment ($p=0.024$).

	Communication (ABaCo), Communications Activities of Daily Living (CADL), Aachener Aphasie test, Attentional Matrices, Trail Making test, Verbal Span, Corsi's Block-Tapping test, immediate and deferred recall test, Tower of London test, Modified Card Sorting test, Raven Colored Progressive Matrices, Sally & Ann, Strange Stories.	3. Between immediate pretreatment scores and immediate posttreatment scores significant differences were only seen on the Verbal Span ($p=0.045$), and the Modified Card Sorting test ($p=0.004$).
Hellgren et al. (2015) Sweden Case Series N=48	**Population:** Cerebral infarction=23%, TBI=21%, Infection=19%, Intracerebral hemorrhage=13%, Subarachnoid hemorrhage=10%, Brain tumor=8%, Other=6%; Mean Age=43.7yr; Gender: Male=30, Female=18; Mean Time Post Injury=51.2mo. **Intervention:** Participants received a working memory training program (Cogmed) consisting of various visuospatial and verbal working memory tasks. There were 4-5 sessions/wk for 5-7wk, consisting of 45-60min of intense exercise with one break. Occupational therapist coaches were present during every session and provided weekly feedback in addition to continuous feedback from the computer program. **Outcome Measures:** Paced Auditory Serial Attention Test (PASAT 2.4), Forward and backward block repetition, Listening Span Task, Canadian Occupational Performance Measure (COPM performance and satisfaction), EuroQol descriptive (EQ-5D Index), EuroQol visual analogue scale (EQ-VAS), Working Memory Index (WM Index).	1. At 20wk post-training, there were significant improvements in PASAT ($p<0.001$), Listening Span ($p<0.001$), Forward block repetition ($p<0.001$), Backward block repetition ($p<0.001$), COPM performance ($p<0.001$), COPM satisfaction ($p<0.001$), EQ-5D index ($p=0.009$), and EQ-VAS ($p<0.001$) compared to baseline. 2. Compared to baseline, all participants significantly improved their WM Index at 20wk follow-up ($p<0.001$). 1. No significant differences in treatment effect were found for all outcomes in terms of sex or time post-injury, except for ≤18 mo since injury exhibiting more improvement than >18mo in terms of WM index difference ($p<0.05$), COPM performance improvement ($p<0.05$), and COPM satisfaction improvement ($p<0.05$).
Serino et al. (2007) Italy Case Series N=9	**Population:** TBI: Age range=16-57 yr; Gender: male=6, female=3; Time since injury=6-78 months. **Intervention:** A long sequence of numbers is presented, and patients were asked to add each new number to the number preceding it and say the sum out loud. Two additional tests (the Months tasks and the Word tasks) were also administered in a similar way. The GST and the WMT were each 4 sessions/week, for 4 weeks. To vary tasks and their level of difficulty, in the interstimulus interval was varied. **Outcome Measures:** Working memory training (WMT); Paced Auditory Serial Addition Test (PASAT); Months task	1. Study results indicate the greatest improvement in performance occurred from the intermediate to the final sessions ($p<0.0005$) after the WMT. 2. Improvement from the initial to intermediate sessions did not show any significant improvement in working memory ($p<0.46$) after GST. 3. Working memory ($p<0.05$), divided attention ($p<0.05$), executive function ($p<0.05$), and long-term memory ($p<0.05$) for subjects were significantly improved in the final session compared to the intermediate session. 2. The same was not noted on the speed processing and sustained attention tasks ($p>0.05$). Working memory training tasks were also found to improve scores on various psychosocial outcomes.
Boman et al. (2004) Sweden Pre-Post N=10	**Population:** TBI: Mean age=47.5yr; Gender: male=5, female=5; Time Post injury=9-40 months. **Intervention:** Each participated in an individual	1. For the following: sustained attention, selective attention and alternating attention significant changes ($p<0.05$, $P<0.05$, $p<0.01$ respectively) were noted in the scores of the APT test and

	cognitive training session for 1 hr/3x a week for 3 weeks at home or work. The program included attention process training (APT), generalization for training and teaching of compensatory strategies for self-selected cognitive problems. Identification of cognitive problems in everyday life was also part of the compensatory strategy. **Outcome Measures:** Digit Span Test; Claeson-Dahl test; Rivermead Behavioural Memory test (RBMT); Assessment of Motor and Process Skills; European Brain Injury Questionnaire.	Digit Span task between the pre to post training session and the 3 mo follow up. 2. Score increases ($p<0.05$) on the RMBT were found at the 3 mo follow up compared to the RMBT scores at the pretest. 3. When looking at changes in the RBMT score pre to post training, changes were not found. 4. No significant changes were found (pre to post and pre to 3 mo follow up) when looking at the scores on the Claeson-Dahl Memory
Park et al. (1999) Canada Case-Control N=46	**Population:** TBI=23; Age matched controls=23. **Intervention:** Attention process training program of 20 two-hour sessions for a total of 40 hr. **Outcome Measures:** Paced Auditory Serial Addition Task (PASAT); Consonant Trigrams; Beck Depression Inventory (BDI).	1. No statistically significant improvements on the BDI from pre- to post-treatment for the TBI group. 2. TBI ($p<0.01$) and control ($p<0.001$) groups improved significantly in PASAT before/after tests. 3. Performance declined with increases in delay ($p<0.001$), and study position ($p<0.001$) on the Consonant trigrams.

Discussion

Many studies examined the effects of goal training or cognitive training (Boman et al., 2004; Chen et al., 2011{Novakovic-Agopian, 2011 #26; Laatsch et al., 1999; Novakovic-Agopian et al., 2011; Sohlberg et al., 2000). Levine et al. (2000) completed an RCT comparing patients using goal management training strategies to a control group exposed to 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. Novakovic-Agonian et al. (2011), found similar results in an RCT crossover where participants were assigned to received goal-training followed by education or the reverse. The goal training first group saw a significant improvement in sustained attention compared to the education-first group, additionally the goal training first group maintained their gains over 10 weeks.

A more recent RCT (Dundon et al., 2015) examined the effect of adaptive training on dichotic listening tasks and attention, interestingly the adaptive training group had significantly higher scores on the listening task compared to non-adaptive training group; however, the non-adaptive training group surpassed the adaptive training group in Test of Everyday Attention (TEA) scores. Overall, both groups significantly improved on measures of attention as a result of time (Dundon et al., 2015).

Park et al. (1999) examined whether Attention Processing Training (APT) had a beneficial effect on attention measures (PASAT, Consonant Trigrams) in a group with severe TBI (tested pre and post training approximately 7 months apart). They compared their results to a convenience sample of controls, given the same measures one week apart without training. Results suggested that the APT did not have a significantly beneficial effect as performance improved on all measures across both groups (indicating practice effects and possibly spontaneous recovery). A pre-post study (Boman et al., 2004) found that

cognitive training for three weeks significantly improved attention task scores compared to pre-test scores. Similarly, Lesniak et al. (2019) found that a three-week comprehensive cognitive training program significantly improved attention, when compared to a three-week waiting list control condition. One study did demonstrate that cognitive training (although beneficial) may not be more beneficial than other interventions such as educational training with respect to processing speed (Chen et al., 2011). In this study both groups significantly improved in attention directed goal completion.

Another study comparing the effects of attentional training to physical exercise found that there was no significant difference between groups post-intervention, but there was a within subjects effect such that both groups reported significantly less cognitive failures (McMillan et al., 2002). Attention process training, was also shown to have greater results in attention remediation compared to education alone (Sohlberg et al., 2000). One study examined the effects of a memory training program on attention and reported positive results; Hellgren et al. (2015) found that a memory training program was successful in improving attentional scores on the Paced-Auditory Serial Attention Test, as well as further enhancing memory in general which is discussed later in this chapter.

In a study directly comparing the effects of an attention training program with that of a memory training program, the authors found that the results were split, with individuals performing better on some measures of attention (Attention Test 2d) but not others (PASAT) (Neiman et al., 1990). The last study to use an attention training program sought to see if the presence of a therapy animal could enhance the effects of training (Gocheva et al., 2018). Both the animal therapy and non-animal therapy groups produced significant improvement on measures of attention and concentration; however, the animal therapy group had a significantly larger increase in concentration (Gocheva et al., 2018).

Emotional regulation was also examined as a potential intervention for the remediation of attention post ABI (Cantor et al., 2014). However, this treatment was not seen to be effective in the recovery of attention, other significant effects on executive functioning from this study are discussed further in section 6.4.1.1. Another study which focused specifically on mindfulness (McHugh & Wood, 2013) found that mindful focused training significantly improved participants' ability to correctly select stimuli compared to controls.

Fasotti et al. (2000) assessed the effectiveness of time pressure management (TPM) training compared to concentration training in patients with slowed processing speed as a result of traumatic brain injury. Though both groups showed improvements on information intake task performance, no significant differences between groups were observed even though specific time pressure management strategies were learned by the experimental group (Fasotti et al., 2000). "Cognitive pragmatic treatment' has been found to significantly improve scores on the card sorting task; however, the specific details of this program were not stated (Bosco et al., 2018).

The inconsistencies between studies may be due to a lack of standardized goal management training or attention process training protocols. The lack of a consensus on the definition of certain cognitive

processes appears to be reflected in the interventions used to attempt to rehabilitate these deficits. Unfortunately, this decreases the ability to compare studies on a more specific level; however, general conclusions can still be made that specific training programs which intend to increase attentional capacity are effective, to what extent they are more beneficial than other training programs needs to be addressed in the future through comparative methodologies. Only one study (Serino et al., 2007) described the specific task that was successful in improving attention. This cognitive task involved mental addition in combination with two other standardized tasks and was an effective strategy for improving attention.

Conclusions

There is level 2 evidence that adaptive training is no more effective than non-adaptive training in remediating attention in ABI populations.

There is level 1b evidence that emotional regulation therapy is not effective in treating attentional disorders compared to waitlist controls in ABI populations.

There is level 1b evidence that the addition of a therapy animal to attention training programs may enhance gains in concentration in those with an ABI.

There is level 2 evidence that mindfulness training compared to no intervention may improve an individual's ability to correctly reject inappropriate stimuli post ABI.

There is level 2 evidence to suggest goal management training, when compared to education, may be effective at improving attention in individuals post ABI.

There is level 2 evidence that goal management training is more effective in remediating task completion times than motor skill training, however it is not more effective in treating attention deficits, in individuals post ABI.

There is conflicting (level 2) evidence that attentional control or processing training may not significantly improve attention in post ABI individuals compared to control training.

There is level 4 evidence that summation tasks may be effective at improving attention in individuals post ABI.

There is level 4 evidence that a working memory training program may remediate attention in individuals post ABI.

There is level 4 evidence that cognitive rehabilitation therapy may not be effective for improving attention post ABI.

KEY POINTS

- Goal management training is effective in assisting those who sustain an ABI in learning to manage life goals through improved attention.
- In general, a variety of non-specific attentional training programs appear to be effective for improving attentional scores following an ABI.
- The addition of a therapy animal to an attentional training program may enhance concentration gains.
- Therapies which focus on emotional regulation do not appear to be effective at improving attention post ABI, while mindfulness may improve some areas.

Brain Stimulation Techniques

Transcranial Direct Current Stimulation (tDCS) is a technique that painlessly delivers electrical currents to specific regions of the brain. These electrical currents modulate neuronal activity through electrodes placed over the head at different regions. Two recent studies have examined the effects of tDCS on attention post ABI.

TABLE 8 | The Effect of Transcranial Direct Current Stimulation on Attention Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
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.

Author Year Country Study Design Sample Size	Methods	Outcome
Lee & Kim (2018) South Korea RCT PEDro=7 N=13	**Population:** *Experimental Group (N=7):* Mean age=42.42yr; Gender: Male=5, Female=2; Mean time post-injury=3.85 months; Mean GCS=13.71. *Control Group (N=6):* Mean age=41.33yr; Gender: Male=4, Female=2; Mean time post-injury=3.88 months; Mean GCS=13.66. **Intervention:** Individuals received either rTMS or sham rTMS for 30mins 5 times a week, for 2 weeks. **Outcomes:** Montgomery-Asberg Depression Rating Scale (MADRS), Trail Making Test (TMT), Stroop Color Word Test (SCWT).	1. The experimental group experienced significant within group differences on the MADRS ($p<0.05$), TMT ($p<0.05$), and SCWT ($p<0.05$). 2. No significant within group differences were seen for the control group. Following intervention, the experimental group had significantly lower scores on the MADRS ($p<0.05$), TMT ($p<0.05$), and SCWT ($p<0.05$). *Lower scores indicate improved performance on TMT and SCWT.
Sacco et al. (2016) Italy RCT PEDro=4 N=32	**Population:** TBI. Mean Time Post Injury=8.73yr; Severity: Severe=32, Moderate=0, Mild=0. *Treatment Group (TG, n=16):* Mean Age=37.7; Gender: Male=12, Female=4. *Control Group (CG, n=16):* Mean Age=35.2; Gender: Male=14, Female=2. **Intervention:** Participants were randomized to receive transcranial direct current stimulation (tDCS, TG) or sham tDCS (CG) with computer-assisted training (2/d, 5d). Outcomes were assessed at baseline (T0), before treatment (T1), after treatment (T2), and 1-month follow-up (T3). **Outcome Measures:** Test for the Examination of Attention, Divided Attention subtest (DA); Repeatable Battery for the Assessment of Neurological Status (RBANS).	1. For DA, the TG performed significantly better at T2 compared to T0 and T1, with faster reaction times ($p=0.004$) and fewer omission errors ($p<0.0001$). 2. For DA, the CG did not perform better at T2 compared to T0 and T1. 3. For DA, there was a significant interaction between time (T0/T1 vs T2) and group (TG vs CG), for both reaction time ($p=0.05$) and omission errors ($p=0.03$). 4. On RBANS, the TG showed a non-significant improvement in performance on attention task ($p=0.057$), but no improvement on visual-spatial abilities, semantic fluency, working memory, and long-term memory.
Carneiro et al., (2019) Brazil Pre-Post $N_{Initial}=10$, $N_{Final}=10$	**Population:** TBI=10; Mean Age=37.8±10.2yr; Gender: Male=9, Female=1; Time Post Injury Range=4mo-4yr; Severity: Mild=0, Moderate=0, Severe=10. **Intervention:** Participants received 30 min of transcranial photobiomodulation therapy (PBMT) 3 times per wk for 6wk, for a total of 18 sessions and 540min of irradiation. Outcome measures were assessed at baseline, 1wk following PBMT, and 3mo following PBMT. **Outcome Measures:** Cerebral Blood Flow (CBF), Beck Depression Inventory II (BDI-II), Beck Anxiety Inventory (BAI), Stroop Test- Version Victoria, Trail Making Test-Forms A and B (TMT A and TMTB), Symbol Digit Test, Rey Figure Test, Rey Auditory Verbal Learning Test (RAVLT), Verbal Fluency.	1. No significant differences were observed across all neuropsychological outcomes and time points with PBMT. However, CBF increased, with a significant improvement in left peak systolic velocity ($p=0.007$).

Discussion

Three RCTs and one pre-post study have examined brain stimulation techniques to improve attention following an ABI (Carneiro et al., 2019; Lee & Kim, 2018; Neville et al., 2019; Sacco et al., 2016). Only Sacco et al. 2016 examined the effects of transcranial direct current stimulation (tDCS), on attention in a population post ABI. The authors found that the addition of transcranial direct current stimulation to

computer-assisted training was superior to sham stimulation for improving divided attention. However, more high-level studies are needed in order to fully examine the potential benefits of adding tDCS to traditional attentional therapies.

Two studies examined the effects of repetitive transcranial magnetic stimulation (rTMS) on attention, with conflicting results. While Lee & Kim (2018) found significant positive effects on attention and depression when compared to sham controls, Neville et al. (2019) found that rTMS had no significant positive effects on attention. In light of this, further research is necessary to determine the efficacy of rTMS for attention remediation following ABI.

One pre-post study examined the effects of transcranial photo biomodulation therapy (PBMT) on attention following TBI. Carneiro et al. (2019) observed an improvement in cerebral blood flow; although, no significant improvements were observed on any neuropsychological outcomes, including attention. As only a single pre-post study evaluated the effects of PBMT on attention, further research is necessary to determine the efficacy of this intervention.

Conclusions

There is level 2 evidence that transcranial direct current stimulation when combined with an attention training program (compared to sham stimulation) may improve divided attention in individuals post ABI.

There is conflicting level 1b evidence that repeated transcranial magnetic stimulation compared to sham stimulation may not improve attention following an ABI.

There is level 4 evidence that transcranial photo biomodulation therapy may not improve attention following an ABI.

KEY POINTS

- **Transcranial direct current stimulation may be effective in remediating attentional deficits when combined with computer assisted training in ABI populations.**
- **Repeated magnetic transcranial stimulation may not be effective in remediating attentional deficits following an ABI.**

Pharmacological Interventions

Donepezil

Donepezil, an acetylcholinesterase inhibitor, was originally developed for improving cognitive function and memory in people with Alzheimer's disease (Cacabelos, 2007), by delaying cognitive impairment in (Takeda et al., 2006). Since evidence suggests that cholinergic dysfunction may contribute to persistent cognitive deficits for people after traumatic brain injury, improvements in attention, memory, and other aspects of cognition related to the acetylcholine system are expected when cholinergic function is reduced (Arciniegas, 2003).

TABLE 9 | The Effect of Donepezil on Memory and Cognitive Functioning Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Zhang et al. (2004) USA RCT PEDro=7 N=18	**Population:** TBI; *Group A (n=9)*: Mean Age=33yr; Gender: Male=6, Female=3; Mean GCS=9.3; Mean Time Post Injury=4.6mo; *Group B (n=9)*: Mean Age=31yr; Gender: Male=7, Female=2; Mean GCS=8.9; Mean Time Post Injury=3.9. **Intervention:** In a randomized crossover trial, Group A received oral donepezil for the first 10wk, followed by a washout period of 4wk, then followed by 10wk of placebo. Group B received the treatments in the opposite order. Donepezil was administered at 5mg/d for the first 2wk, and at 10mg/d for the remaining 8wk. **Outcome Measures:** Auditory (AII) and Visual (VII) subtests of Wechsler Memory Scale-III, and the Paced Auditory Serial Addition Test (PASAT).	1. At week 10, Group A achieved significantly better scores in AII (95.4±4.5 versus 73.6±4.5; p=0.002), VII (93.5±3.0 versus 64.9±3.0; p<0.001), and in the PASAT (p≤0.001) compared to Group B. 2. This increase in scores in Group A were sustained after washout and placebo treatment (week 24), leading to no significant differences in AII (105.9±4.5 versus 102.4±4.5; p=0.588), VII (91.3±3.0 versus 94.9±3.0; p=0.397), and PASAT (p>0.1) compared to Group B at study end. Within-group comparisons showed that patients in both Group A and Group B improved significantly in AII and VII (p<0.05), as well as in PASAT (p<0.001), after receiving donepezil.
Campbell et al. (2018) United States PCT N=129	**Population:** *Donepezil Group (N=55):* Mean Age=34.4yr; Gender: Male=80%, Female=20%; Mean time post injury=28.6d; Injury Severity=Moderate-severe. *Control Group (N=74)*: Mean Age=40.8yr; Gender: Male=71.6%, Female=28.4%; Mean time post injury=25.2d; Injury Severity=Moderate-severe. **Intervention:** Individuals were assigned to receive either donepezil or a placebo treatment for an average of 67.5 days. Those receiving donepezil started with a dosage of 5mg/day, increasing to 10mg/day over the course of 7-10 days. Follow-up assessments took place approximately 61.4 days after treatment. **Outcome Measures:** Trail Making Tests (Part A and B), Digit Span index (DS), California Verbal Learning Test-II (CVLT-II), Logical Memory II (LMII), Functional Independence Measure (FIM), Disability Rating Scale (DRS).	1. For both parts of the Trail Making Test (Part A and B), there was a significant effect of time (p<0.001, p<0.001) respectively. Demonstrating that both groups significantly improved over time. No other significant effects were found for the Trail Making Test. 2. Likewise, in the DS, only a significant effect of time (p<0.001) was observed. 3. For both the learning and memory components of the CVLT-II there was only a significant effect of time observed (p<0.001, p<0.001). 4. The LMII showed similar results with only a significant effect of time observed (p=0.005). 5. For measures of disability, both the DRS and the FIM also only showed a significant effect of time for both groups respectively (p<0.001, p<0.001). 6. Overall, there were no significant effects of treatment found, however both groups did

Author Year Country Study Design Sample Size	Methods	Outcome
		demonstrate significant spontaneous recovery.
Khateb et al. (2005) Switzerland Pre-Post $N_{initial}$=15, N_{final}=10	**Population:** TBI; Mean age=43yr; Gender: Male=8, Female=7; Mean Time Post Injury=42mo. **Intervention:** Patients were administered donepezil 5 mg/day for 1mo, followed by 10 mg/day for 2mos. **Outcome Measures:** Stroop test, Trail Making Test (TMT), Rey Auditory Verbal Memory Test (RAVMT) and Test for Attentional Performance (TAP).	1. 4 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, the comparison of the global score of all questionnaires before and after therapy was marginally significant (p=0.058). 3. 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=0.03); for learning and memory the RAVMT-learning (47.7±6.9 to 53.5±5.0, p=0.05); and for attention, the errors subsection of divided attention (5.8±3.3 to 2.9±2.7, p=0.03).

Discussion

In an RCT, Zhang et al. (2004) demonstrated that donepezil was associated with significantly more improvement in tasks of sustained attention compared to placebo. These improvements were sustained even after the washout period. Once both groups had completed donepezil treatment there were no significant differences between groups on any measures of attention. Khateb et al. (2005) found that individuals performed significantly better on measures of divided attention after donepezil treatment; however, 4 of 15 participants stopped treatment due to negative side-effects. In contrast to the positive effects found by these studies, one prospective controlled trial found no significant effects of donepezil on any measures of cognition, including attention (Campbell et al., 2018). In both the Campbell et al. (2018) and Zhang et al. (2004) studies, individuals received donepezil for approximately the same duration.

Conclusions

There is conflicting level 1b (positive) and level 2 (negative) evidence that donepezil may improve attention compared to placebo post ABI.

KEY POINT

- It is unclear as to whether donepezil may improve attention in individuals with moderate to severe ABI.

Methylphenidate

Methylphenidate is a central nervous stimulant (CNS) which inhibits the reuptake of dopamine and norepinephrine, resulting in increased dopaminergic activity. In healthy individuals, methylphenidate has been found to improve memory but not other cognitive functions such as attention, mood, or executive function (Repantis et al., 2010). Methylphenidate is extensively used as a treatment for attention deficit disorder, as well as narcolepsy (Glenn, 1998). No serious side effects have been observed in clinical trials, though there is a lack of evidence for long term safety (Godfrey, 2009).

TABLE 10 | The Effect of Methylphenidate on Attention, Concentration and Processing Speed Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Jenkins et al., (2019) UK RCT Crossover PEDro=9 $N_{Initial}$=46, N_{Final}=40	**Population:** TBI=40; *Treatment Group (Intervention First; n=20):* Mean Age= 40±12yr; Gender: Male=18, 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.	1. No significant differences (p>0.05) were observed between groups on several measures: • TMT • 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).

Author Year Country Study Design Sample Size	Methods	Outcome
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. **Intervention:** 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 9mo 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.
Zhang and 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. **Intervention:** 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).
Willmott et al. (2013) Australia RCT PEDro=10 N=32	Population: TBI; Gender: Male=21, Female=11; Mean Time Post Injury=68 d; *TBI Val/Val Group (n=11)*: Mean Age=22.64 yr; Mean GCS=4.67; *TBI Val/Met Group (n=14)*: Mean Age=28.57 yr; Mean GCS=5.38; *TBI Met/Met Group (n=7)*: Mean Age=30.57 yr; Mean GCS=6.83. **Intervention:** Participants with TBI, in a crossover design, received 0.3 mg/kg methylphenidate (2 ×/d) for 6 sessions in total (spanning 2 wk), alternating between treatment and placebo for every other session. Results were compared against	1. At baseline, there were no significant differences across various genotypes on attentional performance. 2. Participants with TBI and Met/Met alleles performed significantly poorer on the SDMT (p<0.0005), 2 & 7 ASRS (p=0.001), 2 & 7 CSRS (p<0.0005), DC RT (p=0.005), and SI RT (p=0.002), when compared to controls. Analyses with participants with TBI and Val/Val alleles showed even worse

Author Year Country Study Design Sample Size	Methods	Outcome
	those from healthy controls (n=40). Groups were stratified by the presence of the Val158Met gene. **Outcome Measures:** Ruff 2 & 7 Selective Attention Test – automatic (2 & 7 ASRS) and controlled (2 & 7 CSRS), Selective Attention Task, Four Choice Reaction Time Task (4CRT) – dissimilar compatible (DC) and similar incompatible (SI), Symbol Digit Modalities Test (SDMT), Letter Number Sequencing Task, Wechsler Test of Adult Reading.	outcomes, demonstrating poorer performance on 7/8 outcome measures. 3. Following methylphenidate treatment one significant drug and genotype interaction was seen between Met/Met carriers and performance on the SDMT (F=4.257; p=0.024), suggesting Met/Met carriers were more responsive to methylphenidate than either of the others.
Kim et al. (2012) USA RCT PEDro=7 N=23	**Population:** Moderate/Severe TBI; Mean Age=34.2 yr; Gender: Male=18, Female=5; Mean Time Post Injury=51.1 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 0.3 mg/kg methylphenidate followed by placebo, or the reverse and were assessed after each. **Outcome Measures:** Visual sustained attention task (VSAT), Two-back task.	**1.** Relative to placebo, both accuracy (1.62±1.03 versus 2.23±1.07; p<0.005) and mean reaction time (827.47±291.17s versus 752.03±356.87s; p<0.050) in the VSAT were improved significantly on MPH. **2.** Relative to placebo, mean reaction time (929.31±192.92s versus 835.02±136.12s; p<0.050), but not accuracy, in the two-back task was improved significantly when on MPH.
Willmott & Ponsford (2009) RCT PEDro=10 N=40	**Population:** TBI; Mean Age=26.93 yr; Gender: Male=28, Female=12; Time since injury=68.38 d. **Intervention:** Patients received either methylphenidate (0.3 mg/kg 2 x/d, rounded to the nearest 2.5 mg) or a placebo. Patients were seen for 6 sessions across 2-week period. Patients then crossed-over. **Outcome Measures:** Ruff 2 and 7 Selective Attention Test, Selective Attention Task, Four Choice Reaction Time Task, Sustained Attention to Response Task, Symbol Digit Modalities Test, Letter Number Sequencing Task, Wechsler Test of Adult Reading.	1. Methylphendiate significantly increased speed of information processing on the Symbol Digit Modalities Test (p=0.020); Ruff 2 and 7 Test-Automatic Condition (p=0.003); Simple Selective Attention Task (p=0.001); Dissimilar compatible (p=0.003), and Similar Compatible (p=0.002).
Kim et al. (2006) Korea RCT PEDro=6 N=18	**Population:** TBI; *Methylphenidate Group (n=9)*: Mean Age=30.1 yr; Gender: Male=9, Female=0; Mean Time Post Injury=1.6 yr; *Placebo Group (n=9)*: Mean Age=38.3 yr; Gender: Male=7, Female=2; Mean Time Post Injury=3.6 yr. **Intervention:** Patients were randomly allocated to receive either 20 mg methylphenidate or the placebo. Assessments were done at baseline (T1), 2 hr post treatment (T2), and 2 d later (T3). **Outcome Measures:** Visual sustained attention task (VSAT), Two-back task.	**1.** At T1 there were no significant differences in mean reaction time or in accuracy between the two groups. **2.** For those in the treatment group, the mean reaction time of the two-back task improved significantly compared to those in the placebo group from T1 to T2 (13.74±13.22% versus 4.02±9.48%; p<0.05). **3.** No significant difference in improvement as seen with accuracy of the two-back task (p=0.07), nor with the VSAT.
Whyte et al. (2004) USA RCT PEDro=8 N=34	**Population:** TBI; Mean Age=37 yr; Gender: Male=29, Female=5; GCS<12; Median Time Post Injury=3.2 yr. **Intervention:** Participants received 0.3 mg/kg/dose methylphenidate for 3 wk, 2×/d, and placebo for 3 wk, for a total of 6 wk, with conditions alternating weekly. Washout lasted a day, after which time the groups crossed over. **Outcome Measures:** Attention Tasks.	1. Methylphenidate showed significant improvements in information processing speed (p<0.001), work task attentiveness (p=0.010), and caregiver attention ratings (p=0.010), pre-post. 2. No treatment-related improvements were observed in susceptibility to distraction and divided or sustained attention.

Author Year Country Study Design Sample Size	Methods	Outcome
Plenger et al. (1996) USA RCT PEDro=5 N=23	**Population:** TBI; Gender: Male=17, Female=6; *Placebo Group (n=13)*: Mean Age=26.6 yr; Mean GCS=8.1; *Methylphenidate Group (n=10)*: Mean Age=31.4 yr; Mean GCS=9.3. **Intervention:** Patients were randomly allocated to receive either methylphenidate or placebo. Methylphenidate was administered at 30 mg/kg, 2×/d, for 30 d. **Outcome Measures:** Disability Rating Scale (DRS), Continuous Performance Test (CPT), 2 & 7 Test (2 & 7), Paced Auditory Serial Addition Test (PASAT), Digit Span & Attention/ Concentration from Wechsler Memory Scale-Revised (Attn/Conc from WMS-R).	**1.** At 30 d follow-up (n=15), significant differences were obtained on DRS, suggesting better outcome for the methylphenidate group. This difference however was not seen at 90 d follow-up (n=11). **2.** Significant differences were found on the attention-concentration domain at the 30 d follow-up, as indicated by CPT, PASAT, 2 & 7, and Attn/Conc from WMS-R (p<0.030). The treatment group performed better in these measures compared to the placebo group.
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 1 wk of placebo, or receive the treatment in the 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, Katz Adjustment Scale.	1. No significant differences were found between methylphenidate and placebo condition in any of the outcome measures studied.
Gualtieri & Evans (1988) United States RCT Crossover PEDro=7 N=15	**Population:** Mean age=24.1yr; Gender: Male=10, Female=5; Mean time post-injury=46.8mo. **Intervention:** Participants were assigned to receive three conditions in randomized order. 1) Placebo; 2) Methylphenidate (0.15mg/kg) twice daily; 3) Methylphenidate (0.30mg/kg) twice daily. Each condition was 12 days long, with 2 days washout between conditions. **Outcome Measures:** Adult Activity Scale self-administered (AAS-S), Adult Activity Scale (administrator)(AAS-O), Examiner's Rating Scale (EXRS), Self Rating Scale (SRS), Verbal Fluency Test (VFT), Non-verbal Fluency test (NVFT).	1. There was a significant improvement in AAS-S and AAS-O scores between the placebo and high-dose conditions (p<0.05). 2. There was a significant difference in SRS scores between the placebo group and the high-dose condition (p<0.05). 3. On the EXRS there was a significant difference between baseline and low-dose (p=0.012), placebo and low-dose (p=0.025), baseline and high-dose (p=0.012), with higher doses of methylphenidate having improved effects. 4. There was a significant improvement in VFT scores between baseline and the high-dose groups (p=0.017). 5. There was a significant difference on NVFT scores between baseline and placebo (p=0.008), baseline and low-dose (p=0.008), baseline and high-dose (p=0.008), and the placebo and high-dose group (p=0.018), with methylphenidate improving scores.
Whyte et al. 1997 United States RCT Crossover PEDro=7 N=19	**Population:** Mean age=30.7yr; Gender: Male=15, Female=4; Mean GCS=5.83. **Intervention:** Individuals were randomly assigned to either receive methylphenidate first or placebo, and then the reverse. Methylphenidate was given twice a day at a dose of 0.25mg/kg.	1. There was a significant drug x performance interaction (p<0.001), where performance was differentially impacted by the drug on each assessment. 2. Group stratification revealed that methylphenidate was more effective for

Author Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measures: Sustained arousal task, phasic arousal task, distraction task, choice reaction-time task, behavioral inattention.	improving performance on attentional measures for younger participant than older ones ($p<0.05$). 3. There were no other significant effects.
Pavlovskaysa et al. (2007) Pre-Post Israel N=6	**Population:** TBI; Age Range=18-47 yr; Gender: Male=4, Female=2; GCS ≥8. **Intervention:** Participants were administered 5 to 10 mg of methylphenidate (MHP) over a 2-week period. Participants were evaluated before, during and after the administration of methylphenidate. **Outcome Measures**: Performance on the Visual Spatial Attention Task Analyzing Rightward and Leftward Shifts of Attention.	1. Prior to treatment, patients were found to have great difficulty in shifting attention between hemifields. 2. There was a significant improvement in the asymmetry with MHP ($p<0.001$). 3. The right-side performance was significantly better on average than the left side (0.77 versus 0.59; $p<0.050$). 4. Performance was significantly better for ipsilateral valid cueing ($p<0.010$) than for invalid cross-trials ($p<0.001$). 5. The difference between ipsi- and cross-cueing for left side target performance is significant for each of the stages ($p<0.001$).

Discussion

The majority of studies evaluating the efficacy of methylphenidate have been RCTs. In an RCT, Whyte et al. (2004) indicated that speed of processing, attentiveness during individual work tasks and caregiver ratings of attention were all significantly improved with methylphenidate treatment. No treatment related improvement was seen in divided or sustained attention, or in susceptibility to distraction. Similarly, Plenger et al. (1996) and Pavlovskaysa (2007) found that methylphenidate significantly improved attention and concentration, and visuo-spatial attention, respectively. More recently, Kim et al. (2012) found that reaction time improved significantly while on the methylphenidate. This is in line with Willmott and Ponsford (2009) who found that administering methylphenidate to a group of patients during inpatient rehabilitation significantly improved the speed of information processing. A variety of studies with different dosing regimens and durations have found positive effects of methylphenidate (Gualtieri & Evans, 1988; Whyte et al., 1997; Zhang et al., 2004).

Speech et al. (1993) conducted a double blind placebo controlled trial evaluating the effects of methylphenidate following closed head injury. In contrast to the results noted by Whyte et al. (2004) and Plenger et al. (1996), methylphenidate did not demonstrate significant differences compared to placebo on measures of attention, information processing speed, or learning. Kim et al. (2006) examined the effects of a single-dose treatment of methylphenidate and, although a trend was found in favour of improved working and visuospatial memory for the treatment group, these results did not reach statistical significance. Conflicting results continue to be reported, as two high-quality RCTs reached different conclusions regarding methylphenidate use. While Dymowski et al. (2017) noted no

improvements on any measures of attention and mental processing, Zhang et al. (2017) noted improvements in reaction time, arithmetic tests, and even mental health outcomes after intervention by methylphenidate.

A potential explanation for these conflicting results is proposed by Willmott et al. (2013). The authors hypothesized that an individuals' response to methylphenidate depends on their genotype. More specifically, that individuals possessing the methionine (Met) allele at the catechol-O-methyltransferase (COMT) gene would confer greater response to methylphenidate compared to those with the valine (Val) allele. While both Met/Met and Val/Val carriers performed more poorly in various attentional tasks compared to healthy controls, Met/Met carriers did show greater improvements in strategic control in attention than Val/Val carriers. As well, the authors were able to identify one significant drug and genetic interaction between Met/Met carriers and performance on the Symbol Digit Modalities Test (SDMT). These findings suggest Met/Met carriers may in fact be more responsive to methylphenidate than individuals with the Val genotype.

Jenkins et al. (2019) offer another possible explanation for these conflicting results, suggesting that the variability in treatment effect may be due to variability in dopaminergic damage between individuals. As such, the authors stratified their participants by dopaminergic damage, comparing those with low dopamine transporters to those with normal levels of dopamine transporters. Interestingly, it was found that only individuals with low dopamine transporter levels, demonstrated improvements in attention with methylphenidate. Although further studies are necessary to draw firm conclusions, this study provides insight into tailoring cognitive treatments to the individual.

Conclusions

There is conflicting level 1a evidence regarding the effectiveness of methylphenidate following brain injury for the improvement of attention and concentration in individuals post ABI.

There is level 1a evidence that methylphenidate improves reaction time of working memory compared to placebo in individuals post ABI.

There is level 1b evidence that individuals carrying the Met allele may be more responsive to methylphenidate than those without the Met allele when it comes to the ABI population.

KEY POINT

- **The effectiveness of methylphenidate treatment to improve cognitive function following brain injury is unclear.**
- **Methylphenidate may be effective in improving reaction time for working memory.**
- **Response to methylphenidate may depend on the presence of the Met genotype and/or dopamine transporter levels.**

Bromocriptine

Bromocriptine is a dopaminergic agonist which exerts its effects primarily through the binding of D_2 receptors (Whyte et al., 2008). It has been suggested that dopamine is an important neurotransmitter for prefrontal function (McDowell et al., 1998). 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 reflected in motor abilities. Two studies have been identified investigating the use of bromocriptine as an adequate treatment for the recovery of cognitive impairments following brain injury.

TABLE 11 | The Effect of Bromocriptine on Attention Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Whyte et al. (2008) USA RCT PEDro=7 N=12	**Population**: Moderate/ Severe TBI; Mean Age=35.75 yr; Gender: Male=8, Female=4; Median Time Post Injury=3.3 yr. **Intervention:** In a crossover design, participants were randomly assigned to receive bromocriptine (1.25 mg 2×/d titrated to 5mg 2×/d over a 1 wk), followed by placebo or the reverse order. Each lasted 4 wk with a 1 wk washout period. **Outcome Measures:** Attention Tasks.	1. Though some improvements were observed in certain subtests of attentional tasks (e.g. speed decline, decline in responding, test of everyday attention), they were not significant. 2. Overall results suggest bromocriptine had little effect on attention.
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=27d-300 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 2.5 mg bromocriptine followed by placebo, or the reverse order. **Outcome Measures:** 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), 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=0.05), COWAT (p=0.02), 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).

Discussion

The question of whether bromocriptine improves cognitive function in patients with ABI was explored in two RCTs (McDowell et al., 1998; Whyte et al., 2008). In an earlier investigation, 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. However, a later study by Whyte et al. (2008) found that bromocriptine had little effect on attention and it was noted that several participants did experience moderate to severe drug effects and withdrew or were withdrawn from the study.

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 Whyte et al. (2008). 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. Results from Whyte et al. (2008) noted that the placebo group demonstrated better (although not significant) trends in improvement on the various tasks administered.

Conclusions

There is conflicting evidence as to whether bromocriptine improves performance on attention tasks compared to placebo in patients post TBI.

KEY POINT

- **Bromocriptine does not appear to improve attention in those with an ABI.**

Cerebrolysin

Cerebrolysin has been demonstrated to have neuroprotective and neurotrophic effects and has been linked to increased cognitive performance in an elderly population. As explained by Alvarez et al. (2003), "*Cerebrolysin (*EBEWE Pharma, Unterach, Austria*) is a peptide preparation obtained by standardized enzymatic breakdown of purified brain proteins, and comprises 25% low-molecular weight peptides and free amino acids"* (pg. 272).

TABLE 12 | The Effect of Cerebrolysin on Attention Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Alvarez et al. (2003) Spain Pre-Post N=20	**Population:** TBI; Mean Age=30.1 yr; Gender: Male=15, Female=5; Mean GCS=6.1; Time Post Injury Range=23-1107 d. **Intervention:** Patients with TBI received a total of 20 intravenous infusions of cerebrolysin solution (30 mL/infusion) over 4 wk. Assessments were made at	1. Compared to baseline, patients with TBI showed a significant decrease in slow bioelectrical activity frequencies (delta: p<0.010; theta: p<0.050), and a significant increase in fast frequencies (beta: p<0.010)

Author Year Country Study Design Sample Size	Methods	Outcome
	baseline, during treatment, and after the 4 wk treatment period. **Outcome Measures:** Syndrome Kurztest (SKT), Electroencephalogram (EEG)/brain mapping recordings, Glasgow Outcome Scale (GOS).	after receiving cerebrolysin, suggesting improvement in brain bioelectrical activity. 2. Significant improvements in SKT performance was noted from pre to post treatment (15.9±2.4 versus 12.0±2.1; p<0.010). 3. GOS scores significantly improved from pre to post treatment (3.7±0.3 versus 3.95±0.3; p<0.050).

Discussion

In an open-label trial of 20 patients with TBI Alvarez et al. (2003) found that cerebrolysin was associated with improved brain bioelectrical activity, as evidenced by a significant increase in fast beta frequencies. A brief neuropsychological battery (Syndrome Kurztest) consisting of nine subtests was administered to evaluate memory and attentional functions in patients undergoing treatment with cerebrolysin. There was an overall significant improvement in performance post treatment, suggesting patients experienced cognitive benefits from cerebrolysin treatment. Improvements in the Glasgow Outcome Scale were also observed (Alvarez et al., 2003). Together these findings suggest that cerebroylsin may represent an effective neuroprotective therapy with tangible cognitive benefits for individuals living with an ABI. However, controlled trials are necessary to further explore the efficacy of this drug.

Conclusions

There is level 4 evidence that cerebrolysin may improve attention scores post ABI.

KEY POINT

- **Cerebrolysin may be beneficial for improving clinical outcomes and cognitive functioning following brain injury; however, controlled trials are needed to further evaluate its efficacy**

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 impairments; however, it is also implicated in attentional processing.

TABLE 13 | The Effect of Rivastigmine on Attention and Processing Speed Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Tenovuo et al. (2009) Finland RCT PEDro=10 N=102	**Population:** Mean age=45.5yr; Gender: Males=61, Female=39; Mean time post-injury=8yr; Mean GCS=11. **Intervention:** Individuals were randomized to receive one of two dosing rivastigmine schedules (placebo then rivastigmine or rivastigmine then placebo). Treatment lasted 8 weeks once a max dose of 12mg per day was reached. **Outcome Measures:** Computer-based reaction time (CRT), subtraction test, vigilance test (0-5mins, 5-10mins, 10-15mins, correct responses), Symptom Checklist-90 (SC), Diener satisfaction of life scale, Finnish Traumatic Brain Injury Questionnaire (FITBIQ).	1. The percentage of right answers in the subtraction tests were significantly different between groups ($p<0.05$), with the 2. Vigilance scores were significantly higher during periods of rivastigmine treatment compared to placebo treatments ($p<0.05$). 3. There were no other significant differences between groups on any other measures.
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 Measures:** 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. 40% 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. Further sub-analysis controlling for order effects demonstrated no significant differences between groups.
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 Measures:** 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.

Discussion

Three studies have concluded that rivastigmine most likely does not improve attention following an acquired brain injury (Silver et al., 2006; Silver et al., 2009; Tenovuo et al., 2009). In Silver's (2009) follow-up open-label cohort study to their original RCT (Silver et al., 2006), participants (n=98) showed significant improvement on the CANTAB RVIP A', the HVLT and the trail A and B scales at the end of 38 week study period; however, after further sub-analysis controlling for order effects no significant differences were found between groups. The third study by Tenovuo et al. (2009) found that rivastigmine

significantly improved vigilance following doses of 12mg/day for eight weeks. Tenovuo et al. (2009) on average had higher doses and longer duration of rivastigmine administration compared to both Silver et al. studies; however, it is unclear whether this resulted in their conflicting results. The route of rivastigmine administration (injection versus oral administration) did not appear to influence its efficacy.

Conclusions

There is level 1b evidence that Rivastigmine compared to placebo is not effective for improving concentration or processing speed in post ABI individuals but may increase vigilance.

KEY POINT

- **Rivastigmine may not be effective in treating attention deficits post ABI.**

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).

TABLE 14 | Amantadine for the Treatment of Attentional Disorders Following an ABI.

Author Year Country Study Design Sample Size	Methods	Outcome
Hammond et al. (2018) United States RCT PEDro= 9 N=119	**Population:** Mean age=38.6yr; Mean time post-injury=6.2yr; Injury severity: GCS<13. **Intervention:** Individuals were allocated to receive either the placebo or 100mg amantadine twice a day for 60 days. Assessments were completed at baseline, day 28, and day 60. **Outcome Measures:** Digit-span from Wechsler Memory Scale-III (DS), Trail Making Test (TMT), Controlled Oral Word Association Test (COWAT), Learning/Memory Index (LMI), Attention/Processing Speed Index (APSI), overall composite (GCI).	1. No significant differences were seen on the DS, TMT, COWAT, or the APSI between groups at any time point. 2. The treatment group had significantly lower LMI scores at day 28 compared to the control group (p=0.001), this effect was not present at 60-day follow-up. 3. The treatment group had significantly lower scores on the GCI compared to the control group at day 28 (p=0.002), this effect was not present at day 60 follow-up.

Discussion

Presently, only one study has examined the effects of amantadine on attention and processing speed and found no significant effects on attention or processing speed following treatment. Any results which were found to be significant on other cognitive measures were not maintained at the 60-day follow-up (Hammond et al., 2018). Further studies are needed to examine whether or not amantadine may be a viable treatment for attention and processing speed deficits following an ABI.

Conclusions

There is level 1b evidence that amantadine is not effective for improving attention compared to placebo following an ABI.

KEY POINT

- **Amantadine may not be effective in treating attention deficits following an 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 15 | The Effect of Hyperbaric Oxygen on Attention and Processing Speed 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 ($p<0.0001$).

Author Year Country Study Design Sample Size	Methods	Outcome
		6. Visual spatial processing significantly improved following HBOT treatment (p=0.005). 7. Motor skills significantly improved following HBOT treatment (p<0.0001).

Discussion

From this single case series, hyperbaric oxygen therapy significantly improved both attention and processing speed following treatment five days a week (Hadanny et al., 2018). Also, general improvements in cognitive functioning and visual processing were also reported (Hadanny et al., 2018). However, without proper prospective experimental data it is challenging to make conclusions on the efficacy of this intervention.

Conclusions

There is level 4 evidence that hyperbaric oxygen therapy may improve both attention and processing speed following an ABI.

KEY POINT

- **Hyperbaric oxygen therapy may improve attention and processing speed following an ABI; however, more prospective data is required.**

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 16 | The Effect of Dextroamphetamine on Attention and Engagement Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Hart et al. (2018)	**Population:** *DEX Group (N=17)*: Mean age=39.6yr; Gender: Male=11, Female=6; Mean GCS=8.2; Mean	1. There was a significant difference between groups on the ABS (p=0.04), with the DEX

Author Year Country Study Design Sample Size	Methods	Outcome
United States RCT PEDro=10 N=32	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).	group demonstrating more agitation over time. 2. No other significant differences were found.

Discussion

Based on a single study, it does not appear that dextroamphetamine has any beneficial effects on attention or processing speed following an ABI. However, administration of dextroamphetamine did significantly increase agitation over time.

Conclusions

There is level 1b evidence that dextroamphetamine does not improve attention following an ABI.

KEY POINT

- **Dextroamphetamine may not be an effective treatment for attentional deficits following an ABI and may actually increase agitation.**

CONCLUSION

The rehabilitation of attention, concentration and information processing speed is complicated by the lack of consensus on the definition of attention.

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. Over the past several

years, Cicerone et al. (2000; 2005; 2011) reviewed a series of studies investigating the effectiveness of attentional retraining interventions during rehabilitation following traumatic brain injury and stroke. Not all patients respond equally to all intervention strategies and only a limited number of studies in the current review indicated whether severity of injury was related to the efficacy of a given intervention.

Technology has increased the availability of external aids, although some seem more feasible to use than others (e.g., cell phones or hand-held recorders). Unfortunately, the studies reviewed did not specify the length of time subjects required to master compensatory strategies or the nature of the long-term effects. Generally, if these electronic appliances are used before the injury, they are more likely to be used post-injury as well. It was unclear from the studies if any of the participants had previous knowledge of these tools.

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