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

MOTOR AND SENSORY IMPAIRMENT REHABILITATION POST ACQUIRED BRAIN INJURY

Ali Bateman MD FRCPC, Heather MacKenzie MD FRCPC, Cecilia Flores-Sandoval PhD, Amber Harnett MSc, Shawn Marshall MD FRCPC, Robert Teasell MD FRCPC

Disclaimer

This review has been prepared based on the scientific and professional information available up to May 2022. The ERABI information is provided for informational and educational purposes only. If you have or suspect you have a health problem, you should consult your health care provider. The ERABI contributors shall not be liable for any damages, claims, liabilities, costs, or obligations arising from the use or misuse of this material.

Copyright

Funding

This work is funded by the Ontario Ministry of Health. All work produced by ERABI is editorially independent from its funding source.

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) *Motor and Sensory Impairment Rehabilitation 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

TABLE OF CONTENTS

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.

E. Ali Bateman, MD, FRCPC is a consultant physiatrist at Parkwood Institute in London, Ontario, where she is the medical director of the Acquired Brain Injury Rehabilitation Program; she is an assistant professor in the Department of Physical Medicine & Rehabilitation at Western University. She completed her undergraduate training at McGill University, medical school and residency at Western University, and a Master's degree in quality improvement and patient safety at the University of Toronto.

Heather MacKenzie, MD, FRCPC is a consultant physiatrist in the spinal cord injury and brain injury rehabilitation programs at Parkwood Institute in London, Ontario, and an assistant professor in the Department of Physical Medicine & Rehabilitation at Western University. Her research focuses on the development of prognostic models and predicting outcomes after mild traumatic brain injury and concussion. Most recently, she completed a Master of Science degree in Epidemiology at the Harvard T. H. Chan School of Public Health.

Cecilia Flores-Sandoval, PhD, is the research coordinator of the Evidence-Based Review of Acquired Brain Injury (ERABI). She completed a master's degree and a PhD in Health and Rehabilitation Sciences, field of Health and Aging. Her research interests include aging and rehabilitation, patient engagement and transitional care for older adults.

Amber Harnett, MSc, RN, CNF scholar, completed her MSc in pathology at Western University and 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.

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.

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 • Amytrophic 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 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).

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–May 2022 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 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, 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 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 in which it should be provided, based on their patient. 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 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
	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 test	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.

MOTOR AND SENSORY IMPAIRMENT

REHABILITATION POST AQUIRED BRAIN INJURY

Summary of the Evidence

Intervention	Key Point Level of Evidence
MOTOR IMPAIRMENT	
Upper Extremity Interventions	
Constraint Induced Movement Therapy	Constraint induced movement therapy may improve the amount and quality of use of the more affected upper limb post ABI. - *There is level 4 evidence (Shaw et al., 2005; Page & Levine, 2003) that constraint induced movement therapy (CIMT) or modified CIMT may improve upper extremity function in individuals post ABI.*
Fine Motor Coordination Training	Functional retraining activities may be superior to tabletop fine motor control activities for improving fine motor coordination post ABI. Training in finger sequencing tasks, gesture recognition biofeedback and visual feedback may improve fine motor function post ABI. Visual feedback-based grip force training may enhance accuracy and transfer tasks post ABI. - *There is level 2 evidence (Neistadt, 1994) that functional retraining activities may be more effective than tabletop fine motor control retraining activities for improving fine motor function in the dominant hand in individuals with ABI.* - *There is level 2 evidence (Korman et al., 2018) that finger sequencing training may increase performance speed in individuals with ABI; however, error rates may not improve.* - *There is level 2 evidence (Kriz et al., 1995) that gesture recognition biofeedback may improve fine motor function in individuals with ABI, compared to standard repetitive training without feedback.* - *There is level 4 evidence (Yungher & Craelius, 2012) that visual feedback-based grip force training may improve tracking accuracy and transfer tasks in individuals post ABI.*
Virtual Reality for Upper Extremity Rehabilitation	Virtual reality interventions may be an effective intervention for the recovery of upper extremity function post ABI. - *There is level 2 evidence (Mumford et al., 2012; Sietsema et al., 1993) that virtual reality training may improve hand dexterity, as well as reaching performance in the upper extremities of individuals with TBI.*
Lower Extremity Interventions	
Aquatic Treadmill Walking	Waist to chest-depth water may facilitate gait kinematics in individuals with a TBI during aquatic treadmill walking; neck-depth water may not be ideal for gait training. - *There is level 4 evidence (Narasaki-Jara et al., 2020) that walking in neck-depth water may limit hip and ankle joint kinematics in individuals with TBI.*

Body Weight Supported Gait Training	Partial body weight supported gait training may not improve ambulation, mobility, or balance when compared to conventional gait training post ABI. - *There is level 1b evidence (Wilson et al., 2006) that physical therapy with partial weight-bearing gait training may not improve ambulation, mobility, or balance compared to standard physical therapy in individuals with TBI.* - *There is level 2 evidence (Brown et al., 2005) that body weight supported treadmill training may not improve ambulation or mobility compared to conventional gait training in individuals with TBI.* Robotic assisted treadmill training may be similar to manually assisted treadmill training at improving gait speed and mobility post ABI. - *There is level 2 evidence (Esquenazi et al., 2013) that robotic assisted body weight supported treadmill training may not improve ambulation or gait velocity compared to manually assisted treadmill training in individuals post ABI.* Dynamic body weight support gait training may improve motor function in individuals with TBI when compared to standard rehabilitation. - *There is level 2 evidence (Anggelis et al., 2019) that dynamic body weight support gait training may improve motor function in individuals with TBI when compared to standard rehabilitation.* Body-weight-support treadmill with handrail support may reduce movement instability compared to other methods of training in individuals post ABI. - *There is level 2 evidence (Clark et al., 2012) that body-weight-supported treadmill training combined with handrail support may reduce movement instability compared to other methods of training in individuals post ABI.* Intensive mobility training consisting of body-weight-supported treadmill, balance activities, strength coordination, and range of motion training may improve lower extremity motor function post ABI; however, more research is needed. - *There is level 4 evidence (Peters et al., 2014) that Intensive Mobility Training may improve ambulation and mobility in individuals post ABI.*
Multimodal Interventions	Sit-to-stand training and Intensive Mobility Training may improve lower extremity motor function post ABI. - *There is level 1b evidence (Canning et al., 2003) that sit-to-stand training combined with usual rehabilitation may improve motor performance in sit-to-stand tasks compared to usual rehabilitation alone in individuals post ABI.* Electrical muscle stimulation with passive exercise may improve lower extremity muscle atrophy post ABI. - *There is level 2 evidence (Hirose et al., 2013) that electrical muscle stimulation with passive exercise may reduce lower extremity muscle atrophy compared to passive exercise alone in individuals post ABI.*

	Motor rehabilitation may improve high-level mobility and ankle joint mechanisms during running in individuals with severe TBI. - *There is level 2 evidence (Williams et al., 2019) that motor rehabilitation may improve high-level mobility and ankle joint mechanisms during running in individuals with severe TBI.*
Virtual Reality for Lower Extremity Rehabilitation	Virtual reality based therapy using a Nintendo Wii, or an Xbox system may not be more effective for the rehabilitation of lower extremity function and balance, when compared to standard physiotherapy or home exercise. - *There is level 1b evidence (Cuthbert et al., 2014) that virtual reality-based therapy using a Nintendo Wii system may not be more effective for the rehabilitation of lower extremity function post TBI than standard physical therapy.* - *There is level 2 evidence (Tefertiller et al., 2019) that virtual reality using an Xbox system may noy be more effective for the rehabilitation of balance post TBI than traditional home-based exercise.* - *There is level 2 evidence (Straudi et al., 2017) that video game therapy with the Xbox Kinect system may improve balance in individuals with TBI.* - *There is level 4 evidence (Foo et al., 2013) that visual feedback using a Wii balance board may reduce weight-bearing asymmetry in the lower extremities post ABI.* Virtual reality combined with a robotic device may facilitate lower limb functional recovery post severe ABI. - *There is level 2 evidence (Fusco et al., 2022) that semi-immersive virtual reality combined with a robotic device may facilitate lower limb functional recovery in individuals with severe ABI.*
Combined Upper and Lower Extremity Interventions	
Virtual Reality for Upper and Lower Extremity Rehabilitation	Virtual reality therapy may improve balance, gait and reaching in individuals post ABI; however, it may not be more effective than conventional physiotherapy programs. - *There is level 2 evidence (Schafer & Ustinova, 2013) that reaching activities performed in a virtual environment may lead to improvements in reaching in a physical environment in individuals with TBI.* - *There is level 4 evidence (Ustinova et al., 2014) that virtual reality therapy may improve whole-body balance, gait, and functional reaching in individuals post TBI.*
Yoga	Yoga may be effective for the rehabilitation of motor impairment in individuals with TBI; however, more research is needed. - *There is level 4 (Schmidt et al., 2016) that yoga may improve balance, pain, cervical range of motion and gait speed in individuals with TBI. However, more research is needed.*
Exercise Programs	There is conflicting evidence about whether exercise programs, home-based or administered in the community, may improve motor function, balance, and cardiovascular parameters post ABI. Further research is needed to determine

	which components of exercise are the most effective for motor rehabilitation post ABI. - *There is level 1b (Hassett et al., 2009; 2011) evidence that an exercise program at a fitness-center may not result in different motor outcomes when compared to home-based exercise.* - *There is level 1b evidence (Hassett et al., 2012) that circuit training with encouragement and heart rate monitor feedback may not significantly improve motor performance in individuals post ABI.* - *There is level 1b evidence (Bateman et al., 2001) that exercise programs may not improve balance or mobility compared to relaxation training in individuals post ABI.* - *There is level 2 evidence (Hoffman et al., 2010) that community-based exercise may decrease pain and depression in individuals post ABI.* - *There is level 2 evidence (Driver et al., 2006) that aquatic exercise training may be effective at improving co-ordination, strength, flexibility, and endurance in individuals post ABI.* - *There is level 2 evidence (Bhambhani et al., 2005; Chin et al., 2015; Corral et al., 2014) that exercise programs may improve oxygen uptake and cardiovascular parameters in individuals post ABI.* - *There is level 2 evidence (Ding et al., 2022) that aerobic exercise training may be as effective as stretching and toning at home for endurance in individuals with chronic TBI.* - *There is level 2 evidence (Dault & Dugas, 2002) that aerobic dance training compared to traditional muscular training may improve sensory interaction and balance post ABI.* - *There is level 3 evidence (Damiano et al., 2016) that a home-based exercise program may improve stability, but may not improve motor control, mobility, or dual-task performance in individuals post ABI.* - *There is level 4 evidence (Charette et al., 2016) that multimodal exercise programs may improve gait and mobility in individuals post ABI.* - *There is level 4 evidence (Ustinova et al., 2014) that a therapeutic exercise program may improve balance and gait post ABI.*
Early Intensive Rehabilitation	Early intensive rehabilitation may improve ambulation and motor function following an ABI. - *There is 1b evidence (Fan et al., 2020) that early intensive rehabilitation may improve motor function in individuals with TBI.* - *There is level 4 evidence that early intensive rehabilitation (Mossberg et al., 2002) may improve ambulation in individuals with ABI.*
Aquatic Therapy	Aquatic therapy may not significantly improve motor function compared to conventional rehabilitation in individuals who have sustained a severe TBI. - *There is level 1b evidence (Curcio et al., 2020) that aquatic therapy may not be more effective than conventional training for the rehabilitation of motor function in individuals with severe TBI.*

SPASTICITY	
Non-Pharmacological Interventions	
Electrical Stimulation	Electrical stimulation in combination with tilt table standing and splinting may not be more effective than tilt table standing alone. Electrical stimulation may decrease spasticity for a period of up to 24 hours among persons with TBI. - *There is level 1b (Leung et al., 2014) that electrical stimulation in combination with tilt table standing and splinting may not be better than tilt table standing alone for the management of spasticity in individuals with severe TBI.* - *There is level 4 evidence (Seib et al., 1994) that electrical stimulation may be effective for decreasing lower extremity spasticity for six or more hours in individuals with TBI.*
Acupuncture	Acupuncture may reduce a surrogate measure of muscle hypertonia in individuals with disorders of consciousness following severe TBI. - *There is level 2 evidence (Matsumoto-Miyazaki et al., 2016) that acupuncture may reduce a surrogate measure of spasticity in individuals with disorders of consciousness post severe TBI.*
Physiotherapy	Four to six sessions of physiotherapy per week may improve spasticity and muscle contractures in individuals with disorders of consciousness following ABI, compared with less than four sessions per week. - *There is level 4 evidence (Thibaut et al., 2018) that higher doses of physiotherapy (four to six sessions per week) may improve spasticity and muscle contractures in individuals with disorders of consciousness following ABI compared with lower doses of physiotherapy.*
Casting	Serial casting may improve contractures, spasticity, and joint range of motion in individuals with an ABI compared to stretching; however, contracture improvement may not be maintained long-term. - *There is level 1b evidence (Moseley et al., 2008) that serial casting may be superior to passive stretching at improving spasticity of the elbow in individuals post ABI.* - *There is level 3 evidence (Pohl et al., 2002) that serial casting following a short duration casting change interval (one to four days), or a longer duration casting change interval (five to seven days) may have similar effects on upper and lower extremity range of motion in individuals post ABI; however, complications may be more common when employing a longer casting change interval.* Below-knee casting and stretching might increase passive ankle dorsiflexion in patients post ABI. - *There is level 2 evidence (Moseley et al., 1997) that a below-knee casting and stretching may increase passive ankle dorsiflexion in patients post ABI.* Serial below-knee casting may improve ankle range of motion and muscle extensibility in patients post TBI. - *There is level 4 evidence (Singer et al., 2003) that weekly below-knee casts may improve ankle range of motion, muscle extensibility, and passive torque in patients post ABI. However, this intervention may be associated with tissue breakdown.*

Hand Splinting and Stretching	Overnight hand splinting may not improve upper limb function post ABI. Soft hand splinting may be beneficial for improving hand opening post ABI and spasticity of the finger muscles in individuals with disorders of consciousness. - *There is level 1b evidence (Lannin et al., 2003) that nocturnal hand splinting may not improve upper extremity range of motion or function compared to standard care in individuals post ABI.* - *There is level 2 evidence (Thibaut et al., 2015) that soft hand splinting may improve hand opening in individuals post ABI.*
Pharmacological Interventions	
Focal Treatment with Botulinum Toxin	Botulinum toxin type A injections may be effective in the treatment of spasticity post ABI. - *There is level 1b (Mayer et al., 2008) evidence that botulinum toxin type A injected at a single motor point or using a distributed multisite technique may reduce spasticity to a similar degree in individuals with an ABI.* - *There is level 4 evidence (Intiso et al., 2014) that botulinum toxin type A injections may be effective in the management of localized spasticity following ABI.* - *There is level 4 evidence (Clemenzi et al., 2012; Yablon et al., 1996) that botulinum toxin type A injections, in conjunction with conventional therapies, may improve spasticity and passive ROM in patients with TBI.*
Focal Treatment with Chemodenervation (Phenol Blocks)	Phenol nerve blocks may help to temporarily decrease spasticity and improve joint range of motion in the upper extremities of individuals with TBI. - *There is level 4 evidence (Keenan et al., 1990; Garland et al., 1984) that phenol nerve blocks may temporarily reduce spasticity in the elbow, wrist, and finger flexors in individuals post TBI.*
Oral Baclofen	Oral baclofen may reduce lower extremity, but not upper extremity, spasticity in individuals with an ABI. - *There is level 4 evidence (Meythaler et al., 2004) that oral baclofen may improve lower extremity spasticity, but not upper extremity spasticity, in individuals post ABI.*
Surgical Interventions	
Intrathecal Baclofen	Intrathecal baclofen bolus injections may reduce upper and lower extremity spasticity in individuals with ABI, but it is associated with significant risks. - *There is level 1a evidence (Meythaler et al., 1996) that bolus intrathecal baclofen injections may produce short-term (up to six hours) reductions in upper and lower extremity spasticity compared to placebo following ABI.* A continuous infusion of intrathecal baclofen by a pump may improve spasticity post ABI in both upper and lower extremities, as well as increase ankle range of motion during gait post ABI.

	- *There is level 4 evidence (Wang et al., 2016; Becker et al., 1997; Francois, 2001; Francisco et al., 2005; Stokic et al., 2005; Dario et al., 2002; Margetis et al., 2014; Meythaler et al., 1997; 1999a; 1999b; Posteraro et al., 2013; Hoarau et al., 2012a) that a continuous infusion of intrathecal baclofen may result in long-term reductions in spasticity in both the upper and lower extremities following an ABI.* - *There is level 4 evidence (Chow et al., 2015; Horn et al., 2005; 2010) that intrathecal baclofen may improve ankle range of motion during gait in individuals with ABI.*
Multimodal Interventions	
Multimodal Interventions	The combination of botulinum toxin, serial casting, motor training and splinting may improve dorsiflexion range of motion but may not reduce spasticity, when compared to standard care. - *There is level 1b evidence (Leung et al., 2019) that an intervention consisting of botulinum toxin injections, serial casting, motor training and splinting may improve ankle dorsiflexion range of motion but not improve spasticity in individuals with TBI.* Electrical stimulation in combination with tilt table standing and splinting may improve early presentation of spasticity in patients post TBI. - *There is level 1b evidence (Leung et al., 2014) that electrical stimulation in combination with tilt table standing and splinting may decrease spasticity at 6 weeks post intervention compared to tilt table standing alone in individuals with an TBI.* Neural tension technique may be just as effective as random passive movement for improving lower extremity spasticity post ABI. - *There is level 1b evidence (Lorentzen et al., 2012) that neural tension technique may not be more effective than random passive movement in improving lower extremity spasticity in individuals with ABI.* The combination of casting with botulinum toxin may not be more effective than casting alone for the prevention of calf spasticity and contracture post ABI. - *There is level 2 evidence (Verplancke et al., 2005) that botulinum toxin combined with casting may not be more effective than casting alone in the prevention of calf spasticity and contracture after severe brain injury.*
VISUAL DYSFUNCTION	
Interventions for Visual Dysfunction	Computer-based visual restitution training and reading related rehabilitation may improve visual function in individuals with TBI. - *There is level 1b evidence (Kasten et al., 1998), and level 2 evidence (Kasten et al., 2000) that computer-based visual restitution training may be more effective than visual fixation training in improving visual function post TBI.* The Six Eyes Exercises protocol may reduce visual symptoms post TBI. - *There is level 2 evidence (Berryman et al., 2020) that the Six Eyes Exercises protocol may be more effective for the reduction of visual symptoms than standard of care in persons post TBI.*

	Reading related rehabilitation may facilitate reading tasks in individuals with ABI. - *There is level 2 evidence (Ciuffreda et al., 2006) that reading-related rehabilitation may improve reading tasks in individuals with oculomotor dysfunction post ABI.* Base-in prisms and bi-nasal occluders may improve ambient vision disturbances post ABI. - *There is level 4 evidence (Padula et al., 1994) that base-in prisms and bi-nasal occluders may be effective in the treatment of ambient vision disturbances post ABI.* Home-based computer visual vergence therapy may improve binocular vision disorders in individuals with ABI. - *There is level 4 evidence (Conrad et al., 2017) that home-based computer visual vergence therapy may be effective in the treatment of binocular vision disorders in individuals with ABI.*
Balance Dysfunction	
Interventions for Balance Dysfunction	Aquatic therapy, compared to conventional training, may not improve balance in individuals with severe TBI. - *There is level 1b evidence (Curcio et al., 2020) that aquatic therapy may not be more effective than conventional training for rehabilitation of balance impairment in individuals with severe TBI.* An individualized dual-task home-based rehabilitation program may improve balance in individuals with ABI. - *There is level 1b evidence (Peirone et al., 2014) that an individualized dual-task home-based rehabilitation program may improve balance in individuals with ABI.* For the rehabilitation of balance impairment, virtual reality therapy using an Xbox Kinect system may be more effective than a balance platform; however, virtual reality therapy may not be more effective than a home-based balance program. - *There is level 2 evidence (Tefertiller et al., 2019; Straudi et al., 2017) that virtual reality therapy using an Xbox Kinect system may not be more effective than a home-based program for balance rehabilitation; however, it may be more effective than a balance platform.* A combination of aerobic dancing and slide and step training may be more effective than traditional muscular training for rehabilitation of balance post TBI. - *There is level 2 evidence (Dault & Duga, 2002) that a combined program including aerobic dancing and slide and step training may be more effective for the rehabilitation of balance impairment post TBI than traditional muscular training.*

	Yoga may be effective for rehabilitation of balance post TBI; however, more research is needed. - *There is level 4 evidence (Schmid et al., 2016) that yoga may improve balance in individuals with TBI; however, further research with larger samples is needed to confirm the effectiveness of this intervention.*
VESTIBULAR DYSFUNCTION	
Interventions for Vestibular Dysfunction	Betahistine in combination with vestibular rehabilitation may improve vertigo and balance in individuals with TBI. - *There is level 2 evidence (Naguib & Madian, 2014; Jafarzadeh et al., 2018) that betahistine in combination with vestibular rehabilitation may be more effective than betahistine or rehabilitation alone in improving vertigo and balance disorder after a TBI.* Particle repositioning maneuvers may be effective for the improvement of positional nystagmus post TBI. - *There is level 4 evidence (Motin et al., 2005) that the Particle Repositioning Maneuver may lead to improvements in positional nystagmus in individuals with severe TBI.* A behavioural exposure program may improve vertigo post TBI. - *There is level 4 evidence (Gurr & Moffat, 2001) that a behavioural exposure program may improve symptoms of vertigo in patients after TBI.*
OLFACTORY DYSFUNCTION	
Interventions for Olfactory Dysfunction	Olfactory training using odors such as anise, lemon, rose, vinegar, smoke, and eucalyptus may be effective for the improvement of odor thresholds in individuals with TBI. - *There is level 1b evidence (Langdon et al., 2018) that olfactory training using a variety of odors such as anise, lemon, rose, vinegar, smoke, and eucalyptus, may improve odor thresholds, but not subjective olfactometry.* Olfactory training with a bottle of phenyl ethyl alcohol (PEA) may be more effective for the improvement of odor threshold levels when compared to mineral oil and bottles of PEA with lemon, eucalyptus, and clove oils; however, it may not lead to improvements in odor identification ability. - *There is level 2 evidence (Jiang et al., 2017; 2019) that olfactory training with a bottle of PEA may improve odor threshold levels but not the ability to identify odors, when compared to mineral oil and bottles of PEA with lemon, eucalyptus, and clove oils.* Corticosteroids and olfactory training may improve olfactory dysfunction in individuals with moderate to severe TBI. - *There is level 4 evidence (Bratt et al., 2020) that corticosteroids and olfactory training may improve olfactory dysfunction in individuals with moderate to severe TBI.*

Introduction

Impairment in motor and sensory function affecting upper and lower limbs is common in individuals who have sustained brain injuries. These impairments may include abnormal posture, weakness, paresis, altered muscle tone, impaired balance, abnormal reflexes, exaggerated stretch reflexes and lack of coordination (Subramanian et al., 2022). The primary etiology of motor impairment and movement dysfunction post ABI is upper motor neuron syndrome (UMNS). Individuals who develop UMNS may present positive or negative symptoms, both of which produce abnormal patterns of muscle activity: negative signs include muscle weakness or loss of dexterity and positive signs involve muscle overactivity (e.g., spasticity, clonus, flexor and extensor spasms) (Segal, 2018).

Motor impairment can also result from the independent effects of prolonged immobilization and bed rest during the acute period. Affected muscles may subsequently develop stiffness and contractures, which may further negatively impact movement (Mayer, 1997). Prolonged immobility affects multiple body systems, although it is the direct effect on the musculoskeletal and cardiovascular systems that impact motor function the most (Bushbacher & Porter, 2000).

For motor and sensory impairments following brain injury, both the character and distribution of the individual's symptoms should be considered when deciding on a course of action. Time post injury is another important consideration, as spontaneous neurological recovery may continue for 9 to 15 months post injury. The majority of motor recovery often occurs within the first six months after injury (Iaccarino et al., 2015). However, the potential for functional motor recovery beyond that point is possible through medical interventions, such as the correction of a deformity or the use of pharmacological agents that allow for improved motor control (Mayer et al., 1996).

This module reviews the available evidence pertaining to interventions for motor and sensory rehabilitation following ABI.

MOTOR IMPAIRMENT

Motor rehabilitation is commonly provided to individuals who have sustained an ABI. Rehabilitation is essential to reestablishing independence and helping persons return to basic activities of daily living (ADLs) and reestablishing independence post ABI. Rehabilitation facilitates motor recovery by helping the individual perform accurate repetitions of the desired movement or task, and may also teach adaptive strategies for functional task performance; in addition, rehabilitation promotes motor learning and neuroplasticity (Subramanian et al., 2022). The following sections evaluate interventions available for upper and lower extremity motor impairment, including spasticity.

Upper Extremity Interventions

Upper limb motor impairments are common in individuals with an ABI (Lannin et al., 2003). Interventions for the upper limb can focus broadly on arm mobility or on more specific outcomes such as finger dexterity. Despite the importance of upper extremity rehabilitation post ABI, there are limited studies evaluating interventions.

Constraint Induced Movement Therapy

Constraint Induced Movement Therapy (CIMT) is an intervention directed at improving the function of the more affected upper extremity following brain injury. The two primary components involve: 1) intensive motor training of the more affected upper extremity and 2) motor restriction of the less affected upper extremity (Dettmers et al., 2005). CIMT originated from research suggesting that the affected limb post brain injury is negatively impacted by "learned non-use" due to increased use of the intact limb (Grotta et al., 2004).

Although there is substantial evidence in the stroke population to suggest that CIMT is clinically effective, many patients with stroke/or ABI are not suitable for this type of therapy due to the severity of upper limb dysfunction, as CIMT requires patients to be able to voluntarily extend the wrist and fingers. Uptake of CIMT amongst eligible patients may also be limited due to the resources required for its implementation and patient frustration due to having their less affected limb restrained (Grotta et al., 2004).

TABLE 4 | Constraint Induced Movement Therapy for Upper Extremity Rehabilitation Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Shaw et al. (2005) USA Pre-Post N=22	**Population:** TBI; Mean Age=39.3yr; Gender: Male=14, Female=8; Mean Time Post Injury=8.9yr. **Intervention:** Participants received constraint induced movement therapy (CIMT; 6hr, 5d/wk for 2wk) in the laboratory. Participants engaged in massed practice shaping or task specific procedures with their affected upper limb (UL) while wearing a protective safety mitt on their less-affected UL for ≥90% of the time. Participants were encouraged to use the mitt outside the lab as well. **Outcome Measure:** Fugl Meyer (FM) Motor Performance Assessment, Wolf Motor Function Test (WMFT), and Motor Activity Log (MAL).	1. Significant improvements in real-world use across all post-intervention testing occasions as measured by the MAL (mean change=1.6, p<0.001). 2. Significant post-treatment improvements in more affected ULFM scores (mean change=4.2, p<0.001), and WMFT scores (mean change=0.4, p<0.01). 3. Based on the FM scores, the largest gains were in the upper arm, compared to the hand or wrist. 4. Based on a median split (57%) of adherence to mitt wearing outside the lab, less-adherent participants had smaller treatment gains than those who were more-adherent. 5. On the MAL, less adherent participants showed a trend towards smaller gains than more adherent participants (p=0.065).
Page & Levine (2003) USA	**Population:** TBI; Mean Age=21yr; Gender: Male=2, Female=1; Time Post Injury=1 to 6yr. **Intervention:** Physical and occupational	1. Pre-intervention, participants exhibited learned non-use (MAL, Amount of Use scores <1.0).

Pre-Post N=3	therapy sessions (30min each, 3x/wk for 10 wk) were provided. The less affected upper limb was also restrained (5hr/day for 5days/wk) using modified constraint induced therapy (mCIT). **Outcome Measure:** Action Research Arm Test (ARAT), Motor Activity Log (MAL), and Wolf Motor Function Test (WMFT).	2. After the intervention, MAL scores improved: Amount of use=2.0 and quality of use=2.2. Participants 1, 2 and 3 had functional improvements on the ARAT (14.0, 5.5, and 6.0 respectively) and the WMFT (1.15, 1.7 and 1.35 respectively).

Discussion

The effectiveness of modified CIMT was studied by Page and Levine (2003) in a pre-post study with three participants with TBI. The authors found that participants showed improvements in both the amount and quality of use of the more affected limb. In a larger prep-post study with 22 participants, Shaw et al. (2005) reported similar results. The authors found significant improvements in both laboratory and real-world spontaneous use of the more affected upper limb following two weeks of CIMT. While the gains were maintained at one month post-treatment. The effect was not sustained at two years post-treatment (Shaw et al., 2005).

Conclusions

There is level 4 evidence (Shaw et al., 2005; Page & Levine, 2003) that constraint induced movement therapy (CIMT) or modified CIMT may improve upper extremity function in individuals post ABI.

KEY POINTS

- Constraint induced movement therapy may improve the amount and quality of use of the more affected upper limb post ABI.

Fine Motor Coordination Training

Fine motor impairment refers to the inability to perform tasks that require manual dexterity, and it is usually related to the ability to make precise hand movements (Burr & Choudhury, 2022). Although gross motor function may return early in the recovery period following an ABI, fine motor deficits may persist and present a considerable challenge for individuals and their care providers.

TABLE 5 | Fine Motor Coordination Training in Upper Extremity Rehabilitation Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Neistadt (1994) USA RCT PEDro=5 N=45	**Population:** TBI=42, Anoxia=3; Mean Age=33.2yr; Gender: Male=45, Female=0, Mean Time Post Injury=7.9yr. **Intervention:** Participants were assigned to either the parquetry block assembly (n=22) or the meal preparation group (n=23). Participants received individual training sessions (3, 30 min sessions for 6wk) in addition to their regular program. **Outcome Measure:** WAIS-R (Block Design Test), Parquetry Block Test, RKE-R, and Jebsen-Taylor Test of Hand Function.	1. For picking up small objects with the dominant hand, the meal preparation group showed a significantly greater improvement over the puzzle group (p=0.027). 2. There was no significant difference in improvement between the two groups for simulated page turning with dominant hand (p=0.655), simulated page turning with the non-dominant hand (p=0.182) and picking up small objects with the non-dominant hand (p=0.265).
Korman et al. (2018) Belgium PCT N=20	**Population:** *Experimental Group (N=10):* Mean age=30yr; Mean time post-injury=126.9d; GCS range: 3-12. *Control Group (N=10):* Mean age=29.3yr; Mean time post-injury=118.4d; GCS range: 3-8. **Intervention:** Individuals were either trained or not trained to complete a 5-finger sequence task. Training took place every day for five days, with approximately 100 sequence repetitions in each practice. Assessment occurred pre-intervention, post-intervention, and at 1-month follow-up. **Outcome Measures:** Number of correct and incorrect completed sequences during testing.	1. There were no significant differences between groups in performance on the sequence task before the intervention occurred. 2. The trained group showed a significant improvement over the course of training for performance speed (p<0.001), as did the control group (p<0.001). 3. There were no significant differences in the number of errors produced before the intervention compared to post-intervention for either group. 4. The trained group had significantly greater spontaneous gains over the course of the study (p=0.016). Within session gains became negative over the course of the week with performance degrading closer to the end of training sessions (p<0.05). Between session gains steadily improved over the course of training (p<0.05).
Yungher & Craelius (2012) USA PCT N=19	**Population:** TBI=8, Stroke=4, Healthy Participants=7; *Experimental Group (n=12):* Mean Age=39.8yr; Gender: Male=8, Female=4. *Healthy Control Group (n=7)*: Mean Age=46.4yr; Gender: Not Reported. **Intervention:** The use of Gesture Recognition Biofeedback (GRB), which uses surface muscle pressures of the forearm to provide real-time visual biofeedback, was compared to standard repetitive training without feedback. Measures were completed before and after each condition. **Outcome Measure:** Nine-hole peg test (HPT).	1. HPT scores for the experimental group ranged from 28.6 to 263 sec, and 15.78 to 25.56 sec for the control group. 2. For the experimental group (n=12), GRB training was associated with a decrease in the time needed to complete the NPT by an average of 15.5%. Training without feedback was associated with an increase in time needed to complete the NPT by an average of 2.07%. 3. For the control group, GRB training had a minimal effect. The time to completion on the NPT was faster in this group, compared to the experimental group, at baseline as well as with training with and without feedback (p<0.05).
Kriz et al. (1995) Germany	**Population:** TBI=3, Stroke=2, Intracerebral bleeding=3, Viral Encephalitis=1, Cerebral Abscess=1, Healthy Controls=17. Gender:	1. No significant changes were observed among control participants after feedback training (p>0.10). Nine of 10 participants with

Author, Year Country Study Design Sample Size	Methods	Outcome
Pre-Post N=27	Male=17, Female=10; *Impaired Group (n=10)*: Mean Age=33.8yr; Mean Time Post Injury=14.7mo. *Healthy Control group (n=17):* Age Range=22-42yr. **Intervention:** Patients completed a feedback-based training intervention that involved tracking moving targets with grip force, using a precision grip. Patients trained over 10 weekly 30 min sessions. Training terminated when normal performance was achieved. **Outcome Measure:** Force control using grip strength, Tracking errors, and Transfers.	impairments reduced tracking errors significantly ($p<0.05$) and improved in transfer tasks ($p<0.05$). 2. Impaired initial performance and improvement was not uniform and could be attributed to individual aspects of force control.

Discussion

In an RCT, Neistadt (1994) examined fine motor coordination in a group of adult men with TBI after two types of coordination retraining activities: tabletop activities (i.e., peg board activities, puzzles etc.) and functional activities (i.e., meal preparation). The authors found that functional activities may be more effective than tabletop activities in promoting fine motor coordination in persons with brain injury, as indicated by the improvement in "picking up small objects with the dominant hand" that the meal preparation group experienced (Neistadt, 1994).

In a pre-post study, Kriz et al. (1995) found that visual feedback-based training of grip force is beneficial for individuals who have sustained a brain injury (Kriz et al., 1995). In this study, a light-weight force transducer was held between the pulp of the index finger and thumb of the impaired hand. In response to visual cues delivered via computer monitor, all tasks involved the gradual increase and decrease of grip force in training and transfer protocols. Regardless of the individual pattern of impairments, all but one patient succeeded in improving their tracking performance and transferring regained capabilities to other tasks (Kriz et al., 1995).

In a Prospective Controlled Trial (PCT) study, Youngher and Craelius (2012) compared the use of gesture recognition biofeedback to standard repetitive training without feedback (Yungher & Craelius, 2012). There was a significant decrease in task completion time for those who received feedback, compared to those who did not. The authors suggested that this intervention may lead to improvements in fine motor function of the hand with minimal supervision (Yungher & Craelius, 2012).

In another PCT study, Korman et al. (2018) found that training on a finger-sequencing tasks may not be effective in improving fine motor task performance when compared to no training. While the group who received training showed improvements in performance speed, there were no significant differences in error rates between groups (Korman et al., 2018).

Conclusions

There is level 2 evidence (Neistadt, 1994) that functional retraining activities may be more effective than tabletop fine motor control retraining activities for improving fine motor function in the dominant hand in individuals with ABI.

There is level 2 evidence (Korman et al., 2018) that finger sequencing training may increase performance speed in individuals with ABI; however, error rates may not improve.

There is level 2 evidence (Kriz et al., 1995) that gesture recognition biofeedback may improve fine motor function in individuals with ABI, compared to standard repetitive training without feedback.

There is level 4 evidence (Yungher & Craelius, 2012) that visual feedback-based grip force training may improve tracking accuracy and transfer tasks in individuals post ABI.

KEY POINTS

- Functional retraining activities may be superior to tabletop fine motor control activities for improving fine motor coordination post ABI.
- Training in finger sequencing tasks, gesture recognition biofeedback and visual feedback may improve fine motor function post ABI.
- Visual feedback-based grip force training may enhance accuracy and transfer tasks post ABI.

Virtual Reality for Upper Extremity Rehabilitation

Virtual Reality (VR) has gained popularity in recent years with the introduction of commercially available programs and video game consoles. Virtual Reality (VR) usually involves the use of immersive, interactive, three-dimensional environments; in the rehabilitation context, VR can be used to offer engaging rehabilitation activities in a controlled environment (Aida et al., 2018). VR offers the opportunity to practice real-life meaningful tasks in highly customizable systems; these may be immersive, semi-immersive, or non-immersive, depending on the level of user perception and the display of the virtual environment (e.g., through a head-mounted display or using basic desktop displays) (Brassel et al., 2021).

TABLE 6 | Virtual Reality for Upper Extremity Rehabilitation Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Mumford et al. (2012) Australia Pre-Post N=9	**Population:** Severe TBI; Mean Age=30.9yr; Gender: Male=5, Female=4; Mean Time Post Injury=33.8mo. **Intervention:** Participants had two pre-intervention assessments (4wk apart), then received the Virtual Reality (VR) intervention, followed by a follow-up assessment. The intervention consisted of 12, 1-hr training sessions with the Elements virtual reality system (VR therapy, tracking camera, and tangible working LCD surface), over a 4wk period in addition to their usual care. **Outcome measure:** System-measured variables, Box and Block Test (BBT), McCarron Assessment of Neuromuscular Dysfunction (MAND), Neurobehavioural Functioning Inventory (NFI).	1. The intervention provided significant improvements on accuracy percentage for both left (46.26 to 64.25; p=0.01) and right hands (56.86 to 73.62; p=0.02). 2. No significant changes were seen from pre to post treatment in left hand speed, but a significant improvement in right hand speed was evident (0.23m/s to 0.31m/s; p=0.01). 3. Efficiency scores improved significantly only for the right hands (92.61 to 97.68; p=0.002). 4. BBT showed significant improvements from pre to post test for both the left (30.44 to 35.98; p=0.04) and right (46.66 to 53.33; p=0.007) hands. 5. No significant improvements were noted on the MAND. 6. From pre to post treatment, significant improvements in total NFI scores were demonstrated with a reduction from 128.67 to 112.89 (p=0.005); however, among subscales, only the memory/attention subscale improved significantly (p=0.049).
Sietsema et al. (1993) USA PCT N=20	**Population:** TBI; Mean Age=31.6yr; Gender: Male=17, Female=3; Mean Time Post Injury=6yr. **Intervention**: Two interventions were compared: An Occupational Embedded Intervention and rote exercise. The Occupational Embedded Intervention involved leaning forward and reaching out the affected arm to play a computer-controlled game. The rote exercise involved leaning forward and reaching out the affected arm on command. Each participant had two 20min sessions, separated by 1wk. **Outcome Measure:** Range of motion (trunk inclination, shoulder flexion, elbow extension), Total Movement (leaning forward and reaching).	1. There were no significant order effects. 2. There was a significant increase in range of motion concerning hip to wrist movement in the Occupational Embedded Intervention group compared with the rote exercise group (mean reach length 71.60 cm versus 59.38 cm, p<0.001). 3. The Occupational Embedded Intervention group had a range of motion for scapula-to-wrist that was a mean of 3.52cm greater than the rote exercise group; however, this was not statistically significant.

Discussion

In a small pre-post study, Mumford et al. (2012) used virtual reality therapy with an interactive LCD surface and tracking cameras over twelve 1-hour sessions delivered in addition to standard care. The authors found that accuracy and dexterity improved significantly in both upper extremities, but only the right arm of participants showed speed and efficiency improvements. In a larger PCT study, Sietsema et al. (1993) reported that individuals who used a computer-controlled game aimed at improving reaching had better range of motion in the wrist than individuals who completed rote exercise. More research is needed to characterize the extent of benefit and potential optimal programming for VR.

Conclusions

There is level 2 evidence (Mumford et al., 2012; Sietsema et al., 1993) that virtual reality training may improve hand dexterity, as well as reaching performance in the upper extremities of individuals with TBI.

KEY POINTS

- Virtual reality interventions may be an effective intervention for the recovery of upper extremity function post ABI.

Lower Extremity Interventions

Outcomes targeted by lower extremity interventions following ABI tend to be gait and balance related and aimed at preventing lower extremity contractures. Which can develop within the first few months of injury (Baagoe et al., 2018). Current methods in use for lower extremity rehabilitation include — but are not limited to — casting, orthosis use, and partial body weight supported gait training.

Aquatic Treadmill Walking

Aquatic treadmill walking is a form of low impact exercise, as the water supports the person's body weight while they walk (Parfitt et al., 2017). There is limited evidence regarding the use of aquatic treadmill walking for rehabilitation of individuals with TBI.

TABLE 7 | Aquatic Treadmill Walking for Lower Extremity Rehabilitation Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Narasaki-Jara et al. (2020) USA Post-test N=13	**Population:** TBI; Mean Age=43.23yr; Gender: Male=12, Female=1; Mean time Post Injury=12.67yr. **Intervention:** Participants completed walking trials at three different water depths as follows: waist, chest, and neck level. Participants completed three test trials of 2-minute aquatic treadmill walking at each condition with a 2-minute resting period between each trial. The specific order of water depths was randomized for all participants. **Outcome Measures:** Cadence, Stride Length, Stance/Swing Time Ratio, Peak Sagittal Plane Angles, Range of Motion at hip, knee, and ankle joints.	1. Significant differences were found in spatiotemporal and joint kinematic variables across the three conditions: stance swing ratio (p = .023), peak hip flexion (p = .001), hip range of motion (p = .047), and peak ankle dorsiflexion (p = .000). 2. No significant differences were found in hip extension, knee kinematics, ankle plantarflexion, or ankle range of motion (ROM). 3. Walking in neck-depth water may not be ideal for gait training as it appears to limit hip and ankle joint kinematics. 4. Waist to chest-depth water may be better for aquatic gait rehabilitation.

Author Year Country Study Design Sample Size	Methods	Outcome

Discussion

In a post-test study, Narasaki-Jara et al. (2020) examined the use of aquatic treadmill walking, across three different depths of water, for the rehabilitation of individuals with TBI. The authors found significant differences in kinematic and spatiotemporal variables when comparing the three depths of water, with participants showing significant changes in stance swing ratio, peak hip flexion, hip range of motion, and peak ankle dorsiflexion. However, no differences were found in hip extension, knee kinematics, ankle plantar flexion, or ankle range of motion across the three conditions. In addition, the authors suggested that neck-depth water may not be ideal for aquatic rehabilitation.

Conclusions

There is level 4 evidence (Narasaki-Jara et al., 2020) that walking in neck-depth water may limit hip and ankle joint kinematics in individuals with TBI.

KEY POINTS

- Waist to chest-depth water may facilitate gait kinematics in individuals with a TBI during aquatic treadmill walking; neck-depth water may not be ideal for gait training.

Body Weight Supported Gait Training

The use of a body weight support system reduces the muscle force that a person needs to exert to counteract gravity in order to participate in gait rehabilitation and provides stability (Dragunas & Gordon, 2016). Walking on a treadmill using body weight support has been used to improve motor function in individuals with neurological conditions, such as stroke (Mehrholz et al., 2014); there is limited evidence about this intervention for individuals with brain injury.

TABLE 8 | Body Weight Supported Gait Training for Lower Extremity Rehabilitation Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
	Population: TBI; Gender: Male=7, Female=9. Robotic-Assisted Group (n=8): Mean Age=37.1yr; Mean Time Post Injury=140.3mo. Manually Assisted Group (n=8):	1. For the RATT group, SSV increased by 49.8% (p=0.01), maximal velocity increased by

Author Year Country Study Design Sample Size	Methods	Outcome
Esquenazi et al. (2013) USA RCT PEDro=4 N=16	Mean Age=41.9yr; Mean Time Post Injury=150.4mo. **Intervention**: All participants received gait training for 45min, 3 x/wk for a total of 18 sessions. The training was either Robotic-Assisted Treadmill Training (RATT) or Manually Assisted Treadmill Training (MATT). **Outcome Measure:** Over ground walking Self-Selected Velocity (SSV), Maximal Velocity, Spatiotemporal Symmetry, 6-minute Walk Test (6MWT), and Stroke Impact Scale.	14.9% (p=0.01), step length asymmetry ratio improved during SSV by 33.1% (p=0.01), and the 6MWT improved by 11.7% (p=0.21). 2. For the MATT group, SSV increased by 31% (p=0.06), maximal velocity increased by 30.8% (p=0.01), step-length asymmetry ratio improved during SSV by 9.1% (p=0.73), and the 6MWT improved by 19.3% (p=0.03). 3. No significant between group differences were found for any of the outcome measures.
Clark et al. (2012) Australia RCT PEDro=3 N=42	**Population:** *Experimental Group (n=17)*: TBI=11, Stroke=5, Multiple Sclerosis=1; Mean Age=38.7yr; Gender: Male=10, Female=7; Median Time Post Injury=9 mo. *Control Group (n=25)*: Healthy controls; Mean Age=27.8yr; Gender: Male=16, Female=9. **Intervention:** All participants performed 7 alternative gait training methods in a randomized order. Methods included: therapist manual facilitation, use of gait assistive device, treadmill walking with handrail support, and 4 variations of body weight supported treadmill training with combinations of handrail and/or therapist support. **Outcome Measure:** Mediolateral Center of Mass Movement, Stride Time, Stability of Movement.	1. Body weight supported treadmill training without any additional support resulted in greater amplitude, altered timing, and reduced movement stability compared with non-pathologic gait. 2. Manual facilitation by the therapist most closely matched non-pathologic gait for timing and stability. The use of therapist facilitation or handrail support reduced the effect and resulted in treadmill training having lower movement amplitudes when compared to other methods of training.
Wilson et al. (2006) USA RCT PEDro=7 N=38	**Population:** TBI; Mean Age=29.6yr; Gender: Male=35, Female=3; Mean Time Post Injury: Experimental Group (n=19) =4mo, Control Group (n=19) =2.8mo. **Intervention:** Patients in the control group received standard physical therapy for 8wk. The experimental group had physical therapy supplemented with partial weight-bearing gait training twice weekly. **Outcome Measure:** Functional Independence Measure and Functional Assessment Measure (FIM+FAM), Rivermead Mobility Index (RMI), Gross Motor Subscale (GMS), Standing Balance Scale (SBC), Functional Ambulation Category (FAC).	1. The control group had significant improvements on the SBC ($p<0.0039$), FAC ($p<0.0002$), RMI ($p<0.0001$), GMS ($p<0.0005$), and FIM+FAM ($p<0.0002$). 2. The experimental group had significant improvements on the SBC ($p<0.002$), FAC ($p<0.0002$), RMI ($p<0.0009$), GMS ($p<0.0015$), and FIM+FAM ($p<0.0039$). 3. No between group differences were found for the SBC, FAC, RMI, GMS, or the FIM+FAM.
Brown et al. (2005) USA RCT PEDro=5 N=20	**Population:** TBI; Mean Age=40.2yr; Gender: Male=14, Female=6; Mean Time Post Injury=15.8yr. **Intervention:** Patients received either Body Weight Support Treadmill Training (BWSTT; n=10) or conventional over-ground gait training (COGT; n=9) for 15 min plus 30 min of exercise 2 days/wk for 3 mo. **Outcome Measure:** Functional Ambulation Category, Functional Reach, Timed Up and Go, gait velocity, Stride Width, Left-Right Step Length differential.	1. Step Length Differential improved significantly more for the COGT group than for the BWSTT group after 3mo of intervention (p=0.011). 2. There were no other significant differences between groups at baseline or after 3mo of intervention for any of the outcome measures.

Author Year Country Study Design Sample Size	Methods	Outcome
Anggelis et al. (2019) USA Cohort N=12	**Population:** TBI; *Dynamic Body Weight Support Gait Training Group (DBWS)*=6; Mean Age=34yr; Gender: Male=4, Female=2; *Standard of Care Group (SOC)*=6; Mean Age=30.2yr; Gender: Male=3, Female=3. **Intervention:** Data was collected retrospectively from patients with TBI who received inpatient rehabilitation incorporating DBWS gait training (n = 6) and those who received inpatient rehabilitation without DBWS (SOC, n = 6). **Outcome Measures:** Change in Functional Independence Measures (FIM) scores from admission to discharge.	1. Both groups showed significant improvements in total FIM scores at discharge compared to admission (DBWS group p = 0.001 and SOC group p = 0.007). 2. Both the DBWS and SOC groups showed significant improvements on motor FIM and cognitive FIM subscales. The DBWS group showed significantly greater improvement on both the motor (p = 0.008) and cognitive subscales (p = 0.021) than the SOC group. 3. DBWS leads to greater improvement in total FIM compared to SOC. The use of DBWS allowed the therapists to administer more intense therapy, challenge patients and encourage them to attempt movement, while simultaneously relieving them of their fear of falling.
Peters et al. (2014) USA Pre-Post N=10	**Population:** TBI; Median Age=35.4yr; Gender: Male=6, Female=2; Median Time Post Injury=9.9yr. **Intervention:** Participants went through 20 days of intensive mobility training (5 d/wk for 4wk). Sessions included gait training with body weight supported treadmill, balance activities, strength coordination, and range of motion training. **Outcome Measure:** Berg Balance Scale, Dynamic Gait Index (DGI), 10 Metre Walk Test (10MWT), 6 Minute Walk Test (6MWT), 30 sec Sit-to-Stand test, Timed Up and Go (TUG) test, Walking While Talking Test average errors/ alternating letters, Falls Efficacy Scale (FES), Quality of Life after Brain Injury, Global Rate of Change Scale, Fatigue.	1. The average session was 150.1±2.7min in length. 2. Fatigue scores ranged from 0 to 2.5 (out of 10) before sessions and 3 to 5.5 after sessions. 3. From pre-test to post-test, significant improvements were seen for the FES (p=0.01), DGI (p=0.049), 10MWT (p=0.03), TUG (p=0.01), and 6MWT (p=0.03). From pre-test to follow-up (3mo), significant improvements were sustained for the 10MWT (p=0.02) and the TUG (p=0.03).

Discussion

In an RCT study, Brown et al. (2005) randomized participants to either body weight supported treadmill training or conventional over-ground gait training. The authors reported that body weight supported treadmill training provided no additional benefit over conventional gait training in measures of ambulation following three months of training. Similarly, in another RCT, Wilson et al. (2006) randomized 40 patients with ABI to either standard physical therapy or physical therapy supplemented with partial body weight-bearing gait training. The authors reported that although each group made functional improvements, there were no significant between-group differences on measures of balance, ambulation, and mobility at the end of the 8-week training period (Wilson et al., 2006).

Esquenazi et al. (2013) compared robotic assisted treadmill training to manually assisted treadmill training for individuals with TBI and noted that while both interventions resulted in significant improvement in gait parameters, there were no differences between the two interventions for gait velocity, endurance, or mobility.

In an RCT, Clark et al. (2012) found that using body weight supported treadmill training combined with handrail support reduces the amount of center of mass displacement and movement instability. However, the authors noted that support alters timing and variability components of gait patterns. Although the study explored seven gait training methods, Clark et al. (2012) concluded that no one method provides the optimal stimulus and that combining various methods may be the most beneficial. In a pre-post study, Peters et al. (2014) found that intensive therapy using body weight supported treadmill training, balance activities, strength coordination, and range of motion activities improved walking speed and Timed Up and Go test scores in individuals with TBI.

In a cohort study, Anggelis et al. (2019), examined the use of dynamic body-weight support (DBWS) compared to standard care during in-patient rehabilitation and its effect on function, as measured by the Functional Independence Measure (FIM). The authors found significant improvements in the total FIM scores at discharge, compared to admission for both groups; however, the DBWS group showed significantly greater improvements on the motor subscale, compared to the standard of care group.

Conclusions

There is level 1b evidence (Wilson et al., 2006) that physical therapy with partial weight-bearing gait training may not improve ambulation, mobility, or balance compared to standard physical therapy in individuals with TBI.

There is level 2 evidence (Esquenazi et al., 2013) that robotic assisted body weight supported treadmill training may not improve ambulation or gait velocity compared to manually assisted treadmill training in individuals post ABI.

There is level 2 evidence (Brown et al., 2005) that body weight supported treadmill training may not improve ambulation or mobility compared to conventional gait training in individuals with TBI.

There is level 2 evidence (Clark et al., 2012) that body-weight-supported treadmill training combined with handrail support may reduce movement instability compared to other methods of training in individuals post ABI.

There is level 2 evidence (Anggelis et al., 2019) that dynamic body weight support gait training may improve motor function in individuals with TBI when compared to standard rehabilitation.

There is level 4 evidence (Peters et al., 2014) that Intensive Mobility Training may improve ambulation and mobility in individuals post ABI.

KEY POINTS

- Partial body weight supported gait training may not improve ambulation, mobility, or balance when compared to conventional gait training post ABI.
- Robotic assisted treadmill training may be similar to manually assisted treadmill training at improving gait speed and mobility post ABI.
- Dynamic body weight support gait training may improve motor function in individuals with TBI when compared to standard rehabilitation.
- Body-weight-support treadmill with handrail support may reduce movement instability compared to other methods of training in individuals post ABI.
- Intensive mobility training consisting of body-weight-supported treadmill, balance activities, strength coordination, and range of motion training may improve lower extremity motor function post ABI; however, more research is needed.

Multimodal Interventions

Multimodal interventions combine treatments to better evaluate rehabilitation options. Combining treatments allows multiple physical impairments to be targeted through a single program, while comparing them assists in determining the relative effect of each therapy for motor rehabilitation.

TABLE 9 | Multimodal Interventions for Lower Extremity Rehabilitation Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Canning et al. (2003) Australia RCT PEDro=7 N=22	**Population:** Severe TBI; Gender: Male=16, Female=6. *Experimental Group (n=12):* Mean Age=24.75yr; Mean Time Post Injury=75.25d. *Control Group (n=10):* Mean Age=25.6yr; Mean Time Post Injury=84.6d. **Intervention:** Patients were divided randomly into either a regular rehabilitation program group (control) group or the intervention group which received the rehabilitation program as well as 4wk of intensive training of sit-to-stand and step-up exercises. **Outcome Measure:** Sit-to-stand repetitions, Peak Oxygen Consumption (exercise capacity), Oxygen Consumption Workload Test (exercise efficiency).	1. The experimental group performed a mean of 87 repetitions of sit-to-stand and 42 repetitions of step-ups per working day. 2. The intervention group had a 62% improvement in the number of sit-to-stands performed in 3min (motor performance) compared to an 18% increase seen in the control group (p=0.03). 3. There were no significant between-group differences in the improvements made in exercise capacity (p=0.36) or efficiency (p=0.38). 4. The increase in exercise capacity for the intervention group was significant with an increase in VO_2peak from 0.75L/min to 1.14L/min (p<0.01).
Hirose et al. (2013) Japan PCT N=15	**Population:** TBI=8, Stroke=7; Gender: Male=11, Female=4. *Control Group (n=6)*: Mean Age=59.8yr. *Intervention Group (n=9):* Mean Age=49.9yr. **Intervention:** The control group received passive exercise and the intervention group received	1. There was a significant difference in the rate of atrophy between the EMS and control groups. The EMS group showed less atrophy in all 4 compartments (anterior and posterior thigh and leg) at day 14 (p<0.001).

Author Year Country Study Design Sample Size	Methods	Outcome
	Electrical Muscle Stimulation (EMS) weekly (30min with stimulation cycles of 10 sec) in addition to passive exercise for 6wk. **Outcome measure:** Rate of Atrophy.	2. At 6wk, the cross-sectional limb area was significantly different between groups. The EMS group showed less atrophy ($p<0.001$).
Williams et al. (2019) Australia PCT $N_{Initial}=22$, $N_{Final}=22$	**Population:** TBI=12; Mean Age=25.5±10.7yr; Gender: Male=10, Female=2; Mean Time Post Injury=374±486d; Severity: Mean PTA=57.8±25.9d. **Intervention:** Healthy participants and individuals with TBI completed a 6mo rehabilitation program focused on functional ballistic activities and task-specific practice to compare lower-limb joint mechanics during running. Outcome measures were assessed at baseline and 6mo follow-up. **Outcome Measures:** Average power absorbed and generated at the hip, knee, and ankle joints during stance.	1. When compared to healthy controls, those with TBI ran with greater average power absorption at the hip (-.27W/kg versus -61W/kg; $p<.05$), reduced average power absorption at the knee (-2.03W/kg versus -1.02W/kg; $p<.05$) and reduced average power generation at the ankle (2.86W/kg versus 2.06W/kg; $p<.05$). 2. Only average power generation at the ankle improved following six months of rehabilitation for the participants with TBI (2.06W/kg versus 2.79W/kg; $p<.05$).

Discussion

Studies in this subset of lower extremity motor rehabilitation have evaluated diverse interventions. In an RCT, Canning et al. (2003) compared the addition of an intensive sit-to-stand training program to a traditional rehabilitation program. The experimental group demonstrated an increased ability to repeat sit-to-stand movements within a defined time frame in comparison to the traditional rehabilitation group; however, there were no differences between groups in terms of the observed improvements in exercise capacity or efficiency.

In a PCT study, Hirose et al. (2013) compared passive exercise to electrical muscle stimulation (EMS) to determine the effects of EMS on muscle atrophy in the lower limbs. The authors found that the use of EMS was associated with a significant reduction in atrophy when compared to passive exercise alone.

In a PCT, Williams and Schache (2019) investigated the efficacy of a 6-month rehabilitation program focusing on functional ballistic activities and task-specific practice on deficits identified in biomechanical variables during running. It was found that the average power generation at the ankle improved for the participants with TBI following the intervention period. The authors noted that, compared to healthy controls, participants with TBI ran with greater average power absorption at the hip, reduced average power absorption at the knee, as well as reduced average power generation at the ankle (Williams & Schache, 2019).

Conclusions

There is level 1b evidence (Canning et al., 2003) that sit-to-stand training combined with usual rehabilitation may improve motor performance in sit-to-stand tasks compared to usual rehabilitation alone in individuals post ABI.

There is level 2 evidence (Hirose et al., 2013) that electrical muscle stimulation with passive exercise may reduce lower extremity muscle atrophy compared to passive exercise alone in individuals post ABI.

There is level 2 evidence (Williams et al., 2019) that motor rehabilitation may improve high-level mobility and ankle joint mechanisms during running in individuals with severe TBI.

KEY POINTS

- Sit-to-stand training and Intensive Mobility Training may improve lower extremity motor function post ABI.
- Electrical muscle stimulation together with passive exercise may improve lower extremity muscle atrophy post ABI.
- Motor rehabilitation may improve high-level mobility and ankle joint mechanics during running in individuals with severe TBI.

Virtual Reality for Lower Extremity Rehabilitation

Virtual Reality (VR) has gained popularity in recent years with the introduction of commercially available programs and video game consoles. Virtual Reality (VR) usually involves the use of immersive, interactive, three-dimensional environments created by a computer; in the rehabilitation context, VR can be used to offer engaging rehabilitation activities in a controlled environment (Aida et al., 2018). VR offers the opportunity to practice real-life meaningful tasks in highly customizable systems; these may be immersive, semi-immersive, or non-immersive, depending on the level of user perception and the display of the virtual environment (e.g., through a head-mounted display or using basic desktop displays) (Brassel et al., 2021).

TABLE 10 | Virtual Reality Interventions for Lower Extremity Rehabilitation Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Fusco et al. (2022) Italy RCT Crossover PEDro=5 N_{Inital}=24 N_{Final}=23	**Population:** Virtual Reality-Non-Virtual Reality (VR-NVR): TBI=2, ABI=10; Mean Age=54.7yr; Gender: Male=8, Female=4; Time-Post Injury=20.7mo; Severity: Severe. Non-Virtual Reality-Virtual Reality (NVR-VR): TBI=3; ABI=8; Mean Age=58.6yr; Gender: Male=5, Female=6; Time Post-Injury=39.6mo. Severity: Severe.	1. After 4 weeks of training, both groups (VR-NVR and NVR-VR) significantly improved their functional impairment on all three scales (p<.001). 2. The VR-NVR group showed significant improvements in all outcome measures at the end of the second week (T1).

Author Year Country Study Design Sample Size	Methods	Outcome
	Intervention: Participants were randomized into two groups: VR-NVR (N=12) and NVR-VR (N=11). The VR-NVR underwent a 2-week rehabilitation for the lower limbs training with a robotic device (Omego®) with VR feedback, followed by 2 weeks without VR; NVR-VR performed the protocol in the opposite order. **Outcome Measures:** Level of Cognitive Functioning (LCF), Disability Rating Scale (DRS), Motricity Index for Lower Limb (MI-LL).	3. The NVR-VR group only showed improvements in the MI.
Tefertiller et al. (2019) USA RCT PEDro=5 N_{Inital}=63 N_{Final}=58	**Population:** TBI; Virtual Reality (VR) group (n=31); Mean Age = 48.1yr; Gender: Male=23, Female=8; Mean Time Post Injury= 8.3yr; and Traditional Home-based Exercise Program (HEP) group (n = 32); Mean Age = 49.5yr; Gender: Male=16, Female=16; Mean Time Post Injury=8.5yr. **Intervention:** Participants were randomized into two groups, Virtual Reality (VR) and Traditional Home-based Exercise. The VR program included Xbox system Kinect games that focused on dynamic standing activities. **Outcome Measures:** Community Balance and Mobility Scale (CB&M), Balance Evaluation Systems Test (BESTest), Activities-Specific Balance Confidence Scale (ABC), Participation Assessment with Recombined Tools-Objective (PART-O).	1. No significant differences were found in the Community Balance and Mobility Scale (CB&M) between groups. 2. No significant differences were found in any of the secondary outcomes: Balance Evaluation Systems Test (BESTest), Activities-Specific Balance Confidence Scale (ABC), Participation Assessment with Recombined Tools-Objective (PART-O). 3. Significant improvements in balance were observed in both groups over a 24-week period. 4. Results suggested that VR training is not more beneficial than a Traditional HEP for improving balance in individuals with moderate to severe TBI.
Straudi et al. (2017) Italy RCT PEDro=5 N_{Inital}=21 N_{Final}=20	**Population:** Chronic TBI; VGT group: Mean Age=30.5yr; Gender: Male=10, Female=2; Mean Time Post Injury=2yr; BPT group: Mean Age=37yr; Gender: Male=7, Female=2; Mean Time Post Injury=8yr. **Intervention:** Participants were randomized into two groups: Video Game Therapy (VGT) using the Xbox Kinect system or Balance Platform Therapy (BPT) for three sessions per week for 6 weeks. **Outcome Measures:** Community Balance and Mobility Scale (CB&M), Unified Balance Scale (UBS), Timed Up and Go test (TUG), selective visual attention evaluation (Go/Nogo task).	1. Both groups improved in CB&M scores, but only the VGT group increased on the UBS and TUG with a between-group significance ($p < 0.05$). 2. Selective attention improved significantly in the VGT group ($p < 0.01$). Dynamic balance and overall mobility improved after training.
Cuthbert et al. (2014) USA RCT PEDro=6 N=20	**Population:** TBI; Median Age at Injury=31.5yr (IQR 23-56); Gender: Male=13, Female=7; Range of Time Post Injury=24-122d. **Intervention**: Participants were randomly assigned to either Extra Standard Balance Care (ESC; n=10) (standard physical therapy) or Virtual Reality (VR) balance therapy (n=10) using the Nintendo Wii. Both groups received standard physical therapy 4x/wk. The ESC group had an additional 15min of balance-specific therapy and the VR therapy group had 15min of balance training using the Wii Fit.	1. There was no statistically significant difference between therapy groups on PACES scores at mid-treatment (p=0.59) or at treatment completion (p=0.34). 2. The VR therapy group had a significant improvement on the BBS over time (0.19 points per day, p=0.03); however, there were no significant between group differences (VR therapy had a 1.13-point higher improvement than the ESC group, p=0.70).

Author Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measure: Physical Activity Enjoyment Scale (PACES), Berg Balance Scale (BBS), Functional Gait Assessment (FGA).	3. Within group improvements were found on the FGA (ESC=0.20, p=0.01 and VR therapy=0.23, p<0.01); however, there were no statistically significant differences found between groups (p=0.73).
Foo et al. (2013) Australia Post-Test N=20	**Population:** TBI=11, Tumour=3, Stroke=2, Cerebral Palsy=2, SCI=1, Anoxic Brain Injury=1; Mean Age=43.3yr; Gender: Not Reported; Mean Time Post Injury=23.3mo. **Intervention:** Participants completed two tasks (static standing and sit-to-stand) three times each, with and without visual feedback. Feedback was provided using the Wii Balance Board. **Outcome measure:** Weight-bearing Asymmetry.	1. During the static balance task, weight-bearing asymmetry was significantly reduced with visual feedback (p=0.005). 2. There was no significant difference with visual feedback for the dynamic test (p=0.737); however, those with higher weight-bearing asymmetry were the most responsive to feedback.

Discussion

In an RCT crossover, Fusco et al. (2022) examined the effectiveness of VR combined with lower limb robotic training to enhance functional recovery in individuals with severe ABI. The authors found significant improvements in motricity of the lower limb, particularly for those who received the virtual reality intervention first.

In an RCT, Tefertiller et al. (2019) randomized participants into two groups, a virtual reality program that included Xbox system games addressing dynamic balance and a traditional home-based exercise program. The authors found no significant differences in the Community Balance and Mobility Scale or in secondary outcomes. Similarly, Cuthbert et al. (2014) found that there were no significant differences between participants who received virtual reality-based balance therapy using a Nintendo Wii system and those who received standard physical therapy.

In an RCT, Straudi et al. (2017) randomized participants into video game therapy or balance platform therapy groups. Participants in both groups improved, but those who received video game therapy showed improved balance and overall mobility to a greater extent. In a post-test study by Foo et al. (2013), participants completed two tasks, static standing and sit-to-stand with and without visual feedback provided using a Wii balance board. The authors found that during static balance tasks, visual feedback provided using a Wii Balance board helped reduce weight-bearing asymmetry.

Conclusions

There is level 1b evidence (Cuthbert et al., 2014) that virtual reality-based therapy using a Nintendo Wii system may not be more effective for the rehabilitation of lower extremity function post TBI than standard physical therapy.

There is level 2 evidence (Fusco et al., 2022) that semi-immersive virtual reality combined with a robotic device may facilitate lower limb functional recovery in individuals with severe ABI.

There is level 2 evidence (Tefertiller et al., 2019) that virtual reality using an Xbox system may noy be more effective for the rehabilitation of balance post TBI than traditional home-based exercise.

There is level 2 evidence (Straudi et al., 2017) that video game therapy with the Xbox Kinect system may improve balance in individuals with TBI.

There is level 4 evidence (Foo et al., 2013) that visual feedback using a Wii balance board may reduce weight-bearing asymmetry in the lower extremities post ABI.

KEY POINTS

- Virtual reality-based therapy using a Nintendo Wii, or an Xbox system may not be more effective for the rehabilitation of lower extremity function and balance, when compared to standard physiotherapy or home exercise.
- Virtual reality combined with a robotic device may facilitate lower limb functional recovery post severe ABI.

Combined Upper and Lower Extremity Interventions

Some studies evaluated interventions that addressed both the upper and lower extremity motor impairments in individuals with brain injuries. Although these combined studies may more closely approximate real-life rehabilitation contexts, conducting methodologically sound research in this area is challenging due to the inherent differences in upper and lower extremity function and this outcome measures.

Virtual Reality for Upper and Lower Extremity Rehabilitation

Virtual Reality (VR) has gained popularity in recent years with the introduction of commercially available programs and video game consoles. Virtual Reality (VR) usually involves the use of immersive, interactive, three-dimensional environments created by a computer; in the rehabilitation context, VR can be used to offer engaging rehabilitation activities in a controlled environment (Aida et al., 2018). VR offers the opportunity to practice real-life meaningful tasks in highly customizable systems; these may be immersive, semi-immersive, or non-immersive, depending on the level of user perception and the display of the virtual environment (e.g., through a head-mounted display or using basic desktop displays) (Brassel et al., 2021).

TABLE 11 | Virtual Reality Interventions for Upper and Lower Extremity Rehabilitation Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Ustinova et al. (2014) USA Pre-Post N=30	**Population:** TBI; Mean Age=30.6yr; Gender: Male=10, Female=5; Mean Time Post Injury=6.1yr. **Intervention:** Participants had completed physical therapy previously and had reached a plateau. All participants received virtual reality (VR) therapy which was a series of games that re-trained whole-body coordination, posture, and gait. All games allowed for advancement into more difficult levels. Therapy was a total of 15 sessions, each 50-55 min (typically 2-3 sessions/wk, over 5-6wk). **Outcome Measure:** Berg Balance Scale (BBS), Functional Gait Assessment (FGA), Functional Reaching Test (FRT).	1. BBS scores increased by a mean of 4.5 points (45.6±5.15 to 50.2±4.4, p<0.01). 2. FGA scores improved by a mean of 4.6 points (20.3±5.6 to 24.9±4.6, p<0.05). 3. FRT scores increased by a mean reaching distance of 2.3 inches (12.5±2.3 to 14.8±2.3, p<0.01).
Schafer & Ustinova (2013) USA PCT N=30	**Population:** TBI=15, Healthy Controls=15. *TBI Group (n=15)*: Mean Age=35.3yr; Gender: Male=6, Female=9; Mean Time Post Injury=6.6yr; *Control Group (n=15)*: Mean Age=33.4yr; Gender: Male=7, Female=8. **Intervention:** Participants completed reaching activities in a physical environment (PE; reach to the farthest point possible) and a virtual environment (VE; touching furthest flower seen on the screen with hand avatar). VE touches were done from 50° and 10° angles. In each setting, three reaches were completed with the dominant hand. **Outcome measure:** Centre of Mass (COM) Displacement, Endpoint Displacement Amplitude, Movement Time, Peak Velocity.	1. The control group showed greater endpoint displacement amplitude (p<0.01) and COM displacement (p<0.01) than the TBI group. 2. Reaches were performed more slowly among participants with TBI, but the difference between groups was not significant (p>0.05). 3. Reaching amplitude was ~9% further for both groups in the VE than the PE (p<0.05). 4. For both groups, reaches were farther in the PE after performing in the VE. The TBI group increased their reach by ~5% (p<0.05).

Discussion

In a pre-post study, Ustinova et al. (2014) examined the effectiveness of virtual reality therapy that included a series of games that addressed whole-body coordination, gait and posture. The authors found that participants showed significant improvements for balance and dynamic stability following VR therapy. In a PCT study, Schafer and Ustinova (2013) compared reaches in the physical environment after having participants with TBI and controls practice reaches in a virtual environment. The authors found that reaching distances in the physical environment increased for both groups, but a greater effect was noted among those with TBI.

Conclusions

There is level 2 evidence (Schafer & Ustinova, 2013) that reaching activities performed in a virtual environment may lead to improvements in reaching in a physical environment in individuals with TBI.

There is level 4 evidence (Ustinova et al., 2014) that virtual reality therapy may improve whole-body balance, gait, and functional reaching in individuals post TBI.

KEY POINTS

- Virtual reality therapy may improve balance, gait and reaching in individuals post ABI; however, it may not be more effective than conventional physiotherapy programs.

Yoga

Yoga is a practice that promotes the unity of mind and body. It involves the use of meditation, slow and synchronized poses, as well as breathing to influence spiritual well-being, physical and mental health (Green et al., 2019). Yoga has been used in the rehabilitation of individuals with stroke, dementia, and cancer as well as in the treatment of sleep disorders and depression (Wen et al., 2022). There is limited evidence on the use of yoga for motor impairment post ABI.

TABLE 12 | Yoga for Motor Rehabilitation Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Schmid et al. (2016) USA Pre-post N=3	**Population:** TBI; Mean Age=44.33yr; Gender: Male=1, Female=2; Time Post Injury=19.33yr. **Intervention:** One-on-one yoga with a therapist. Therapy included 1-h sessions twice a week for 8 weeks. **Outcome Measures:** Berg Balance Scale (BBS), the Activities Balance Confidence scale (ABC), the PEG (measure of pain), cervical Range of motion (ROM), chair-to-stand test and 6-min/10-min walk to assess gait.	1. All three study participants had baseline BBS scores of ≤46, indicating impaired balance and increased fall risk. 2. After the 8-week intervention, two individuals improved their BBS score to be >46, indicating improved balance. All three participants improved their balance, with average BBS scores improving by 36% from 34± 9.6 to 46.3± 5.5. Average ABC scores increased by 39%. 3. On average, pain interference scores decreased by 6% (5.1±1.26 to 4.8±2.67). 4. All three participants increased left and right cervical rotation and lateral flexion. 5. Gait-speed, as measured with the 10-min walk test, increased by an average of 19% from 1.08± 0.73 m/s to 1.28±0.78 m/s,. 6. Yoga is feasible and safe for individuals with chronic TBI, and it may bring benefits in physical functioning.

Discussion

Schmid et al. (2016) examined the effectiveness of one-on-one yoga sessions on multiple outcome measures in 3 participants. Each session lasted one hour, and yoga postures involved the use of the whole body. The authors found that the yoga program resulted in improvements in balance, pain, cervical range of motion and gait speed. Further research with larger samples is necessary to determine the effectiveness of this intervention.

Conclusions

There is level 4 evidence (Schmid et al., 2016) that yoga may improve balance, pain, cervical range of motion and gait speed in individuals with TBI; however, more research is needed.

KEY POINTS

- Yoga may be effective for the rehabilitation of motor impairment in individuals with TBI; however, more research is needed.

Exercise Programs

Individuals with ABI may experience prolonged immobility and resultant cardiovascular changes cardiovascular changes, muscular atrophy, and loss of lean body mass (Boake et al., 2000). Aerobic exercise is often used to improve these and other outcomes such as fatigue, in healthy populations, and has numerous evidence-based health benefits (Warburton & Bredin, 2017). General aerobic training programs have been found to improve balance, gait, and physical fitness in persons with brain injury (Dault & Dugas, 2002; Ustinova et al., 2015). Additional research on the impact of exercise programs on outcomes in persons with ABI is reviewed in this section.

TABLE 13 | Aerobic Training for Motor Rehabilitation Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Hassett et al. (2012) Australia RCT PEDro=6 N=40	**Population:** Severe TBI=40; Experimental Group (n=20): Mean Age=39yr; Gender: Male=14, Female=6; Mean Time Post Injury=3.7mo. Control Group (n=20): Mean Age=29yr; Gender: Male=13, Female=7; Mean Time Post Injury=3.1mo. **Intervention:** All participants wore a heart rate monitor and attended a 1hr circuit class 3/wk which included 10 workout stations, an abdominal exercise portion and a walk for 6min. The experimental group received encouragement from a physiotherapist and had their heart rate monitor uncovered which beeped when they did not reach their target heart rate. Those	1. Participants spent <20min in their heart rate training zone (mean 13min, SD 14) and expended >300kcal (mean 377kcal, SD 137). 2. For the class, the exercise intensity was low (mean heart rate reserve of 34.3%, SD 16.7) but the duration of exercise was long (mean of 52.1min, SD 3.1). 3. For time spent in the heart rate training zone, the experimental group (mean 10.9min, SD10.8) performed better than the control group (mean 6.1min, SD7.5) but this

Author Year Country Study Design Sample Size	Methods	Outcome
	in the control group did not receive encouragement and had their heart rate monitor covered and muted. **Outcome Measure:** Duration of Time spent in Heart Rate Target Zone.	was not significant (mean difference 4.8min, p>0.05).
Hoffman et al. (2010) USA RCT PEDro=5 N=80	**Population:** TBI; Exercise Group (n=40): Mean Age=39.7yr; Gender: Male=15, Female=25. Control Group (n=40): Mean Age=37.1yr; Gender: Male=20, Female=20. **Intervention:** Participants were randomly assigned to the exercise or control group. The 10wk community-based exercise intervention consisted of supervised aerobic exercise (1/wk) involving 30min of aerobic exercise. Participants were also instructed to complete aerobic exercise at home (30min, 4x/wk). The control group was waitlisted. **Outcome Measure:** Borg Scale of Perceived Exertion, Brief Pain Inventory, Beck Depression Inventory (BDI), SF-12 Health Survey (SF-12), Perceived Quality of Life Scale (PQOL), Craig Handicap Assessment and Reporting Technique-Short Form (CHART-SF).	1. The exercise intervention group reported exercising more days of the week than the control group (3.68 versus 2.05, p=0.004); however, the increase in minutes per week of exercise was not significantly different between groups (p=0.064). 2. The exercise group also reported less pain interference (p=0.021) and greater improvement on the Brief Pain Inventory (p=0.031) in comparison to the control group. 3. Post-hoc analyses compared highly active (>90min/wk) and low activity (<90min/wk) participants, regardless of initial grouping. Highly active participants reported significantly more community activity on the CHART-SF (p=0.028), greater PQOL scores (p=0.034) and greater SF-12 general mental health scores (p=0.024) than the low activity group. 4. The highly active group scored lower on the BDI after the 10wk intervention than the low active group (p=0.033).

Author Year Country Study Design Sample Size	Methods	Outcome
Hassett et al. (2009) Australia RCT PEDro=7 N=62	**Population:** Severe TBI; Fitness Center Group (n=32): Mean Age=35.4 yr; Gender: Male=27, Female=5; Median Time Post Injury=2.6 mo. Home-Based Group (n=30): Mean Age=33 yr; Gender: Male=26, Female=4; Median Time Post Injury=2.3 mo. **Intervention:** Participants were randomly assigned to either an exercise intervention group at a fitness-center or to a home-based exercise group. Fitness center participants were supervised by a personal trainer (1hr, 3x/wk, 12wk), whereas the home-based exercise group followed an exercise plan prescribed before discharge and were monitored by a physiotherapist. Assessment at baseline, end of intervention and 3mo follow-up. **Outcome Measure:** Modified 20-metre Shuttle Test (MST), Depression Anxiety Stress Scale, Profile of Mood States (POMS), Sydney Psychosocial Reintegration Scale (SPRS), Brain Injury Community Rehabilitation Outcome.	1. On average, the fitness center group had better adherence than the home-based group (77% versus 44%, p≤0.001). The fitness center group completed a mean of 2.4 sessions/wk compared to the home group who completed 0.5 sessions/wk. 2. At the end of the program, both groups improved their fitness levels on the MST; however, there were no significant differences between groups (p>0.05). 3. Those in the fitness centre group achieved a significantly greater percentage of goals at the end of the intervention (76% versus 52%, p=0.005), but this difference diminished at follow-up (p=0.650). 4. No significant differences were noted when comparing psychosocial functioning or community integration measures between groups except for the POMS Confusion-Bewilderment (p=0.007) and the SPRS Living Skills (p=0.009) subscales at the end of intervention only, with greater improvements in the fitness center group.
Hassett et al. (2011) Australia RCT follow-up N=30	**Population:** Severe TBI=30; Mean Age=33yr; Gender: Male=26, Female=4; Mean Time Post Injury=2.3mo. **Intervention:** An in-home exercise program (36 sessions over 12wk) was completed in a previous study. Participants were then retrospectively divided into adherers (n=10) and non-adherers (n=20) and compared. **Outcome Measure:** Modified 20-metre Shuttle Test, Wechsler Memory Scale III, Wechsler Adult Intelligence Scale III, Controlled Oral Word Association Test, Depression Anxiety and Stress Scale.	1. Non-adherers were significantly younger than adherers (30 versus 39yr, p=0.04). 2. Results indicate that a greater number of participants in the adherence group reported walking or jogging pre-injury compared to non-adherers (7 versus 5, p≤0.05). 3. A greater portion of adherers had extremely severe injuries compared to non-adherers (90% versus 50%, p≤0.05). 4. There were no significant differences between groups on any of the cognitive functioning or psychological health measures.

Author Year Country Study Design Sample Size	Methods	Outcome
Driver et al. (2006) USA RCT PEDro=4 N=18	**Population:** TBI; Exercise Group (n=9): Mean Age=37.8yr; Gender: Male=5, Female=4; Mean Time Post Injury=40.3 mo. Control Group (n=9): Mean Age=35.5yr; Gender: Male=5, Female=4; Mean Time Post Injury=41.2 mo. **Intervention:** Participants were randomly assigned to either an 8wk aquatic exercise program involving 1hr sessions 3x/wk consisting of aerobic and resistance training or to a control group that received 8wk of vocational rehabilitation class to improve reading and writing skills. **Outcome Measure:** Health Promoting Lifestyle Profile II (HPLP-II), Physical Self-Description Questionnaire (PSDQ).	1. The exercise group experienced significant improvements on the health responsibility, physical activity (both $p<0.05$), nutrition, spiritual growth (both $p<0.01$), and inter-personal relationships ($p<0.001$) subscales of the HPLP-II after the intervention, but not the stress management subscale. The control group showed no significant improvements on any of the subscales ($p>0.05$). 2. At the end of the program, the aquatic exercise group showed significant improvements on the self-esteem, co-ordination, body fat, strength, flexibility, and endurance sub-scales of the PSDQ (all $p<0.001$). The control group showed no significant improvements on any of the subscales. No between-group calculations were completed.
Bateman et al. (2001) UK RCT PEDro=7 N=157	**Population:** TBI=44, Stroke=70, Subarachnoid Hemorrhage=15, Other=28; Gender: Male=97, Female=60. Training Group (n=79): Mean Age=41.7yr; Mean Time Post Injury=22.2 wk. Control Group (n=79): Mean Age=44.7yr; Mean Time Post Injury=25.5wk. **Intervention:** Participants were divided to receive either an exercise intervention (intervention group, cycle training) or relaxation training (control group). The interventions were 30 min sessions, 3x/wk for 12 wk. **Outcome Measure:** Peak Work Rate, Berg Balance Scale, Rivermead Mobility Index (RMI), Barthel Index, Functional Independence Measure (FIM), Nottingham Extended Activities of Daily Living (NEDLI).	1. The mean increase in peak work rate from baseline to 12wk was 25.8W and 11.7W for the intervention and control groups, respectively ($p=0.02$). 2. No significant differences were found between groups on the Berg Balance Scale, RMI, or the Barthel Index. 3. There was a trend towards significance, with the control group making greater improvements on the Berg Balance scale ($p=0.06$) and RMI ($p=0.07$) than the intervention group. 4. Greater FIM gains and improvements on the NEADLI were found for the control group between 12 and 24wk ($p<0.05$) compared to the intervention group.
Ding et al. (2022) USA PCT N=20	**Population:** TBI; AET (n=10); Mean Age=58yr; Gender: Male=8, Female=2; Mean Time Post Injury=6.2yr; SAT (n=10); Mean Age=58.1yr; Gender: Male=9, Female=1; Mean Time Post Injury=6.9yr. **Intervention:** A 3-month individualized exercise program. One in-person training session on the Personalized Mobile Trainer (PMT) and an individualized exercise prescription, followed by either aerobic exercise training (AET) or stretching and toning (SAT) performed at home. The PMT system was comprised of a workout app (TBICare), chat app (TBICare Chat), and a Cloud-based Provider Portal. **Outcome Measures:** 6-Minute Walk Test (6MWT), Exercise Compliance.	1. Five out of 10 participants in the AET group had improved exercise endurance with 4.6–7.1% increase in the 6MWT. In comparison, in the SAT group, two participants improved on the 6MWT (5% and 25.8%). 2. No significant correlation was noted between compliance and improvement on 6MWT in either group. 3. There were no significant changes in exercise endurance in either group.

Author Year Country Study Design Sample Size	Methods	Outcome
Charrette et al. (2016) USA Pre-Post $N_{Initial}$=16, N_{Final}=14	**Population:** TBI=9, Stroke=3, Tumour=1, Encephalopathy=1; Mean Age=44.8yr; Gender: Male=12, Female=2; Mean Time Post Injury=20.5yr; Injury Severity: Moderate-Severe. **Intervention:** Participants took part in an intensive exercise program consisting of endurance, full-body strength, stretching, and balance exercises (3d/wk for 6wk). Assessments took place at baseline, 6wk (exercise completion) and 12wk (follow-up). **Outcome Measure:** 6-Minute Walk Test (6MWT), High Level Mobility Assessment Tool (HiMAT), 10-Metre Walk Test (10MWT).	1. There was a significant increase in distance walked from baseline (431ft) to 6wk (1016ft) and 12wk (712ft) during the 6MWT ($p<0.05$). 2. There was a significant increase in mobility from baseline (3.5) to 6wk (9) and 12wk (8) on the HiMAT ($p<0.05$). 3. There was a significant increase in gait velocity from baseline (0.59m/s) to 6wk (1.11m/s) and 12wk (1.10m/s) measured by the 10MWT ($p<0.05$).
Damiano et al. (2016) USA Case Control $N_{Initial}$=31, N_{Final}=24	**Population:** TBI; *TBI group* (n=12); Mean Age=31.3yr; Gender: Male=7, Female=5; Time Post Injury>6 mo. *Healthy Participants* (n=12); Mean Age=32.5yr; Gender: Male=7, Female=5. **Intervention:** Participants with TBI followed a home-based exercise program with an elliptical (30 min 5d/wk for 8wk). Resistance was added progressively each week. Controls did not complete the exercise intervention. Assessments were completed at baseline, and at 8wk follow-up. **Outcome Measure:** Limits of Stability Test (LOS), Motor Control Test (MCT), High-Level Mobility Assessment Tool (HiMAT), Hamilton Depression Inventory (HAM-D), Sensory Organization Test, Gait, Cadence, Dual-Task performance (DT), Hopkins Verbal Learning Test-Revised (HVLT-R), Finger Tapping Test (FTT), Pittsburgh Sleep Quality Index (PSQI), Beck Anxiety Inventory, PTSD Checklist-Civilian Version (PCL-C).	1. There was a significant difference in LOS between the TBI group and controls in 2 directions; backwards (TBI=71.6%, HV=89.3%, p=0.042) and left (TBI=37%, HV=49.6%, p=0.037). 2. The TBI group had a significantly poorer DT performance on both motor (p=0.047) and cognitive (p=0.045) tasks when compared to controls. 3. The TBI group performed significantly worse than controls on HVLT-R (p=0.004), PCL-C (p=0.02) and HAM-D (p=0.04). 4. Within the TBI group, maximal movement during the LOS test had a strong relationship with HVLT-R total recall (r=0.74, p=0.008) and delayed recall (r=0.81, p=0.003) and was related to fewer depressive symptoms (r=-0.63, p=0.04). 5. Within the TBI group, slower walking velocity and slower FTT was related to higher depression scores (r=-0.65, p=0.03 & r=-0.72, p=0.04, respectively). FTT was also related to poorer sleep quality (r=-0.75, p=0.048). 6. Within the TBI group, poorer DT performance was related to higher anxiety (r=0.71, p=0.02). 7. MCT and LOS improved following 8 wk of exercise and did not change at follow-up aside from increased LOS forward endpoint excursion (p=0.001).
Ustinova et al. (2015) USA	**Population:** TBI; Mean Age=29.2yr; Gender: Male=13, Female=9; Mean Time Post Injury=23.6mo; Mean GCS=11.2. **Intervention:** Participants completed a therapeutic exercise program supervised by a physical therapist	1. There was a significant improvement in static and dynamic balance from pre to post intervention on the BBS (45.2 versus 49.2, p=0.011).

Author Year Country Study Design Sample Size	Methods	Outcome
Pre-Post N=22	designed for retaining whole-body coordination, posture, and gait. The program included twenty 30-40 min sessions, increasing to 55-60 min as the participant became more comfortable (4-5d/wk for 4-5wk). **Outcome Measure:** Berg Balance Scale (BBS), Functional Independence Measure (FIM), Functional Gait Assessment (FGA), Ataxia Scale.	2. There was a significant improvement in gait, as measured by the FGA, from pre to post intervention (22.8 versus 26.9, p=0.009). 3. Ataxia symptoms significantly decreased from pre to post intervention (7.3 versus 5.9, p=0.012) 4. There was no significant difference between pre and post intervention on FIM.
Chin et al. (2015) USA Pre-Post N=10	**Population: TBI;** Mean Age=32.9yr; Gender: Male=4, Female=6; Mean Time Post Injury=6.6yr; Severity: Mild=5, Moderate=4, Severe=1. **Intervention:** All participants underwent a supervised exercise training program with each session performed on a treadmill (30min 3d/wk for 12wk). The goal was to complete 30 minutes of continuous exercise at a target heart rate (HR) calculated from baseline measures. **Outcome Measure:** Treadmill Time, Oxygen Consumption (VO2), Work Rate (WR), Heart Rate (HR), Respiratory Exchange Ratio (RER), and Fatigue Severity Scale (FSS).	1. There was a significant increase in treadmill time after training at both peak exercise (16.4 versus 17.8 min; p<0.001) and submaximal exercise (9.3 versus 11.0 min; p<0.001). 2. There was a significant increase in VO2 after training at both peak exercise (37.1 versus 40.2 mL/kg/min; p=0.002) and submaximal exercise (18.9 versus 22.5 mL/kg/min; p<0.001). 3. There was a significant increase in WR after training at both peak exercise (324 versus 383 W; p=0.002) and submaximal exercise (123 versus 160 W; p=0.007). 4. There was no significant difference in HR (p=0.369) or RER (p=0.448) between pre and post exercise. 5. There was a significant reduction (less fatigue) in FSS scores after training (4.1 versus 3.2; p=0.029).
Corral et al. (2014) Spain PCT $N_{Initial}$=21, N_{Final}=17	**Population:** TBI; Mean Age=35yr; Gender: Male=17, Female=0; Time Post Injury>1yr; Mean GCS=6.8. **Intervention:** Participants were assigned to 1 of 4 groups: 1) Exercise electro-stimulation group (EEG; n=5; exercise sessions 5d/wk, electro-stimulation 2x20min periods per session), 2) Cycling group (CyG; exercise sessions 3d/wk), 3) Intermittent-hypobaric-hypoxia (IHH) and muscle electro-stimulation group (HEG; n=6; IHH 2h 2d/wk, electro-stimulation 3h 3d/wk) or 4) Control group (CG; n=5; cognitive activities 1h 1d/wk). All groups continued sessions over 12wk. **Outcome Measure:** Rey Auditory Verbal Learning Test (RAVLT), Trail Making Test A & B (TMT A & B), Stroop Test, Wechsler Adult Intelligence Scale (WAIS III), Barcelona Test, Tower of London Test (ToL), Reduced Paced Auditory Serial Addition Test (PASAT-G), Physical Stress Rest & VO2 Uptake, and Circulating Progenitor Cell (CPC) levels.	1. There were no significant within group differences found for any of the psychological tests (RAVLT, TMT-A & B, Stroop, WAIS III, Barcelona and ToL). 2. The EEG group showed improvement in VO2 uptake and CPC levels. 3. CyG group showed a significant difference in VO2 uptake after 12wk (2.2 versus 2.67 L/min; p=0.043), as well as an improvement on the PASAT-G test. 4. HEG group showed a significant improvement in stress test load (200 versus 218 W; p=0.043); however, there was no significant change in CPC levels. 5. CG showed no significant change on any outcome measure.

Author Year Country Study Design Sample Size	Methods	Outcome
Bhambhani et al. (2005) Canada Post-Test N=14	**Population:** TBI; Mean Age=31.8yr; Gender: Male=10, Female=4; Mean Time Post Injury=17.4mo; Mean GCS=4.6. **Intervention**: Participants took part in a 12wk circuit training program consisting of 32 sessions, 60min each, designed to enhance muscular strength and aerobic fitness. Five evaluations (T1-T5) were administered during the study period. The circuit training program began at T3. **Outcome Measure:** Vo2 Levels, Peak Heart Rate, Power Output, Exercise Time, Body Mass Index, and Basal Metabolic Rate.	1. No significant changes were observed in the body mass, basal metabolic rate, or body fat percentage during the study. 2. There were significant increases in peak values of power output, oxygen uptake, and ventilation rate (p values not listed).
Dault & Dugas (2002) Canada PCT N=8	**Population:** TBI; Mean Age=29.6yr; Gender: Male=6, Female=2; Mean Time Post Injury=44.4mo. **Intervention:** An individualized 12wk training program (TP; n=5) combining aerobic dance, and slide and step training for 30 min, 2x/wk was compared to traditional muscular training (TMT; n=3) for 60min, 2x/wk for 12wk. **Outcome Measure:** Test for Sensory Interaction in Balance (CTSIB).	1. Significant pre- and post-training differences were found in the temporal delay for the wrist ($p<0.01$), knee improvement ($p<0.001$), and sway area ($p<0.05$) for the TP group; no significant changes were noted for the TMT group. 2. The temporal delay in the wrist was 83ms in the TP group and 13ms in the TMT group.

Discussion

The available evidence suggests that aerobic training programs may have a positive effect on various outcome measures, including motor rehabilitation, in individuals with ABI. Numerous studies of varying methodologies established benefits from participation in exercise programs. In a pre-post study, Charrette et al. (2016) examined the effectiveness of an intensive exercise program, consisting of endurance and full body strength training. The authors found that an intensive combination of interventions improved gait distance and velocity, as well as mobility (Charrette et al., 2016). Aquatic exercise was also found to improve coordination, body fat, strength, flexibility and endurance, as well as self-esteem (Driver et al., 2006).

In an RCT, Hassett et al. (2009) found that individuals assigned to exercise programs showed significant improvements in their cardiorespiratory fitness levels regardless of where they worked out (in a gym or at home) or how often (2.4 sessions per week versus 0.5 sessions per week). Both groups, regardless of treatment condition, significantly improved on the shuttle test. In this study, those with greater adherence were found to be older, with more severe injuries, and had exercised before the injury

(Hassett et al., 2011). In a case control study, Damiano et al. (2016) found that lower extremity stability improved in persons with TBI over 8 weeks of exercise therapy.

Several studies demonstrate benefits of an exercise program on cardiorespiratory or psychological outcomes, but not motor outcomes. In an RCT, Bateman et al. (2001) compared cycling training to relaxation training and found that cycling training was associated with a significant improvement in exercise capacity; however, there was no significant difference between the groups in regards to balance, mobility, and functional independence (Bateman et al., 2001). Similarly, in a PCT study, Corral et al. (2014) found that cycling training resulted in increased oxygen uptake capacity. In an RCT, Hoffman et al. (2010) compared a group of individuals who exercised in a community-based program to individuals who did not participate in this program but were able to exercise on their own. Although the intervention group was working out more days per week than controls, the total amount of time spent exercising per week was similar between groups, making comparisons challenging. When comparing groups, the authors found that mood was significantly higher in the participants who were exercising for more than 90 minutes each week, regardless of what treatment group they were originally placed in.

Two studies examined the cardiovascular parameters of exercise programs as it relates to motor recovery (Bhambhani et al., 2005; Chin et al., 2015). In a pre-post study, the authors found that after completing an exercise program, participants showed significant increases in treadmill time (Chin et al., 2015). In a post-test study, the authors found there was a significant increase in oxygen uptake and ventilation rate (Bhambhani et al., 2005). Overall, cardiovascular, and respiratory parameters were seen to improve in both studies.

Two studies did not find that exercise programming did not improve their studied outcomes. In an RCT, Hassett et al. (2012) examined the benefits of circuit training with encouragement from a physiotherapist and heart rate monitor feedback in individuals with severe TBI. The authors found that there was no significant difference between the two groups regarding the amount of time spent in the heart rate target zone. In a PCT study, Ding et al. (2022) examined the effectiveness of a 3-month home-based individualized exercise program comprised of aerobic exercise or stretching and toning following one in-person training session. The authors found that, while participants in the aerobic exercise group showed improvements in endurance, differences between groups were not significant.

Conclusions

There is level 1b (Hassett et al., 2009; 2011) evidence that an exercise program at a fitness-center may not result in different motor outcomes when compared to home-based exercise.

There is level 1b evidence (Hassett et al., 2012) that circuit training with encouragement and heart rate monitor feedback may not significantly improve motor performance in individuals post ABI.

There is level 1b evidence (Bateman et al., 2001) that exercise programs may not improve balance or mobility compared to relaxation training in individuals post ABI.

There is level 2 evidence (Hoffman et al., 2010) that community-based exercise may decrease pain and depression in individuals post ABI.

There is level 2 evidence (Driver et al., 2006) that aquatic exercise training may be effective at improving co-ordination, strength, flexibility, and endurance in individuals post ABI.

There is level 2 evidence (Bhambhani et al., 2005; Chin et al., 2015; Corral et al., 2014) that exercise programs may improve oxygen uptake and cardiovascular parameters in individuals post ABI.

There is level 2 evidence (Ding et al., 2022) that aerobic exercise training may be as effective as stretching and toning at home for endurance in individuals with chronic TBI.

There is level 2 evidence (Dault & Dugas, 2002) that aerobic dance training compared to traditional muscular training may improve sensory interaction and balance post ABI.

There is level 3 evidence (Damiano et al., 2016) that a home-based exercise program may improve stability, but may not improve motor control, mobility, or dual-task performance in individuals post ABI.

There is level 4 evidence (Charette et al., 2016) that multimodal exercise programs may improve gait and mobility in individuals post ABI.

There is level 4 evidence (Ustinova et al., 2014) that a therapeutic exercise program may improve balance and gait post ABI.

KEY POINTS

- There is conflicting evidence about whether exercise programs, home-based or administered in the community, may improve motor function, balance, and cardiovascular parameters post ABI.
- Further research is needed to determine which components of exercise are the most effective for motor rehabilitation post ABI.

Early Intensive Rehabilitation

Early intensive rehabilitation has been associated with improvements in motor outcomes among individuals with conditions such as stroke (Han et al., 2013) and moderate to severe brain injury (Fan et al., 2020).

TABLE 14 | Early Intensive Rehabilitation for Motor Rehabilitation post ABI.

Author Year Country Study Design Sample Size	Methods	Outcome
Fan et al. (2020) China RCT PEDro=9 $N_{Initial}$=87, N_{Final}=81	**Population:** TBI=87; *Intervention Group (Intensive Rehabilitation, n=41)*: Mean Age=39.25±9.57yr; Gender: Male=22, Female=19; Time Post Injury=7d; Severity: Mean GCS=9.89±2.94. *Control Group (Standard of care; n=40):* Mean Age=38.41±10.39yr; Gender: Male=23, Female=17; Time Post Injury=14d; Severity: Mean GCS=10.01±3.25. **Intervention:** Participants in the intervention group received early and high-intensity rehabilitation management (7 days after injury, 7d/wk, 4times/d, 1hr session). Rehabilitative treatment training included correct limb positioning and caring of the limbs; passive, assisted, and active movements; strength training; and practice of functional activities. Participants in the control group received the standard of care (14 days after injury, 5d/wk, 2times/d, 1hr session). Outcome measures were assessed at baseline, 1, 3 and 6mo following intervention. **Outcome Measures:** Glasgow Outcome Scale (GOS), Fugl-Meyer Assessment (FMA), Barthel Index (BI).	1. One month following rehabilitation, no significant differences were observed between groups (p>.05). 2. Three months following rehabilitation, the FMA score was significantly higher in the group that received early intensive rehabilitation when compared to the control (59.83±11.87 versus 44.56±8.32; p<.05). 3. No significant group differences were observed on the GOS or BI (p>.05). 4. Six months following rehabilitation, the FMA score, and BI score significantly improved with early intensive rehabilitation when compared to the control group (FMA: 73.18±16.55 versus 57.86±10.67, p<.01; BI: 87.17±13.85 versus 60.68±11.98, p<.01).
Mossberg et al. (2002) USA Pre-Post N=40	**Population:** TBI=35, Stroke=5; Mean Age=33yr; Gender: Male=29, Female=11; Mean Time Post Injury=2.1yr. **Intervention:** Participants took part in early rehabilitation. Participants performed a treadmill test within 1wk of admission and again within 1wk of discharge. Assessments were conducted at baseline and post-intervention. **Outcome Measure:** Peak Heart Rate, Total Ambulation Time (TAT), and Vo2 Levels.	1. TAT increased significantly from 10.3±3.1ms at baseline to 13.6±3.5ms at post intervention (p<0.01). 2. Peak Heart Rate (168±20 versus 167±21) and VO2 levels (23.5±6.6 versus 24.3±6.4, p=0.09) did not change significantly between baseline and post-intervention.

Discussion

Early intensive rehabilitation for motor rehabilitation following ABI was addressed in two studies. In an RCT, Fan et al. (2020) found that, after receiving early intensive rehabilitation involving correct limb positioning and caring of the limbs, passive, assisted, and active movements, strength training, and practice of functional activities, participants showed significant improvements in motor function compared to those who received standard care alone. In a pre-post study, Mossberg et al. (2002) also found significant improvements in motor outcomes, with total ambulation times increasing post-treatment.

Conclusions

There is level 1b evidence (Fan et al., 2020) that early intensive rehabilitation may improve motor function in individuals with TBI.

There is level 4 evidence that early intensive rehabilitation (Mossberg et al., 2002) may improve ambulation in individuals with ABI.

KEY POINTS

- Early intensive rehabilitation may improve ambulation and motor function following an ABI.

Aquatic Therapy

Aquatic therapy has been considered a safe and adaptable therapy for the rehabilitation of individuals with musculoskeletal, neurological and cardiopulmonary conditions (Becker, 2009).

TABLE 15 | Aquatic Therapy for Motor Rehabilitation post ABI.

Author, Year Country Study Design Sample Size	Methods	Outcome
Curcio et al. (2020) Italy RCT PEDro=6 N_{Inital}=22 N_{Final}=20	**Population:** Severe TBI; GCS: ≤8; ATG (n=10); Mean Age=37.4yr; Gender: Male=4, Female=6; Mean Time Post Injury=5.8mo; CTG (n=10); Mean Age=43yr; Gender: Male=5, Female=5; Mean Time Post Injury=4.8mo. **Intervention:** Participants were randomly assigned to the Aquatic Therapy Group (ATG) or to the Conventional Training Group (CTG). Participants underwent twelve individual rehabilitation sessions (3 days/week, 4 weeks), in a rehabilitation pool. **Outcome Measures:** Berg Balance Scale (BBS), Modified Barthel Index (MBI), Disability Rating Scale (DRS), Tinetti Gait Balance Scale (TBG), and Quality of Life After Brain Injury (QOLIBRI).	1. The within-subjects comparison showed a significant improvement in both groups in MBI, BBS, TBG, and QOLIBRI. 2. No significant differences were found in the between-subjects analysis. 3. Both groups statistically improved in motor function and quality of life suggesting that aquatic therapy could be safely performed in persons with severe TBI during post-acute neurorehabilitation.

Discussion

In an RCT, Curcio et al. (2020) compared the effectiveness of aquatic therapy and standard care for the rehabilitation of balance, gait and activities of daily living in persons with severe TBI. The authors found improvements in motor function in both groups but there were no statistically significant differences between the two groups.

Conclusions

There is level 1b evidence (Curcio et al., 2020) that aquatic therapy may not be more effective than conventional training for the rehabilitation of motor function in individuals with severe TBI.

KEY POINTS

- Aquatic therapy may not significantly improve motor function compared to conventional rehabilitation in individuals who have sustained a severe TBI.

SPASTICITY

Spasticity often occurs as a result of various neurological conditions affecting the central nervous system and producing upper motor neuron patterns of impairment, including brain injury, and can present in a range of ways causing minor discomfort to complete immobility with presence of contractures and pressure sores (Stevenson, 2010). Spasticity has been defined as "a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes with exaggerated tendon reflexes, resulting from excitability of the stretch reflex" (Lance, 1980). Spasticity affects upper and lower extremities, and it can cause muscle stiffness, painful spasms, loss of function, deformities and mobility restriction (Anwar et al., 2019).

Factors that must be taken into consideration when proposing treatment of spasticity include the chronicity, severity, pattern of distribution (focal versus diffuse), and comorbidities (Gormley et al., 1997). Typically, the treatment of focal spasticity includes the use of non-pharmacologic modalities, oral pharmacologic agents, botulinum toxin, nerve and motor point blocks, and neurosurgical procedures such as dorsal rhizotomy and intrathecal baclofen pump insertion (Anwar et al., 2019).

Note that this section also includes discussion of treatment of contracture along with spasticity. Contracture refers to reduced range of motion about a body joint due to shortening of the soft tissues around the joint. Contracture can occur in a joint affected by spasticity, but also occurs in other conditions.

Non-Pharmacological Interventions

Electrical Stimulation

Electrical stimulation uses an electrical current to elicit a muscle contraction either directly by stimulating the skeletal muscle (Gregory & Bickel, 2005), or indirectly by stimulating the nerve supplying that muscle. Electrical stimulation has seen some applications with regards to assisting paraplegic patients with standing and walking (Katz et al., 2000).

TABLE 16 | Electrical Stimulation for the Treatment of Spasticity Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Leung et al. (2014) Australia RCT PEDro=8 $N_{Initial}$=35, N_{Final}=32	**Population:** TBI; *Experimental Group (EG; n=17)*: Mean Age=38yr; Gender: Male=14, Female=3; Mean Time Post Injury=140d; Mean GCS=5. *Control Group (CG; n=18)*: Mean Age=38yr; Gender: Male=15, Female=3; Mean Time Post Injury=83d; Mean GCS=5. **Intervention:** Participants were randomly allocated to either the EG or CG group. The EG group underwent a treatment of tilt table standing and electrical stimulation (30 min 5d/wk) and splinting (12hr 5d/wk) for a total of 6 wk. For the next 4wk EG group participants underwent tilt table standing alone (30 min 3d/wk). The CG group underwent tilt table standing (30min 3d/wk) for the full 10 wk. Measures were taken at baseline, 6wk and 10wk. **Outcome Measure:** Passive ankle dorsiflexion, 5-point Tardieu Scale, Functional Independence Measure (FIM).	1. The CG group had a greater range of motion for passive ankle dorsiflexion than the EG group at 6 wk (3 degrees) and 10 wk (-1 degree). 2. There was a mean reduction in spasticity of 1 point (95% CI 0.1 to 1.8) at Week 6, favoring the experimental group, but this effect disappeared at Week 10. 3. There was no between group differences in walking speed. 4. There were no differences between groups for tolerance to treatment, perceived treatment benefit, perceived treatment worth, and willingness to continue with treatment.
Seib et al. (1994) USA Pre-Post N=10	**Population:** TBI=5, Spinal Cord Injury=5; Mean Age=38yr; Gender: Male=6, Female=4; Mean Time Post Injury=6.3yr. **Intervention:** After baseline assessments, participants received 20 min of Surface Electrical Stimulation to the ipsilateral (the more spastic side) tibialis anterior. Parameters: 2sec rise time, 15sec on, instant fall, 20sec off. Rate of stimulation was 30 pulses/sec. Intensity varied according to participant tolerance. Assessments occurred at baseline, immediately post intervention, and 24hr after the intervention. **Outcome Measure:** Path length, Spasticity Measurement System.	Ipsilateral Effect: 1. There was a significant reduction in spasticity immediately following stimulation for all participants ($p<0.05$). However, the change in path lengths pre to post stimulation was not significantly different in the TBI group alone (median length 82nm/rad before versus 73nm/rad after). 2. Twenty-four hours after stimulation, ipsilateral path length (spasticity) reduced significantly in 8 of 9 participants ($p<0.01$). Contralateral Effect: 3. Six of 9 participants showed increased contralateral path lengths immediately post intervention. 4. TBI median path length increase was from 14nm/rad to 34nm/rad. 5. Twenty-four hours post stimulation, 4 patients had decreased spasticity, 3 had an increase and 1 patient had no change.

Discussion

In a pre-post study, Seib et al. (1994) examined the effects of electrical stimulation applied to the lower extremity in participants with either a TBI or spinal cord injury. Electrical stimulation significantly decreased spasticity in the treated extremity, whereas the tone in the untreated extremity did not change; in addition, the effect of one stimulation session was noted to last up to 24 hours post intervention. In an RCT study, Leung et al. (2014) examined the use of electrical stimulation combined

with tilt table standing and splinting, compared to tilt table standing alone. The authors found that, while there was a small reduction of spasticity in the experimental group, it disappeared at week 10.

Conclusions

There is level 1b evidence (Leung et al., 2014) that electrical stimulation in combination with tilt table standing and splinting may not be better than tilt table standing alone for the management of spasticity in individuals with severe TBI.

There is level 4 evidence (Seib et al., 1994) that electrical stimulation may be effective for decreasing lower extremity spasticity for six or more hours in individuals with TBI.

KEY POINTS

- Electrical stimulation in combination with tilt table standing and splinting may not be more effective than tilt table standing alone.
- Electrical stimulation may decrease spasticity for a period of up to 24 hours among persons with TBI.

Acupuncture

Acupuncture, is part of traditional Chinese medicine, and it has been used to treat symptoms such as spasticity in a variety of neurological conditions, such as stroke, cerebral palsy, spinal cord injury and brain injury (Zhu et al., 2019). However, methodologically rigorous studies evaluating its effectiveness are limited, particularly in brain injury.

TABLE 17| Acupuncture for the Treatment of Spasticity Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Matsumoto-Miyazaki et al. (2016) Japan RCT Crossover PEDro=5 N=11	**Population:** Severe TBI; Mean age=33yr; Gender: Male=11, Female=0; Mean Time Post Injury=19mo. **Intervention:** Participants with disorders of consciousness (DOC) and refractory upper extremity spasticity post TBI received Japanese style acupuncture. Acupuncture treatment was performed at GV 26, Ex-HN3, bilateral LI 4, and ST 36 for 10 minutes. F-waves were recorded from the abductor pollicis brevis muscle before treatment (baseline), 10 minutes after needle insertion (phase 1), and 10 minutes after needle removal (phase 2). The same procedure was followed in a control session without acupuncture on a separate day. **Outcome Measures:** F/M Amplitude Ratio.	1. The F/M Amplitude Ratio was significantly reduced from baseline to phase 1 ($p<0.001$) and phase 2 ($p<0.001$) in the acupuncture session. 2. No significant changes were observed in the controls session. 3. Changes in the F/M Amplitude Ratio from baseline to phase 1 and phase 2 were greater in the acupuncture session than the control session ($p=0.001$ and $p<0.001$, respectively).

Author Year Country Study Design Sample Size	Methods	Outcome

Discussion

In an RCT crossover trial of 11 participants with disorders of consciousness (DOC) post TBI, Matsumoto-Miyazaki et al. (2016) examined the effect of acupuncture on spinal motor neuron excitability. The authors found that the F/M Amplitude ratio was reduced significantly from baseline to phase 1 and phase 2 of the study in the acupuncture session, while no changes occurred in the control session. The results of this study indicated that treatment with acupuncture reduced the excitability of the spinal motor neurons, suggesting that acupuncture may be beneficial for reducing spasticity in individuals with DOC post TBI. However, no clinical outcome measures were reported, and the clinical impact of this finding is unclear.

Conclusions

There is level 2 evidence (Matsumoto-Miyazaki et al., 2016) that acupuncture may reduce a surrogate measure of spasticity in individuals with disorders of consciousness post severe TBI.

KEY POINTS

- Acupuncture may reduce a surrogate measure of spastic muscle hypertonia in individuals with disorders of consciousness following severe TBI.

Physiotherapy

Physiotherapy focuses on the biomechanics of the body and helps improve strength, mobility, range of motion, and pain. There is limited evidence on the use of physiotherapy to treat spasticity following brain injury; however, clinical involvement of physiotherapy as part of brain injury recovery is part of the standard of care for ABI due to observations of effectiveness in persons with ABI and other neurological conditions.

TABLE 18 | Physiotherapy for the Treatment of Spasticity post ABI.

Author Year Country Study Design Sample Size	Methods	Outcome
Thibaut et al. (2018) USA Case Series N=109	**Population:** ABI; Mean Age=40yr; Gender: Male=70, Female=39; Mean Time Post-Injury=38mos. **Intervention:** Individuals with a history of Disorders of Consciousness (DOC) received 0 to 3 (low) or 4 to 6 (high) physiotherapy sessions per week based on their needs. Physiotherapy sessions lasting 20-30min and consisted of conventional stretching of the four limbs. Individuals had all experienced a disorder of consciousness including vegetative state/unresponsive wakefulness syndrome, minimally conscious state, or had emerged from a minimally conscious state. **Outcome Measures:** Modified Ashworth Scale (MAS), frequency of muscle contracture.	1. There was a significant negative correlation between the frequency of PT and associated MAS scores ($p<0.01$)as well as the presence of muscle contracture ($p<0.01$). Patients receiving less than 4 sessions of PT per week were more likely to be spastic and suffer from muscle contracture than patients receiving 4 or more PT sessions per week. When patients were stratified (subacute 3-12mo post insult, chronic >12mo post insult), this correlation was only significant for those in the chronic phase ($p<0.001$).

Discussion

In a case series, Thibaut et al. (2018) found that individuals with disorders of consciousness post ABI who received higher doses of physiotherapy (4 or more sessions per week compared to less than 4 sessions per week) showed a significant improvement in scores on the Modified Ashworth Scale, had fewer spastic events, as well as lower rates of muscle contracture.

Conclusions

There is level 4 evidence (Thibaut et al., 2018) that higher doses of physiotherapy (four to six sessions per week) may improve spasticity and muscle contractures in individuals with disorders of consciousness following ABI compared with lower doses of physiotherapy.

KEY POINTS

- Four to six sessions of physiotherapy per week may improve spasticity and muscle contractures in individuals with disorders of consciousness following ABI, compared with less than four sessions per week.

Casting

Casting, applied once or several times in succession (serial casting), has been used as an adjunct therapy to other treatments for the management of spasticity and contracture in patients post TBI (Farag et al., 2020). Casts also often provide firm and consistent pressure that is distributed across the skin which may improve spasticity by reducing the sensory input to the spinal cord from cutaneous, muscle and joint

receptors (Farag et al., 2020). The theoretical premise for the effect of casting on hypertonia and joint mobility is based on neurophysiological and biomechanical principles (Mortenson & Eng, 2003). Neurophysiologically, casting may improve spasticity by the effect of maintaining prolonged stretch, or possibly the effects of prolonged pressure which may in turn reduce the cutaneous sensory input to the spinal cord. From a biomechanical perspective, muscle and connective tissues are may be elongated when immobilized in a stretched position, thus combating the development of contractures from soft tissue shortening (Mortenson & Eng, 2003).

TABLE 19 | Casting for the Treatment of Spasticity Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Moseley et al. (2008) RCT PEDro=8 N=26	**Population:** TBI; *Positioning Group (n=12)*: Gender: Male=11, Female=1; Mean Age=30.8yr; Median Time Post Injury=71d; Median Glasgow Coma Scale (GCS) Score=3. *Serial Casting Group (n=14)*: Gender: Male=12, Female=2; Mean Age=32.3yr; Median Time Post Injury=59d; Median GCS Score=4.5. **Intervention:** Participants were randomized to one of two interventions for elbow flexion contracture: serial casting or passive stretch (positioning group). Those in the serial casting group had long arm synthetic casts applied for 2wk with the elbow in a stretched position. Casts were changed regularly to gradually progress the stretch. After 2wk, the cast was removed, and the participants underwent passive stretching 1hr/wk for 4wk. The second group had passive stretch applied to the elbow flexor muscles for 1hr/day, 5x/wk. **Outcome Measure:** Torque controlled passive elbow extension, Modified Tardieu Scale.	1. The stretching group received a mean of 13 hr of stretching during the intervention and the serial casting group had stretch applied for a mean of 13.6 days. 2. Those in the serial casting group had a greater reduction in contracture in the short term (2wk). Serial casting reduced contracture by a mean of 22º ($p<0.001$) when compared to the positioning group. The next day the mean reduction was only 11° for the casting group, and differences between groups were less ($p=0.052$). 3. At follow up assessment (4wk), there was no significant or clinically meaningful difference between groups (mean effect 2°, $p=0.782$). 4. At post-intervention assessment, the serial casting group had slightly lower spasticity than the stretching group ($p<0.05$).
Moseley (1997) Australia RCT Crossover PEDro=4 N=9	**Population:** TBI; Mean Age=29.1yr; Gender: Male=8; Female=1; Time Post Injury=72.2d. **Intervention:** Participants in the experimental group were placed in a below-knee cast and participated in gastrocnemius stretching (standing on a tilt table, or knee extension in sitting) for at least 1hr/d for 7d. The control group did not receive a cast or stretching. Participants then received the other intervention. **Outcome Measure:** Passive ankle dorsiflexion (PAD) movement.	1. PAD movement increased by a mean of 13.5° in association with the experimental condition. In comparision, PAD movement decreased by a mean of 1.9° during the control condition ($p<0.05$). There was a mean difference between the experimental and control conditions of 15.4° ($p<0.05$).
Singer et al. (2003) Australia Pre-Post	**Population:** Stroke=3, Subarachnoid Hemorrhage=4, Intra-Cerebral Hemorrhage=1, Diffuse Axonal Injury=1; Mean Age=30.7yr;	1. Post-casting, all individuals had at least 10° dorsiflexion with the knee flexed and 6 had maximal passive range of motion of 10° dorsiflexion with knee extended.

Author, Year Country Study Design Sample Size	Methods	Outcome
N=9	Gender: Male=6, Female=3; Mean Time Post Injury=3.9mo. **Intervention:** A serial casting procedure addressing extensibility, passive resistance torque and stretch reflex response of the ankle was implemented. Casts were applied weekly and continued until the goal was reached or no measurable gain was recorded. **Outcome Measure:** Maximal Passive Range of Motion, Transfer Dependency, and Rancho Los Amigos Levels of Cognitive Functioning (RLA).	2. Muscle extensibility and passive torque improved significantly (p<0.0001). Functional range was maintained in 8 participants at 6mo follow-up. 3. All participants improved RLA scores by at least one point. 4. Significant improvements were noted for transfer dependency scores from initial to post intervention (p<0.0015). 5. Casting did lead to some tissue breakdown.
Pohl et al. (2002) Germany Case Control N=105	**Population:** TBI=43, Stroke=19, Intracerebral Hemorrhage=19, Cerebral Hypoxia=11, Subarachnoid Hemorrhage=6, Other=7; Gender: Male=81, Female=24. *Control Group (n=56):* Median Age=38.2yr. *Intervention Group (n=49):* Median Age=44.6yr. **Intervention:** A stepwise reduction of fixed, flexed joint contracture via serial casting. Patients were treated with conventional casting changing intervals of 5-7d (control) or 1-4d (Intervention), until maximum possible extension (<10% of extension deficit) was reached or when the extension deficit failed to reduce after two cast changes. **Outcome Measure:** Maximum deficits of different joints (elbow, wrist, knee, ankles), Range of Motion (ROM), Number of Complications.	1. The median casting change interval was 6.9 days for 92 joints of 56 control group patients. 2. The median casting change interval was 2.7 days for 80 joints of 49 intervention group patients. 3. Mean casting time in the control and intervention group was 32.6±20.6 days and 9.3±5.6 days, respectively. 4. ROM improved after casting and 1mo follow-up in both groups (p<0.001) but no between group differences were found (p=0.72). 5. Casting complications were observed in 29.3% in group 1, and 8.8% in group 2 (p=0.001).

Discussion

When compared to passive stretching, casting was reported to be effective in improving spasticity and contracture of the elbow; however, these between group differences were no longer significant 4 weeks after the discontinuation of casting (Moseley et al., 2008). The results from this study suggest that while serial casting may be more effective initially when compared to passive stretching, these benefits may not be maintained in the longer term. In a pre-post study, Singer et al. (2003) found that serial casting contributed to a significant change in triceps surae extensibility and passive resistive torque, both surrogate for spasticity.

In an RCT crossover trial, Moseley et al. (1997) compared one week of casting combined with stretching to a week of no therapy (control) for ankle plantar flexion contractures. The experimental group had a significantly improved range of passive ankle dorsiflexion whereas the control group showed overall deterioration of ankle dorsiflexion range of motion (Moseley, 1997).

In a case control study, Pohl et al. (2002) compared short casting (one to four days) to a longer casting change interval (five to seven days), for both upper and lower extremity joints. Although improvements in range of motion were seen in each group immediately following the intervention and at a one-month follow-up, there were no significant differences found between groups. However, the discontinuation rate in the longer casting change interval group due to complications was significantly higher than that seen in the shorter casting change interval group.

Conclusions

There is level 1b evidence that serial casting may improve contractures of the elbow initially when compared to passive stretching in individuals with an ABI; however, these improvements may not be maintained in the longer term.

There is level 1b evidence (Moseley et al., 2008) that serial casting may be superior to passive stretching at improving spasticity of the elbow in individuals post ABI.

There is level 2 evidence (Moseley et al., 1997) that a below-knee casting and stretching may increase passive ankle dorsiflexion in patients post ABI.

There is level 3 evidence (Pohl et al., 2002) that serial casting following a short duration casting change interval (one to four days), or a longer duration casting change interval (five to seven days) may have similar effects on upper and lower extremity range of motion in individuals post ABI; however, complications may be more common when employing a longer casting change interval.

There is level 4 evidence (Singer et al., 2003) that weekly below-knee casts may improve ankle range of motion, muscle extensibility, and passive torque in patients post ABI. However, this intervention may be associated with tissue breakdown.

KEY POINTS

- Serial casting may improve contractures, spasticity, and joint range of motion in individuals with an ABI compared to stretching; however, these differences may not be maintained long-term.
- Below-knee casting and stretching may increase passive ankle dorsiflexion in patients post ABI.
- Serial below-knee casting may improve ankle range of motion and muscle extensibility in patients post TBI.

Hand Splinting and Stretching

The purpose of hand splinting following an ABI is to prevent contractures and deformities, and to reduce spasticity. There are biomechanical and neurophysiologic rationales for splinting the spastic hand

(Lannin et al., 2003); the biomechanical approach attempts to prevent contractures by physically preventing shortening of muscle and connective tissues.

TABLE 20 | Hand Splinting and Stretching for the Treatment of Spasticity Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Thibaut et al. (2015) Belgium RCT PEDro=4 N=17	**Population:** TBI=7, Anoxia=5, Aneurysm=5; Mean Age=41yr; Gender: Male=9, Female=8; Mean Time Post Injury=35mo; Severity: Severe. **Intervention:** Participants were randomized to receive one of the following exercise protocols on each of their upper limbs: manual stretching and control (no Intervention) (G1, n=8), soft splinting and control (G2, n=12), or soft splinting and manual stretching (G3, n=14). Each exercise was done for 30min followed by a 60min break. Outcomes were assessed before (T1) and after (T2) each protocol, and after each break (T3). **Outcome Measures:** Modified Ashworth Scale (MAS), Modified Tardieu Scale (MTS), Range of Motion (ROM), and Hand Opening (HO).	1. In G1, there were no significant changes in MAS, MTS, ROM, or HO after stretching or after the control protocol. 2. In G2, the mean MAS score of flinger flexor muscles improved significantly after splinting from T1 to T2 (p=0.014) and the improvement was maintained at T3 (p=0.022). There was no significant change for the control. 3. In G3, the mean MAS score of finger flexor muscles improved significantly after both splinting (p=0.014) and stretching (p=0.022) from T1 to T2, but neither improvement was maintained at T3. 4. In G2, the mean HO score improved significantly after splinting from T1 to T2 (p=0.009), but the improvement was not maintained at T3. There was no significant change for the control. 5. In G3, the mean HO score improved significantly after splinting (p=0.005) from T1 to T2, but the improvement was not maintained at T3. There was no significant change in mean HO score after stretching (p=0.249). 6. In G3 and G2, there were no significant changes in MTS or ROM after the interventions.
Lannin et al. (2003) Australia RCT PEDro=8 N=28	**Population:** ABI**;** Gender: Male=13, Female=15. *Experimental Group (n=17)*: Mean Age=65yr; Mean Time Post Injury=47 days. *Control Group (n=11):* Mean Age=68yr; Mean Time Post Injury=57d. **Intervention:** The experimental group wore an immobilizing hand splint in a functional position (10^{o}-30^{o} wrist extension) for 4wk, for no longer than 12hr each night. The control group received standard care (motor training and stretching). **Outcome Measure:** Length of wrist and finger flexor muscles, Hand and arm function, and Visual Analog Scale for Pain (VAS), and Motor Assessment Scale (MAS).	1. Effects of splinting were not statistically significant. 2. Splinting increased wrist extension by a mean of 1° post intervention and reduced wrist extension by a mean of 2° at follow-up. 3. Splinting decreased upper-limb function after intervention (MAS; mean 0.3 points) and at follow-up (mean 0.8 points). 4. Splinting decreased performance of hand movements by a mean of 0.4 points (MAS) post intervention and 0.5 points at follow-up. 5. Splinting decreased overall upper-limb function by 0.1 points after intervention and by 0.2 points at follow-up (MAS). Increased reported intensity of upper-limb pain (mean: 0.2cm) on VAS after intervention and by 1cm at follow-up.

Discussion

One RCT study evaluated the effect of nighttime hand splinting in conjunction with conventional therapy compared to therapy alone (Lannin et al., 2003). Overall, the authors did not find significant benefits of nocturnal hand splinting. A second randomized controlled trial (RCT) compared manual stretching, soft hand splinting, and manual stretching plus soft hand splinting to determine the optimal intervention (Thibaut et al., 2015). The authors reported that soft hand splinting for 30 minutes resulted in improved hand opening and reduced spasticity of the flexor finger muscles; however, improvements in hand opening were not maintained after the break period. The hand splint was said to be feasible to use in daily care, as the splint was comfortable and easy to apply. There is a need to further research the effect of splinting in individuals with ABI as this practice is used in both acute and rehabilitation settings.

Conclusions

There is level 1b evidence (Lannin et al., 2003) that nocturnal hand splinting may not improve upper extremity range of motion or function compared to standard care in individuals post ABI.

There is level 2 evidence (Thibaut et al., 2015) that soft hand splinting may improve hand opening in individuals post ABI.

KEY POINTS

- Overnight hand splinting may not improve upper limb function post ABI.
- Soft hand splinting may be beneficial for improving hand opening post ABI and spasticity of the finger muscles in individuals with disorders of consciousness.

Pharmacological Interventions

Focal Treatment with Botulinum Toxin

Botulinum toxin (BTX-A) injections inhibit the release of acetylcholine into the neuromuscular junction and are widely used for the treatment of focal spasticity (Stevenson, 2010). When selectively injected into a specific muscle, botulinum toxin is thought to cause local muscle paralysis, thereby alleviating hypertonia caused by excessive neural activity (Jankovic & Brin, 1991).

TABLE 21 | Botulinum Toxin for the Treatment of Spasticity Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Mayer et al. (2008)	**Population:** TBI=21, Stroke=8, Hypoxic Encephalopathy=2; *Motor Point Group:* Mean	1. The median decrease in Ashworth Scale scores after injection was 1 point in both

Author Year Country Study Design Sample Size	Methods	Outcome
USA RCT PEDro=6 N=31	Age=37.9yr; Gender: Male=13, Female=5; Mean Time Post Injury=256.7 d. *Distributed Group:* Mean Age=34.7yr; Gender: Male=17, Female=1; Mean Time Post Injury=481.9yr. **Intervention:** Patients with severe elbow flexor hypertonia received botulinum toxin according to one of two injection protocols: the motor point injection technique (1 site biceps and 1 site brachioradialis), or the distributed quadrants technique (4 sites rectangularly configured – 2 sites biceps and 2 sites brachioradialis). Following two baseline measures, each elbow was randomized to receive injections of botulinum toxin. A total of 90 units were administered to patients in each group; however, the injection sites and techniques differed between groups. Mean follow up was 23.5±4.4d. **Outcome Measure:** The Ashworth Scale, Modified Tardieu Scale.	groups (p=0.53). The Tardieu catch angle post injection did not differ significantly between groups (p=0.31). 2. Both groups showed significant improvements from baseline on all outcomes measured (all p<0.01); however, there were no between-group differences at 3wk. 3. For both groups, a clinicophysiologic effect was observed at 3wk post-intervention.
Intiso et al. (2014) Italy Pre-Post N=22	**Population:** ABI=16, Cerebral Palsy=6; Mean Age=38.1yr; Gender: Male=12, Female=10; *Brain Injury*: Mean Time Post Injury=3.8yr. **Intervention:** Patients with severe spasticity of the upper and lower limbs received injections of onabotulinum toxin A (BoNT-A; up to 840 IU). **Outcome Measure:** Modified Ashworth Scale (MAS), Glasgow Outcome Scale (GOS), Frenchay Arm Test (FAT), Barthel Index (BI), Visual Analog Scale, Visual Analogue Scale–Pain (VAS).	1. Seventeen patients had spastic hemiparesis and 5 had paraparesis. 2. A significant reduction in spasticity was seen at 4 and 16wk post intervention, shown by a decrease in mean MAS score at the elbow, wrist, finger, and hand (all p<0.05) and ankle (p<0.03). 3. No significant improvements were seen on the GOS, BI, or FAT at 4 or 16 wk. 4. A significant reduction in pain was seen from baseline (7.6±1.1) to 4 (3.5±0.7) and 16 wk (3.6±0.5) post intervention (p<0.001).
Clemenzi et al. (2012) Italy Pre-Post N=21	**Population:** TBI=11, ABI=10; Mean Age=42.2yr; Gender: Male=16, Female=5; Median Time Post Injury=5yr; Severity: Severe. **Intervention:** Patients were evaluated on admission (T0), after 1mo of rehabilitation treatment (T1). Patients who did not demonstrate significant improvements at T1 received injections of Botulinum Toxin Type A (maximum dose 600 U diluted in 50 ml^{-1}) followed by a rehabilitation program that consisted of hand and/or foot adhesive taping, passive or active stretching, and occupational therapy. All patients were followed prospectively for 12mo after the first injection and received repeated injections no more frequently than every 3mo according to their clinical response. Evaluations were performed at the second injection (T2) and the last injection (T3).	1. Spasticity was in the lower limb in 33.3% of patients, upper limb in 9.5%, and both in 57.1%. 2. All patients were treated at least twice during the 12 mo follow up. 3. Improvement in spasticity was seen at the second and last injection (T3) time points compared to baseline (p<0.0001). 4. BI significantly improved by the end of the follow up compared to baseline (p=0.0001). 5. VAS score improved at the end of the second injection, with a reduction in score noted after each injection. 6. Greater improvement on BI was correlated to a shorter period between ABI onset and

Author Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measure: Barthel Index (BI), Modified Ashworth Score (MAS), Visual Analogue Scale- pain (VAS).	first injection (p<0.0001), the same effect was not discovered for MAS or VAS.
Yablon et al. (1996) USA Case Series N=21	**Population:** TBI; Mean Age=28.2yr; Gender: Male=12, Female=9; Mean Time Post Injury: Acute Group=142.7d, Chronic Group=89.5mo. **Intervention:** Participants received Botulinum Toxin A injections (20-40 units per muscle) into the upper extremity. Targeted muscles included: the flexor carpi radialis, flexor carpi ulnaris, flexor digitorum profundus, and flexor digitorum superficialis. Some patients also received injections into the biceps and brachialis due to coexisting spasticity in the elbow flexors. After injection, patients received therapeutic modalities as needed. Patients were grouped based on time between injury and injection: acute (<12mo; n=9) or chronic (≥12mo; n=12). **Outcome Measure:** Modified Ashworth Scale (MAS), passive ROM at the wrist.	1. The acute group showed significant improvements in ROM (wrist extension improved by a mean of 42.9±24.7°, p=0.001) and spasticity severity (mean MAS improvement 1.5±0.5 points, p=0.01). 2. All patients in the acute group showed an improvement in spasticity and no patient worsened or remained unchanged. 3. The chronic group showed significant improvements in ROM (wrist extension improved by a mean of 36.2±21.7°, p<0.001) and spasticity severity (mean MAS improvement 1.47±0.9 points, p=0.002).

Discussion

Four studies examining the effects of botulinum toxin type A on spasticity following ABI were identified. In a case series, Yablon et al. (1996) reported that botulinum toxin type A injections into the upper extremities improved spasticity in 21 patients with ABI, with improvements noted for patients who received the injections within 1 year of injury and those who received the injections more than 1 year post injury (Yablon et al., 1996). Similar findings were reported by Clemenzi et al. (2012) in a pre-post study. In this study, botulinum toxin was associated with improvements in both pain and spasticity; additionally, patients with a shorter period of time between their injury and first injection showed greater functional improvements as measured using the Barthel Index (Clemenzi et al., 2012).

In an RCT, Mayer et al. (2008) found that improved spasticity from BTX-A administration was obtained whether using a single motor point injection technique or multisite distributed injection technique, and that outcomes were similar, with both groups showing a clinical effect of improved spasticity at three weeks post intervention. In a pre-post study, Intiso et al. (2014) found a reduction in spasticity for the upper extremity (elbow, wrist, and hand), as well as ankle joints at 1 and 4 months post intervention with BTX-A administration. Several of the above studies also reported improvements in secondary outcomes such as pain post BTX-A administration.

Conclusions

There is level 1b (Mayer et al., 2008) evidence that botulinum toxin type A injected at a single motor point or using a distributed multisite technique may reduce spasticity to a similar degree in individuals with an ABI.

There is level 4 evidence (Intiso et al., 2014) that botulinum toxin type A injections may be effective in the management of localized spasticity following ABI.

There is level 4 evidence (Clemenzi et al., 2012; Yablon et al., 1996) that botulinum toxin type A injections, in conjunction with conventional therapies, may improve spasticity and passive ROM in patients with TBI.

KEY POINTS

- Botulinum toxin type A injections may be effective in the treatment of spasticity post ABI.

Focal Treatment with Chemodenervation (Phenol Blocks)

Treatment of focal spasticity using Chemodenervation involves the application of a chemical agent, such as phenol, to impair nerve functioning, which produces weakness and reduces spasticity in muscles controlled by the targeted muscle. The effect of the chemical agent is typically temporary (Katz et al., 2000). Agents used for permanent nerve blocks to treat spasticity last between 2 and 36 months and include ethyl alcohol (>10% concentrated solution) and phenol (>3% concentrated solution). These agents act on the targeted peripheral nerve to impair both voluntary and involuntary activation of the muscle, producing weakness, facilitating the treatment of spasticity (Gaid, 2012). The degree to which the nerve is damaged and the greater the distance of the focal administration of nerve treatment from the muscle belly determines the duration of effect. Administration of Chemodenervation at the motor point (i.e., where the peripheral nerve innervates the muscle) results in a shorter duration of treatment than administration of Chemodenervation more proximally along the course of the nerve.

TABLE 22| Percutaneous Phenol Block for the Treatment of Spasticity Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Keenan et al. (1990) USA Case Series N=17	**Population:** TBI; Mean Age=25yr; Gender: Male=12, Female=5; Mean Time Post Injury=6mo. **Intervention:** Participants received percutaneous phenol block (3ml of 5% phenol solution in sterile saline) of the musculocutaneous nerve to decrease elbow flexor spasticity followed by a daily program of active/passive range of motion therapy. Assessments	1. Ninety-three percent of extremities showed a short-term decrease in motor tone and improved resting position of the elbow. 2. Maximum improvements occurred 4wk post block.

Author Year Country Study Design Sample Size	Methods	Outcome
	conducted pre-post block, 24hr after, then at weekly intervals while patients were hospitalized for rehabilitation. Post discharge follow-up occurred for a minimum of 2yr. **Outcome Measure:** Muscle tone/control, Range of Motion.	3. Resting position improved from 120° to 69°, active arc increased from 46° to 60°, and passive arc from 65° to 118°. 4. At follow-up (mean 27mo post injection), nine extremities that had relief of spasticity, had recurrence of flexor tone and loss of motion in the elbow.
Garland et al. (1984) USA Case Series N=11	**Population:** TBI; Mean Age=24yr; Gender: Male=8, Female=3; Mean Time Post Injury=5.8mo. **Intervention:** Participants received percutaneous phenol injections (1-2ml of 3 or 5% phenol solution) at motor points of spastic wrist and finger flexors identified using a nerve stimulator. Injected muscles included: the flexor carpi radialis, flexor carpi ulnaris, flexor digitorum sublimus, flexor digitorum profundus, and flexor pollicis longus. **Outcome Measure:** Resting Angle of Wrist, Passive/active Extension of Wrist.	1. Mean resting position of the wrist prior to injection was 53°. Nine patients increased resting extension by a mean of 34° and 2 patients lost a mean of 15° of extension. 2. Overall, there was a mean increase in resting wrist angle following motor point injections of 25°. 3. Active wrist extension improved an average of 30°. Mean increase in passive wrist extension with finger flexed of 5°.

Discussion

Two studies evaluated the efficacy of focal Chemodenervation as a treatment for spasticity. In a case series, Keenan et al. (1990) evaluated the effect of percutaneous phenol block of the musculocutaneous nerve to decrease elbow flexor spasticity; the authors found that there was improved range of motion of the elbow lasting a mean duration of five months. In another case series, 11 persons with closed head injury with spastic paralysis of the upper extremity were treated with percutaneous phenol injections into the spastic wrist and finger flexors (Garland et al., 1984). The authors reported that the associated reduction in muscle tone persisted for up to two months post injection; furthermore, there was a mean increase in resting wrist angle, active wrist extension, and passive wrist extension with fingers flexed of 25, 30, and 5°, respectively (Garland et al., 1984). These studies found that percutaneous phenol blocks are effective in temporarily controlling spasticity in patients post TBI; however, due to the retrospective nature of the studies and lack of controls there is insufficient evidence to make definitive conclusions on the efficacy of phenol injections.

Conclusions

There is level 4 evidence (Keenan et al., 1990; Garland et al., 1984) that phenol nerve blocks may temporarily reduce spasticity in the elbow, wrist, and finger flexors in individuals post TBI.

KEY POINTS

- Phenol nerve blocks may help to temporarily decrease spasticity and improve joint range of motion in the upper extremities of individuals with TBI.

Oral Baclofen

Oral agents are often used to manage diffuse spasticity, particularly when a patient requires treatment for upper and lower extremity spasticity (Gracies et al., 1997). Oral baclofen is one of the more commonly used agents in the treatment of spasticity; it works by enhancing GABA, an inhibitory neurotransmitter, within the central nervous system thereby reducing muscle stretch reflexes (Ertzgaard et al., 2017). There is limited evidence on the use of oral baclofen in individuals with moderate to severe brain injury.

TABLE 23 | Oral Baclofen for the Treatment of Spasticity Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Meythaler et al. (2004) USA Case Series N=35	**Population:** TBI=22, ABI=6, Stroke=7; Mean Age=31yr; Gender: Male=22, Female=13. **Intervention:** Oral baclofen regimen beginning at 5 mg 3x/day increased per protocol to 80mg/day. Follow-up occurred between 1 and 3mo after initiation of oral baclofen. **Outcome Measure:** Ashworth Rigidity Scale (ARS), Spasm Frequency Scale (SFS), Deep Tendon Reflexes (DTR).	1. Mean dose was 57±26mg/day for all patients and 55±28mg/day for patients with TBI. 2. After treatment, average lower extremity ARS (3.5±1.1 to 3.2±1.2, p=0.0003) and DTR scores (2.5±0.9 to 2.2±1.2, p=0.0274) decreased significantly. There was no statistical difference in the spasm score. 3. When patients with TBI were analyzed separately, average lower extremity ARS (p=0.0044) and DTR (p=0.0003) decreased significantly, but not the SFS (p>0.05). 4. There was no significant change in upper extremity tone, spasm frequency or reflexes after 1-3 months of treatment (p>0.05). 5. There was a 17% incidence of somnolence that limited the maximum daily dosage of the medication.

Discussion

Meythaler et al. (2004) completed a retrospective study evaluating the use of oral baclofen to manage spasticity in a mixed brain injury and stroke population. Pre and post testing revealed that oral baclofen improved spasticity in the lower extremity; however, no changes for tone, spasm frequency, or reflexes

were found for the upper extremity (Meythaler et al., 2004). The authors suggest that the lack of effect may be due in part to receptor specificity issues in that GABA-B receptors may be less involved in the modulation of upper extremity spasticity. Of note, a common adverse effect of the oral baclofen was the onset of sleepiness, which occurred in 17% of patients in this study (Meythaler et al., 2004).

Conclusions

There is level 4 evidence (Meythaler et al., 2004) that oral baclofen may improve lower extremity spasticity, but not upper extremity spasticity, in individuals post ABI.

KEY POINTS

- Oral baclofen may reduce lower extremity, but not upper extremity, spasticity in individuals with an ABI.

Surgical Interventions

Intrathecal Baclofen

A limitation of oral baclofen is the inability to achieve sufficiently high concentrations in the cerebrospinal fluid (CSF) without causing significant unwanted side effects (Gracies et al., 1997). Intrathecal baclofen (ITB) delivered directly into the CSF using a needle (for 1-time administration) or by surgically inserting a pump into the CSF permits using a much lower dose to achieve desired improvements in spasticity and consequently results in fewer side effects (Ertzgaard et al., 2017). ITB can be used to treat severe spasticity in individuals who have failed to respond to the recommended doses of oral medications (Schiess et al., 2020). However, it should be noted that this procedure is invasive and associated with complications including infection, pump failure, and other pump tube complications such as kinking or disconnection (Gracies et al., 1997).

TABLE 24| Intrathecal Baclofen for the Treatment of Spasticity Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Meythaler et al. (1996) USA RCT Crossover PEDro=7 N=11	**Population:** TBI=10, Anoxia=1; Mean Age=25yr; Gender: Male=9, Female=2; Time Post Injury=Not Reported. **Intervention:** Patients with chronic spastic hypertonia received either a bolus injection of intrathecal baclofen (50µg) or placebo (normal saline). Crossover occurred	1. For the lower extremity, after intrathecal baclofen injection, AS scores decreased by a mean of 2 points (p=0.0033), spasm scores decreased by a mean of 2.1 points (p=0.0032), and reflex scores by 2.3 points (p=0.0032) at 4h.

Author Year Country Study Design Sample Size	Methods	Outcome
	a minimum of 48hr later. Assessment occurred at 1, 2, 4, and 6hr post injection. **Outcome Measure:** Ashworth Scale (AS), Spasm Score, Deep Tendon Reflexes.	2. For the upper extremity, after baclofen injection, AS scores decreased by a mean of 1.4 points (p=0.0033), spasm scores decreased by a mean of 1.2 points (p=0.0070), and reflex scores decreaesed by a mean of 1.0 points (p=0.0111) at 4h. 3. No significant within-group differences were shown for placebo. Between group differences were significant for all measures for both the lower and upper extremity (p≤0.0272).
Wang et al. (2016) Singapore Case Series $N_{Initial}$=6, N_{Final}=5	**Population:** TBI=5, Encephalopathy=1; Mean Age=31.6yr; Gender: Male=3, Female=2; Mean Time Post Injury=39.4mo. **Intervention:** A retrospective review was conducted of patients that were recruited to undergo surgical implantation of an intrathecal baclofen (ITB) pump. After implantation, patients received daily physical therapy. Upon discharge, patients continued to receive regular outpatient rehabilitation therapies for 3mo as well as ITB pump refills and monitoring by the neurosurgical team for 3-4 mo. Outpatient follow-up was 3-6mo. **Outcome Measure:** Modified Ashworth Scale (MAS).	1. The mean reduction in MAS was 1.2 (SD 1.1; p<0.05) at 3mo and 1.0 (SD 1.2; p=0.06) at the last follow-up. All patients but 1 (no change) had significant reductions in spasticity.
Chow et al. (2015) Canada Pre-Post N=19	**Population:** TBI=11, Stroke=8; Mean Age=34.2yr; Gender: Male=9, Female=10; Mean Time Post Injury=48.7mo. **Intervention:** All patients underwent a 50µg intrathecal baclofen (ITB) bolus injection via lumbar puncture. Patients were evaluated at baseline, 2hr, 4hr, and 6hr post injection. **Outcome Measure:** Gait speed, stride length, cadence, stance duration, ankle range of motion (ROM)-stance & swing, peak medial gastrocnemius (MG) lengthening velocity, average Ashworth Score, Plantar Flexors Ashworth Score, Electromyography-lengthening Velocity (EMG-LV), Coactivation Duration (CoD), Coactivation Index (CoI).	1. There was no significant difference in gait speed, stride length, cadence, or stance duration across evaluation points. 2. Ankle ROM in the more-affected leg during stance phase was significantly increased from baseline to 6hr (p=0.009); however, was not significantly different during swing phase. 3. Peak MG lengthening velocity significantly increased from baseline to 4hr in the less-affected leg (p=0.005) and from baseline to 6hr in both legs (p≤0.01). 4. Average Ashworth Score and plantar flexors Ashworth Score were significantly lower across all time posts in the more-affected leg only (p<0.001). 5. Compared with baseline, both frequency (p=0.02) and average gain (p=0.007) of EMG-LV were significantly lower at 2 hr post but did not reach significance at 4hr and 6hr post injection (p≤0.040). 6. Slope parameters of EMG-LV in the less-affected leg did not change over time (p≥0.129).

Author Year Country Study Design Sample Size	Methods	Outcome
		7. CoD significantly decreased over time in the more affected leg during all phases of gait (p≤0.013); and CoI did not significantly change over time in either leg (p>0.107).
Margetis et al. (2014) Greece Pre-Post N=8	**Population:** TBI=6, Hydrocephalus=1, Cardiac Arrest=1; Mean Age=31.5yr; Gender: Male=8, Female=0; Mean Time Post Injury=37.25mo. **Intervention:** Patients who were resistant to oral spasticity treatments received an implanted intrathecal baclofen pump. Mean follow-up period was 38.4mo. **Outcome Measure:** Modified Ashworth Scale.	1. All patients showed improvement in their spasticity scores; mean Modified Ashworth Scale scores were 3.375 pre- and 1.125 post-intervention.
Posteraro et al. (2013) Italy Pre-Post N=12	**Population:** TBI=8, Hemorrhage=2, Anoxia=2; Mean Age=36yr; Gender: Male=9, Female=3; Time Post Injury Range=31-150d. **Intervention:** Patients not experiencing reductions in spasticity following initial interventions with oral baclofen received intrathecal baclofen (ITB). The initial dosage was 50 or 100mcg depending on the severity of the impairment and was increased by 10% every 3d until the maximum dosage of 800mcg was achieved. Assessments occurred before the implant, and at 3mo and 12mo follow-ups. **Outcome Measure:** Modified Ashworth Scale (MAS), Spasm Frequency Scale (SFS), Disability Rating Scale (DRS), Level of Cognitive Functioning (LCF).	1. Mean ITB dose for participants was 380mcg. 2. Six patients received ITB within 3mo of injury (early); 6 patients received ITB between 3 and 6mo post injury (late). 3. At 3mo, both spasticity and spasms were significantly decreased compared to baseline, based on MAS and SFS scores (p<0.001 and p<0.002, respectively). 4. At 3mo, improvements in DRS and LCF were seen (p<0.001 and p=0.002, respectively). 5. At 12mo (n=5) all patients demonstrated further improvements in spasticity and spasms, but this was non-significant compared to results at 3 mo. 6. There were no differences in global outcomes (DRS and LCF) between patients in the early ITB initiation group and those in the late ITB initiation group.
Hoarau et al. (2012a) France Post-Test N=43	**Population:** TBI; Mean Age=23.3yr; Gender: Male=33, Female=10; Mean GCS Score=4.6. **Intervention:** After initial injury, participants who were started on Intrathecal Baclofen Therapy (ITB) to treat dysautonomia and hypertonia and were included for evaluation of long-term outcomes (mean 10±0.6yr post implantation). **Outcome Measure:** Coma Recovery Scale-Revised (CRS-R), Modified Ashworth Scale (MAS), Barthel Index (BI).	1. At follow-up, 9 participants had died, 13 were severely disabled or in an unresponsive wakefulness syndrome state and 21 had a good recovery of consciousness. 2. Mean CRS-R score was 18.9 (Range 1-23), mean BI score was 50.1 (Range 0-100), 34.9% were living at home, and mean MAS for upper limb was 1.6 (Range 0-4). 3. Most of the participants who had a positive recovery received ITB later than the other participants. 4. Complications occurred in 62.8% of patients; the most common being operative site infections (20.9%) and overdoses with profound flaccidity, sedation, and vomiting (16.3%).

Author Year Country Study Design Sample Size	Methods	Outcome
Horn et al. (2010) USA Pre-Post N=28	**Population:** TBI=12, Hypoxic Encephalopathy=3, Stroke=13; Mean Age=35yr; Gender: Male=12, Female=16; Mean Time Post Injury=45mo. **Intervention:** Participants received a 50µg bolus of baclofen injected into the lumbar intrathecal space. **Outcome Measure:** Ashworth Scale, Video-based Motion Analysis Program.	1. The range of motion (ROM) increased in the ankle on both the more involved side (13±6 versus 15±7, p=0.008) and the less involved side (22±8 versus 24±8, p=0.031) from baseline to post-injection. 2. ROM improvement occurred most often at 4 and 6hr after injection (p<0.05). 3. There was a significant correlation between the magnitude of change in ROM at the time of peak response and the magnitude of gait speed change (r=0.1, p<0.001). 4. Significant reductions in Ashworth scores compared to baseline (2.0±0.5) were observed at 2hr (1.6±0.4), 4 hr (1.4±0.4) and 6 hr (1.3±0.3) post-injection (all p<0.001).
Stokic et al. (2005) USA Case Series N=30	**Population:** TBI=17, Anoxia=4, Stroke=9; Mean Age=31yr; Gender: Male=17, Female=13; Mean Time Post Injury=3yr. **Intervention:** Participants received a single 50µg intrathecal baclofen bolus injection via a lumbar puncture. **Outcome Measure:** Ashworth Scale, H-Reflex from Soleus Muscle, F waves from Abductor Hallucis in Supine Position.	1. Ashworth score on the more involved side significantly decreased between baseline (2.4±0.7), 4 hr (1.5±0.6) and 6 hr (1.4±0.6) post-injection (p<0.001). 2. Maximal individual change in Ashworth scores ranged from 0 to 2.6 points (mean 1.0±0.7). 3. H/M ratio significantly decreased bilaterally (p<0.001). 4. F-wave persistence significantly decreased on the more involved side (p<0.05) with no change in F/M ratio.
Francisco et al. (2005) USA Case Series N=14	**Population:** Anoxic Encephalopathy=6, TBI=5, Stroke=3; Mean Age=35.9yr; Gender: Male=6, Female=8. **Intervention:** Patients were surgically fitted with an infusion pump for continuous intrathecal baclofen delivery. This took place a mean of 5.62mo (range 2-12mo) post injury. Follow up occurred at a mean of 13.9mo post pump implantation. **Outcome Measure:** Modified Ashworth Scale (MAS), Disability Rating Scale (DRS).	1. Participants received a mean daily intrathecal baclofen dose of 591.5µg (93-2000.2µg). 2. From baseline to follow-up, the mean decrease in MAS scores for upper extremities was 1±1.4 (p<0.020) and lower extremities was 2.1±1.4 (p<0.001). 3. The changes in DRS scores were not significant.
Horn et al. (2005) USA Pre-Post N=28	**Population:** TBI=12, Stroke=13, Hypoxic Encephalopathy=3; Mean Age=35yr; Gender: Male=12, Female=16; Mean Time Post Injury=45mo. **Intervention:** Participants received a single 50µg intrathecal baclofen bolus injection via lumbar puncture. **Outcome Measure:** Walking Performance, Ashworth Scale.	1. Significant reductions were seen in Ashworth scores compared to baseline (2.0±0.5) at 2hr (1.6±0.4), 4hr (1.4±0.4) and 6hr (1.3±0.3) post-injection (all p<0.001). 2. The greatest change from baseline occurred at 2, 4, and 6 hours in 6, 14, and 8 patients, respectively. 3. There were no significant correlations between change in Ashworth score and change in any temporospatial gait parameter.

Author Year Country Study Design Sample Size	Methods	Outcome
		4. There was a significant correlation between baseline velocity and peak change in velocity after ITB bolus (p<.05).
Dario et al. (2002) Italy Pre-Post N=14	**Population:** TBI=6, Anoxic ABI=8; Mean Age=38.8yr; Gender: Male=10, Female=4; Mean Time Post Injury=36.7mo. **Intervention:** Patients received continuous intrathecal baclofen infusions through the implantation of a subcutaneous pump. **Outcome Measure:** Ashworth Scale (AS), Spasm Frequency Scale (SFS).	1. Between the pre-operative assessment and final follow up assessment, there was a significant decrease in AS scores in both lower (4.3±0.5 versus 2.7±0.7) and upper (4.1±0.8 versus 2.3±0.9) extremities (both p<0.05). 2. A significant reduction in SFS scores was found between preoperative and postoperative values (2.5±0.5 versus 0.4±0.6, p<0.001). 3. Mean daily dose of baclofen was 305µg (range 90-510µg).
Francois (2001) France Case Series N=4	**Population:** TBI; Mean Age=19.5yr; Gender: Male=1, Female=2, Unknown=1; Mean GCS=3.5. **Intervention:** Patients received intrathecal baclofen infusions within 1mo following injury onset. **Outcome Measure:** Ashworth scores, Frequency, and Intensity of Autonomic Disorders.	2. Reductions in spasticity, and lower limb Ashworth scores at 6mo post intervention were reported in three of the four cases. In the last case, a substantial reduction in autonomic dysfunction and spasticity enabling passive physiotherapy was reported.
Meythaler et al. (1999) USA Pre-Post N=17	**Population:** ABI; Mean Age=29yr; Gender: Male=14, Female=3. **Intervention:** Patients with spasticity and/ or dystonia were surgically fitted with an infusion pump into the lower abdominal wall for continuous administration of intrathecal baclofen (100µg/day). Patients were assessed at 1yr. **Outcome Measure:** Ashworth Rigidity Scale (ARS), Spasm Frequency Scale (SFS), Deep Tendon Reflex (DTR) Score.	1. One year of intrathecal baclofen treatment (average dose: 302ug/d) resulted in a decrease in ARS (mean 2.2 points), SFS (mean 1.6 points), and DTR scores (mean 2.4 points) for the lower extremity (all p<0.0001) 2. For the upper extremity, the ARS, SFS, and DTR scores decreased by a mean of 1.4, 1.0, and 1.2 points respectively (all p<0.0001). 3. No cognitive side effects were observed after 1yr.
Meythaler et al. (1999) USA Pre-Post N=6	**Population:** TBI=3, Stroke=3; Mean Age=50yr; Gender: Male=2, Female=4. **Intervention:** Patients were surgically fitted with a programmable infusion pump into the lower abdominal wall for continuous administration of baclofen using the same methodology as Meythaler et al. (1997). **Outcome Measure:** Ashworth Rigidity Scale (ARS), Spasm Frequency Scale (SFS), Deep Tendon Reflex (DTR) scores.	1. Lower extremities showed a significant reduction in the ARS (p<0.0001), affected side DTR (p=0.021), unaffected side DTR (p=0.0051). No significant changes were seen in affected side SFS (p=0.500). 2. Upper extremities showed a significant reduction in the ARS (p=0.0002). No significant changes were seen for Biceps DTR (affected and unaffected: p=0.109 and p=0.068), or affected side SFS (p=0.1797). 3. No patients complained of subjective weakness on the normal side.
Meythaler et al. (1997)	**Population:** TBI=9, ABI=3; Mean Age=28yr; Gender: Male=11, Female=1.	1. For the lower extremity, ARS decreased by a mean of 1.4 points, SFS decreased by a

Author Year Country Study Design Sample Size	Methods	Outcome
USA Pre-Post N=12	**Intervention:** Patients received continuous intrathecal baclofen delivery for 3mo via an implanted infusion pump-catheter system. **Outcome Measure**: Ashworth Rigidity Scale (ARS), Spasm Frequency Score (SFS), Deep Tendon Reflex (DTR) Score.	mean of 1.5 points, and DTR scores decreased by a mean of 2.5 points (all p<0.0001). 2. For the upper extremity, the mean decrease in scores was 1.4 points for the ARS (p=0.003), 1.2 points for the SFS (p=0.007) and 1.0 points for the DTR (p=0.011).
Becker et al. (1997) Germany Case Series N=18	**Population:** TBI=9, Hypoxic Brain Injury=9; Mean Age=41yr; Gender: Male=13, Female=6; Mean Time Post Injury=11.6mo. **Intervention:** Patients received continuous intrathecal baclofen infusion. **Outcome Measure:** Ashworth Scale, Spasm Frequency Scale.	1. In all patients, spasticity was reduced. 2. Mean Ashworth scores reduced from 4.5 to 2.33, and the mean spasm frequency scores decreased from 2.16 to 0.94. 3. Reduction in spasticity was associated with a reduction in pain.

Discussion

In an RCT, Meythaler et al. (1996) found that intrathecal baclofen was effective in decreasing upper and lower extremity spasticity. In subsequent studies, the authors found that intrathecal baclofen was effective in decreasing spasticity for up to three months (Meythaler et al., 1997) and 1 year (J. M. Meythaler et al., 1999). While other studies reported efficacy of intrathecal baclofen for the management of spasticity post ABI (Becker et al., 1997; Chow et al., 2015; Dario et al., 2002; Francisco et al., 2005; Hoarau et al., 2012b; Margetis et al., 2014; Posteraro et al., 2013; Stokic et al., 2005; Wang et al., 2016), these studies did not use a control group.

In addition to spasticity management, some studies found that intrathecal baclofen may result in changes in ankle joint range of motion during gait and velocity improvements (Chow et al., 2015; Horn et al., 2010; Horn et al., 2005). Future studies using a prospective controlled trial or RCT study design that includes a control group are needed to further establish the efficacy of intrathecal baclofen for the management of spasticity post ABI.

Although effective for the treatment of spasticity, adverse effects, including known complications and risks associated with invasive ITB treatment, were common. In the study by Hoarau et al. (2012a), 62.8% of participants presented with a complication, including infections at the operative site (20.9%), and overdose characterized by profound flaccidity, sedation, and vomiting (16.3%).

Conclusions

There is level 1a evidence (Meythaler et al., 1996) that bolus intrathecal baclofen injections may produce short-term (up to six hours) reductions in upper and lower extremity spasticity compared to placebo following ABI.

There is level 4 evidence (Wang et al., 2016; Becker et al., 1997; Francois, 2001; Francisco et al., 2005; Stokic et al., 2005; Dario et al., 2002; Margetis et al., 2014; Meythaler et al., 1997; 1999a; 1999b; Posteraro et al., 2013; Hoarau et al., 2012a) that a continuous infusion of intrathecal baclofen may result in long-term reductions in spasticity in both the upper and lower extremities following an ABI.

There is level 4 evidence (Chow et al., 2015; Horn et al., 2005; 2010) that intrathecal baclofen may improve ankle range of motion during gait in individuals with ABI.

KEY POINTS

- Intrathecal baclofen bolus injections may reduce upper and lower extremity spasticity in individuals with ABI, but it is associated with significant risks.
- A continuous infusion of intrathecal baclofen by a pump may improve spasticity post ABI in both upper and lower extremities, as well as increase ankle range of motion during gait post ABI.

Multimodal Interventions

Multimodal interventions involve an examination of the combination of two or more treatments or compare different interventions to one other.

TABLE 25 | Multimodal Interventions for the Treatment of Spasticity Post ABI.

Author, Year Country Study Design Sample Size	Methods	Outcome
Leung et al. (2019) Australia RCT PEDro=7 $N_{Initial}$=13, N_{Final}=11	**Population:** TBI=13; *Intervention Group (n=7)*: Median Age=27yr (27-57); Gender: Male=3, Female=7; Median Time Post Injury=125d (78-150); Severity: Median GCS=3 (3-4). *Control Group (n=6):* Median Age=39yr (28-53); Gender: Male=3, Female=3; Median Time Post Injury=113d (73-159); Severity: Median GCS=9 (3-9) **Intervention:** Participants in the intervention group received botulinum toxin injections and serial casting, while those in the control group were placed on a waiting list for six weeks and then received the same intervention. Both groups received splinting and motor training following serial casting. Outcome measures were assessed at baseline, completion of casting, 2 and 8wk after casting.	1. Passive ankle dorsiflexion range significantly improved following completion of casting in the intervention group compared with the control group (26°, 95% CI: 17-35) and improvements were sustained at 2 wk (24°, 95% CI: 14-33) following casting. 2. No significant between groups differences were observed for strength and spasticity (p>.05). 3. There were 3 incidents of grade 1 pressure injury from casting and 4 incidents of grade 1 pressure injury from splinting. None of the participants suffered grade 2 pressure injury. There were no long term consequences from any of these incidents.

Author, Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measures: Passive ankle dorsiflexion range, spasticity, ankle dorsiflexor strength, Functional Independence Measure (FIM).	
Leung et al. (2014) Australia RCT PEDro=8 $N_{Initial}$=35, N_{Final}=32	**Population:** TBI; *Experimental Group (EG; n=17)*: Mean Age=38yr; Gender: Male=14, Female=3; Mean Time Post Injury=140d; Mean GCS=5. *Control Group (CG; n=18)*: Mean Age=38yr; Gender: Male=15, Female=3; Mean Time Post Injury=83d; Mean GCS=5. **Intervention:** Participants were randomly allocated to either the EG or CG group. The EG group underwent a treatment of tilt table standing and electrical stimulation (30 min 5d/wk) and splinting (12hr 5d/wk) for a total of 6 wk. For the next 4wk EG group participants underwent tilt table standing alone (30 min 3d/wk). The CG group underwent tilt table standing (30min 3d/wk) for the full 10 wk. Measures were taken at baseline, 6wk and 10wk. **Outcome Measure:** Passive ankle dorsiflexion, Functional Independence Measure (FIM).	1. The CG group had more range of motion in passive ankle dorsiflexion than the EG group at 6 wk (3 degrees) and 10 wk (-1 degree). 2. The EG group had a greater mean reduction in spasticity (1 point) at 6 wk; however, the effect disappeared at 10 wk. 3. There was no between group difference in walking speed. 4. There were no differences between groups for tolerance to treatment, perceived treatment benefit, perceived treatment worth, and willingness to continue with treatment.
Lorentzen et al. (2012) Denmark RCT-Crossover PEDro=6 N=10	**Population:** TBI=6, Stroke=2, Subarachnoid Hemorrhage=1, Post-Operative Hemorrhage=1; Mean Age=31.5yr; Gender: Male=6, Female=4; Mean Time Post Injury=3.6mo. **Intervention:** Participants received either a Neural Tension Technique (NTT) or a Random Passive Movement (RPM) treatment on knee joints. The NTT and RPM treatments lasted for 20min, with clinical tests conducted immediately before and after each treatment. **Outcome measure:** Modified Ashworth Scale (MAS), Range of Motion (ROM).	1. The blinded reviewers found no significant change on the MAS for knee flexors after the NTT (Mean change=0.4–0.6, p=0.10–0.31) or the RPM (Mean change=0.4–0.5, p=0.1–0.3). No significant between group differences were found (p=0.12-0.71). 2. No significant between or within group differences were found based on the MAS for knee extensors after the intervention. 3. The blinded reviewers found no significant difference in ROM after RPM (p=0.13) but did see a significant difference in ROM after NTT (p<0.05). No significant between group differences for ROM were found (p>0.32).
Verplancke et al. (2005) UK RCT PEDro=4 N=35	**Population:** TBI=20, Neurosurgery=11, Anoxia=4; Gender: Male=25, Female=10. *Group 1 (n=11)*: Median Age=40yr; Mean Time Post Injury=9.3d, Mean Glasgow Coma Scale (GCS) score 4.3. *Group 2 (n=12):* Median Age=33.5yr; Mean Time Post Injury=13.25 days; Mean GCS score=4.7. *Group 3 (n=12):* Median Age=41.5yr; Mean Time Post Injury=10.6d; Mean GCS score=5.2. **Intervention:** Participants entered one of three groups: Group 1 received a physical intervention (controls), Group 2 received casting plus injections of saline (4 ml), and Group 3 received casting plus injections of	1. Eighty-eight percent of patients developed spasticity within 14 days of injury. 2. Mean change in angle of passive ankle dorsiflexion was 4.59° in controls, 11.69° in group 2 and 13.59° in group 3. 3. There were significant improvements in MAS scores in treated groups (Group 2, p<0.03; Group 3, p=0.04) but not controls (p>0.05).

Author, Year Country Study Design Sample Size	Methods	Outcome
	botulinum toxin (100 units per leg) into the gastrocnemius and soleus muscles. Patients were re-cast if a 10° change in dorsiflexion occurred. **Outcome Measure:** Calf contracture, Modified Ashworth Scale (MAS), Passive Range of Motion.	

Discussion

Studies of combined or multimodal interventions for spasticity showed mixed results. In an RCT of casting alone versus casting combined with botulinum toxin injections (BTX-A). In an RCT, Verplancke et al. (2005) found that casting to prevent leg spasticity was beneficial but that there was no incremental benefit to combining casting with BTX-A. In contrast, in an RCT, Leung et al. (2019) found no significant differences in spasticity or strength in patients who received botulinum toxin injections, serial casting, motor training, and splinting when compared with waitlist controls who received standard care; however, the intervention group did demonstrate a significant increase in passive ankle dorsiflexion range of motion at completion of casting compared to the control group and this treatment effect was maintained at 2 weeks post casting.

Leung et al. (2014) investigated the effects of electrical stimulation and casting combined with standing on a tilt table compared to standing in a tilt table alone. The authors found a significant reduction in spasticity favoring the multimodal intervention group at 6 weeks, but this benefit disappeared in ten weeks. Since the experimental group received a combination of 3 treatments (tilt table, electrical stimulation, and casting), while the control group only underwent tilt table treatment, it is unclear whether the short-term reduction in spasticity in the experimental group is attributable to all 3 interventions or could be achieved with the tilt table and one of the other two treatments alone, or with the other treatments without using the tilt table, either of which might improve the feasibility of implementing such an initiative. Moreover, it should be noted that some participants showed difficulties adhering to the tilt table procedure due to fainting, fatigue, or behavioural issues

In a RCT by Lorentzen et al. (2012), participants received either neural tension technique (NTT) treatment or random passive movement (RPM) therapy on knee joints. No significant changes in spasticity were observed between groups in the knee flexor or extensor muscles.

Conclusions

There is level 1b evidence (Leung et al., 2019) that an intervention consisting of botulinum toxin injections, serial casting, motor training and splinting may improve ankle dorsiflexion range of motion but not improve spasticity in individuals with TBI.

There is level 1b evidence (Leung et al., 2014) that electrical stimulation in combination with tilt table standing and splinting may decrease spasticity at 6 weeks post intervention compared to tilt table standing alone in individuals with an TBI.

There is level 1b evidence (Lorentzen et al., 2012) that neural tension technique may not be more effective than random passive movement in improving lower extremity spasticity in individuals with ABI.

There is level 2 evidence (Verplancke et al., 2005) that botulinum toxin combined with casting may not be more effective than casting alone in the prevention of calf spasticity and contracture after severe brain injury.

KEY POINTS

- The combination of botulinum toxin, serial casting, motor training and splinting may improve dorsiflexion range of motion but may not reduce spasticity, when compared to standard care.
- Electrical stimulation in combination with tilt table standing and splinting may improve the early presentation of spasticity in patients post TBI.
- Neural tension technique may be just as effective as random passive movement for improving lower extremity spasticity post ABI.
- The combination of casting with botulinum toxin may not be more effective than casting alone for the prevention of calf spasticity and contracture post ABI.

VISUAL DYSFUNCTION

Visual system dysfunction is frequent following TBI; the incidence is particularly high in individuals who have sustained a blast-related TBI (Dougherty et al., 2011). The visual system is highly integrated and also acts as a primary sensory receptor for motor, social, cognitive, communicative, and emotive tasks. (Morton, 2004). Visual dysfunction post TBI can present with abnormalities in visual acuity, colour vision, stereopsis or depth perception, visual fields, pupillary function, accommodation, eye movements, vestibulo-ocular reflex, or visual perception as well as symptoms including photophobia or nystagmus (Armstrong, 2018). According to a systematic review by Riggs et al. (2007), the majority of the research investigating visual rehabilitation has focused on stroke populations, with fewer studies addressing persons with TBI.

TABLE 26 | Interventions for the Treatment of Visual Dysfunction Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Berryman et al. (2020) USA RCT PEDro=3 $N_{Initial}$=20, N_{Final}=14	**Population:** TBI; SEE Group (n=8); Mean Age=37.6yr; Gender: Male=6, Female=2; Mean Time Post Injury=33.1d; SOC Group (n=6); Mean Age=33yr; Gender: Male=6, Female=0; Mean Time Post Injury=46d. **Intervention:** Participants were randomized into an experimental group (SEE) or a control group (SOC). The experimental group received the Six Eyes Exercises (SEE) protocol, and the control group received the standard-of-care (SOC) protocol. **Outcome Measures:** Craig Hospital Eye Evaluation Rating Scale (CHEERS), King-Devick Test, Delis-Kaplan Executive Function System Trail Making Test: Condition 1 Visual Scanning, Modified Nelson-Denny Reading Test, and Subjective Vision Symptom Scale.	1. Participants in both groups improved in functional status over the course of treatment. Posttreatment, the number and severity of symptoms improved in both groups, with the SEE group exhibiting a greater reduction in average number of symptoms. 2. Posttreatment, 38% of the SEE group was asymptomatic compared with 17% of the SOC group. 3. The SEE protocol may be useful as a preparatory activity in activity-based vision treatment or as a stand-alone intervention to comprehensively treat oculomotor impairments post TBI.
Kasten et al. (2000) Germany RCT PEDro=5 N=32	**Population:** ABI=23; Vascular Disease=9; Mean Age=51.1yr; Gender: Male=20, Female=12; Mean Time Post Injury=6.8yr. **Intervention:** Participants were randomly assigned to either the Control Group (foveal fixation training only - FixTrain) or Restitution Group (PC-based training program – Visure, SeeTrain). Both groups trained for 1hr/day at home for ≥150hr over a 6mo period. **Outcome Measure:** High-Resolution Campimetry (PeriMa), Conventional Perimetry (TAP-2000), Pattern Recognition (PeriForm), Colour Discrimination (PeriColor).	1. The Restitution Group showed an increase in PeriMa and TAP-2000 after training ($p<0.01$ and $p<0.04$, respectively). 2. The Restitution Group had non-significant improvements in PeriForm and PeriColor ($p=0.06$ and $p=0.12$, respectively) within the defective area of the visual field. 3. There was a correlation between PeriMa and PeriForm ($r=0.67$, $p<0.05$) and PeriForm and PeriColor ($r=0.37$, $p<0.05$) for improved color and form perception. 4. The PeriMa, PeriForm, and PeriColor all demonstrated a shift of the visual field border in the direction of the blind area for participants in the Restitution Group.
Kasten et al. (1998) Germany RCT PEDro=7 N=38	**Population:** Stroke=10, ABI=28; Mean Age=51.5yr; Gender: Male=24, Female=14; Mean Time Post Injury=7.0mo. **Intervention:** Participants were randomly assigned to either the Restitution Group (visual restitution training (VRT)) or the Control Group (fixation training program which required eye movement toward stimuli within the foveal region). Both groups completed 150hr of training over 6mo at home in a darkened room. **Outcome Measure:** High-Resolution Perimetry (HRP), Response Frequency, Area of Absolute Defect, Tübinger Automatic Perimeter 2000 (TAP).	1. Performance on HRP showed improved ability to perceive visual stimuli above detection threshold in the VRT group post-training (post-chiasmic: $p<0.05$, optic nerve: $p<0.01$). 2. The VRT group demonstrated a higher response frequency to stimuli than the control group ($p<0.05$). 3. TAP scores showed a decrease in the area of absolute defect for participants in the VRT group with optic nerve injuries ($p<0.01$). 4. Participants with optic nerve damage benefitted most from VRT; 72.2% of participants who received VRT reported subjective improvement compared to only 16.6% of the Control Group participants ($p<0.03$).

Author, Year Country Study Design Sample Size	Methods	Outcome
Conrad et al. (2017) USA Pre-Post $N_{Initial}$=19, N_{Final}=13	**Population:** TBI=15, Stroke=3, Organic Brain Syndrome=1; Mean Age=45.2yr; Gender: Male=12, Female=7; Time Post Injury=2.2 yr. **Intervention:** Participants were prescribed home-based computer vergence therapy (5d/wk for 12wk). Participants were assessed at baseline, 4, 8 and 12wk. **Outcome Measure:** Negative Fusional Vergence, Positive Fusional Vergence, Near Point of Convergence, Vergence Facility, Convergence Insufficiency Symptom Survey (CISS).	1. Negative Fusional Vergence showed significant improvements over 12wk in blur (p=0.037), break (p=0.003) and recovery (p=0.006). 2. Positive Fusional Vergence showed significant improvements over 12wk in blur, break and recovery (p<0.0001). 3. Near Point of Convergence showed significant improvements over 12wk in break (p=0.002) and recovery (p<0.001). 4. Vergence Facility showed a significant improvement from baseline to 12wk (p<0.0001). 5. CISS scores improved significantly from baseline to 12wk (p=0.0001).
Ciuffreda et al. (2006) USA PCT N=14	**Population:** TBI=9, Stroke=5; Mean Age=48.4yr; Gender: Male=9, Female=5; Mean Time Post Injury=2.4yr. **Intervention:** Patients with oculomotor-based dysfunction received reading-related rehabilitation. Participants were assigned to either Visual (V) Feedback Training (modes included normal internal oculomotor visual feedback in isolation - T1 for 4 weeks) or combined Visual and Auditory (V+A) Feedback (concurrent with external oculomotor auditory feedback - T2 for 4wk) with a cross-over design. Participants underwent single-line (SL) and multiple-line (ML) simulated reading, and basic versional tracking (fixation, saccade, and pursuit) 2x/wk for an 8wk period. **Outcome Measure:** Simulated Reading, Visagraph, Basic Versional Eye Movements, Reading Rating Scale.	1. Significant improvements were found for each of the five questions on the Reading Rating Scale (p<0.01). 2. Simulated Reading Saccade Ratio showed significant improvements for ML (TI: p<0.05) and SL (TI: p<0.01; T2: p<0.01) training compared to pre-training levels. 3. The TBI subgroup had more improvements Simulated Reading and Visagraph, compared to individuals with stroke. 4. There was a trend for greater reading improvement in the V+A Feedback training, compared to visual feedback in isolation.
Padula et al. (1994) USA Pre-Post N=20	**Population:** TBI=10, Healthy Control=10; Age Range=22-46yr; Gender: Male=8, Female=12. **Intervention:** Visual evoked potentials (VEP) were performed using a Nicolet Compact Four Electrodiagnostic System and a Visual Stimulator over three trials. During the baseline trial, participants were tested without bi-nasal occluders and base-in prisms. In the experimental trial, participants were tested with bi-nasal occluders and two diopters of base-in prisms. In the last phase, the bi-nasal occluders and prisms were removed, and the participants were re-evaluated. **Outcome Measure:** Visual Evoked Potential (VEP).	1. The use of base-in prisms and bi-nasal occluders produced a large increase in VEP amplitude in individuals with TBI (p<0.01). 2. Using base-in prisms and bi-nasal occluders resulted in a significantly larger increase in VEP amplitude in individuals with TBI compared with the healthy controls (mean difference between groups 1.78, p<0.01).

Discussion

In an RCT, Berryman et al. (2020) compared the Six Eyes Exercises (SEE) protocol to standard care. The authors found that the symptoms in both groups improved, with the SEE group showing a greater reduction in average number of symptoms. When comparing outcomes post treatment, 38% of participants in the SEE group were asymptomatic, compared to 17% of participants in the control group.

In an RCT of persons with visual fields deficits due to stroke or TBI, Kasten et al. (1998) found that individuals with optic nerve or post-chiasmic injury post ABI who completed computer-based Visual Restitution Training (VRT) experienced reduction in the extend of their visual field deficit and increased light detection, compared to the control group. In a subsequent RCT study, the authors found that VRT was associated with in improvements in visual detection as well as other visual functions such as shape and color recognition (Kasten et al., 2000).

In a pre-post study, Conrad et al. (2017) found that participants who underwent home-based computer vergence therapy five days a week for 12 weeks showed significant improvements in negative vergence, positive vergence, near point convergence and vergence facility (Conrad et al., 2017). In a PCT study, participants received reading-related rehabilitation to improve oculomotor-based dysfunction (Ciuffreda et al., 2006). The authors found that repetitive oculomotor conditioning reduces the cognitive and attentional load of reading, resulting in significant improvements in reading tasks, concentration and visual scanning (Ciuffreda et al., 2006).

A small pre-post study by Padula et al. (1994) reported that visual dysfunction post ABI can be improved with base-in prisms, as they affect the ambient visual process by increasing the effectiveness of binocular cortical cells. The authors found that the addition of bilateral base-in prisms and bi-nasal occluders increased the amplitude of visual-evoked potentials (Padula et al., 1994).

Conclusions

There is level 1b evidence (Kasten et al., 1998), and level 2 evidence (Kasten et al., 2000) that computer-based visual restitution training may be more effective than visual fixation training in improving visual function post TBI.

There is level 2 evidence (Berryman et al., 2020) that the Six Eyes Exercises protocol may be more effective for the reduction of visual symptoms than standard of care in persons post TBI.

There is level 2 evidence (Ciuffreda et al., 2006) that reading-related rehabilitation may improve reading tasks in individuals with oculomotor dysfunction post ABI.

There is level 4 evidence (Padula et al., 1994) that base-in prisms and bi-nasal occluders may be effective in the treatment of ambient vision disturbances post ABI.

There is level 4 evidence (Conrad et al., 2017) that home-based computer visual vergence therapy may be effective in the treatment of binocular vision disorders in individuals with ABI.

KEY POINTS

- Computer-based visual restitution training and reading related rehabilitation may improve visual function in individuals with TBI.
- The Six Eyes Exercises protocol may reduce visual symptoms post TBI.
- Reading related rehabilitation may facilitate reading tasks in individuals with ABI.
- Base-in prisms and bi-nasal occluders may improve ambient vision disturbances post ABI.
- Home-based computer visual vergence therapy may improve binocular vision disorders in individuals with ABI.

BALANCE DYSFUNCTION

Balance and postural difficulties are commonly experienced by individuals with TBI, affecting gait, function in activities of daily living, and participation in social activities; in addition, balance dysfunction may be associated with longer in-patient lengths of stay and delayed recovery (Alashram et al., 2020).

TABLE 27 | Interventions for the Treatment of Balance Dysfunction Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Aquatic Therapy		
Curcio et al. (2020) Italy RCT PEDro=6 N_{Inital}=22 N_{Final}=20	**Population:** Severe TBI; GCS: ≤8; ATG (n=10); Mean Age=37.4yr; Gender: Male=4, Female=6; Mean Time Post Injury=5.8mo; CTG (n=10); Mean Age=43yr; Gender: Male=5, Female=5; Mean Time Post Injury=4.8mo. **Intervention:** Participants were randomly assigned to the aquatic therapy group (ATG) or to the Conventional Training Group (CTG). Participants underwent twelve individual rehabilitation sessions (3d/wk x 4wk), in a rehabilitation pool. **Outcome Measures:** Berg Balance Scale (BBS), Modified Barthel Index (MBI), Disability Rating Scale (DRS), Tinetti Gait Balance Scale (TBG), and Quality of Life After Brain Injury (QOLIBRI).	1. The within-subjects comparison showed a significant improvement both in ATG and CTG in MBI, BBS, TBG, and QOLIBRI. 2. No significant differences were found in the between-subjects analysis. 3. Both groups demonstrated statistically significant improvements in motor function and quality of life suggesting that Aquatic Therapy could be safely offered to persons with severe TBI during the course of post-acute neurorehabilitation.
Virtual Reality		
Tefertiller et al. (2019) USA RCT PEDro=5 N_{Inital}=63 N_{Final}=58	**Population:** TBI; VR group (n=31) Mean Age=48.1yr; Gender: Male=23, Female=8; Mean Time Post Injury=8.3yr; HEP group (n=32); Mean Age=49.5yr; Gender: Male=16, Female=16; Mean Time Post Injury=8.5yr. **Intervention:** Participants were randomized into two groups: Virtual Reality (VR), and	1. No significant between group differences were found in the CB&M. 2. No significant between group differences were found in any of the secondary outcomes: BESTest, ABC, or PART-O. 3. Significant improvements in balance were observed in both groups over a 24-week

Author, Year Country Study Design Sample Size	Methods	Outcome
	traditional Home-based Exercise Program (HEP). The VR intervention focused on dynamic standing and single limb stance while using an Xbox Kinect system. **Outcome Measures:** Community Balance and Mobility Scale (CB&M), Balance Evaluation Systems Test (BESTest), Activities-Specific Balance Confidence Scale (ABC), Participation Assessment with Recombined Tools-Objective (PART-O).	period. These results suggest that VR training is not more beneficial than a traditional HEP for improving balance in individuals with moderate to severe TBI.
Straudi et al. (2017) Italy RCT PEDro=5 N_{Inital}=21 N_{Final}=20	**Population:** Chronic TBI; VGT group: Mean Age=30.5yr; Gender: Male=10, Female=2; Mean Time Post Injury=2yr; BPT group: Mean Age=37yr; Gender: Male=7, Female=2; Mean Time Post Injury=8yr. **Intervention:** Participants were randomized into two groups: Video Game Therapy (VGT) using the Xbox Kinect system or Balance Platform Therapy (BPT) for 3 sessions/wk x 6wk. **Outcome Measures:** Community Balance and Mobility Scale (CB&M), Unified Balance Scale (UBS), Timed Up and Go test (TUG), selective visual attention evaluation (Go/No go task).	1. Both groups improved in CB&M scores. 2. Significant between group differences were noted with the VGT group showing greater increases on the UBS and TUG compared to the BPT group ($p < 0.05$). 3. Selective attention improved significantly in the VGT group ($p < 0.01$).
Dual-Task Rehabilitation		
Peirone et al. (2014) Italy RCT PEDro=6 N=16	**Population:** TBI=7, Stroke=7, Other=2; Mean Age=40.5yr; Gender: Male=9, Female=7; Mean Time Post Injury=14.3mo. **Intervention:** Participants were randomized into a control (n=8) or intervention group (n=8). Both groups received standard physiotherapy in 50min sessions (3x/wk for 7wk). The intervention group performed an individualized dual-task home-based program (6d/wk for 7wk). **Outcome Measure:** Balance Evaluation System Test (BEST), Activities-Specific Balance Confidence Scale, Goal Attainment Scaling (GAS).	1. Post-intervention scores differed significantly between groups on the BEST, with the intervention group improving more (p=0.008). 2. There were no significant between group differences on the Activities-Specific Balance Confidence Scale (p=0.110), or the GAS (p=0.093). 3. The control group made significant improvements on the BEST (mean change=5.5±3.53, p=0.020) and the GAS (mean change=16.28±6.58, p=0.010). 4. The intervention group made significant improvements from pre to post intervention on the BEST (mean change=17.87±6.05, p=0.014), the Activities-Specific Balance Confidence Scale (mean change=25.25±25.51, p=0.01) and the GAS (mean change=19.37±9.03, p=0.02).
Yoga		
Schmid et al. (2016) USA Pre-post N=3	**Population:** TBI; Mean Age=44.33yr; Gender: Male=1, Female=2; Time Post Injury=19.33yr. **Intervention:** One-on-one session of yoga with a therapist. Therapy included 1-h sessions twice a week for 8 weeks.	1. All three study participants had baseline BBS scores of ≤46, indicating impaired balance and increased fall risk. 2. After the 8-week intervention, two individuals improved their BBS score to be >46, indicating

Author, Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measures: Berg Balance Scale (BBS), Activities Balance Confidence Scale (ABC), Pain, Enjoyment and General Activity Scale (PEG), Cervical Range of Motion (ROM), Chair-to-Stand Test and 6-min/10-min Walk Tests.	a lower risk of falling. All three participants improved their balance, with average BBS scores improving from 34± 9.6 to 46.3± 5.5 (36% increase). Average ABC scores also increased by 39%. 3. On average, pain interference scores decreased by 6% (5.1±1.26 to 4.8±2.67). 4. All three participants increased left and right cervical rotation and lateral flexion. 5. Gait-speed, as measured with the 10-min Walk Test, increased by 19% from 1.08± 0.73 m/s to 1.28±0.78 m/s. 6. Yoga is feasible and safe for individuals with chronic TBI, and it may bring benefits in physical functioning.
Aerobic Dance		
Dault and Duga (2002) Canada PCT N=8	**Population:** TBI=8; Mean Age=29.6yr; Gender: Male=6, Female=2; Mean Time Post Injury=44.4mo. **Intervention:** Participants completed an individualized 12-wk Specific Training Program (STP) combining aerobic dance and slide and step training for 30min 3x/wk or traditional muscular training (TMT) for 60min 2x/wk for 12wk. **Outcome Measure:** Clinical Test for Sensory Interaction in Balance (CTSIB), Jumping Jack movement.	1. Over time, all of the participants' performance of the exercises improved. 2. The analysis of balance revealed a significant difference between pre- and post-training sway area for the STP group ($p<0.05$) but not for the TMT group.

Discussion

In an RCT, Curcio et al. (2020) compared aquatic therapy to conventional training for the rehabilitation of motor function and balance in individuals with severe TBI. While both groups demonstrated improvements, the authors found no significant differences in balance between groups, as measured by the Berg Balance Scale (BBS) and the Tinetti Gait Balance Scale (TGBS).

The use of virtual reality was examined in two RCT studies. Tefertiller et al. (2019) found that dynamic standing exercises and single limb stance using an Xbox Kinect system was not more effective than a traditional home-based exercise program for the rehabilitation of balance in individuals with TBI. Straudi et al. (2017) found that training using an Xbox Kinect system was more effective in improving balance than training using a balance platform.

In an RCT study, Peirone et al. (2014) compared standard physiotherapy alone or in combination with a dual-task home-based rehabilitation program. The authors found that both groups demonstrated significant differences in balance, as measured by the Balance Evaluation System Test (BEST). However,

those who received the dual-task home-based rehabilitation program showed significantly greater improvements (Peirone et al., 2014). Despite these findings, this study was underpowered and further investigation is needed before definitive conclusions are made.

The effectiveness of yoga was examined in a pre-post study by Schmid et al. (2016). The authors found that yoga improved balance in individuals with TBI; however, results need to be interpreted with caution given that the study only had three participants. In a PCT study with a small sample size, Dault and Dugas (2002) found that aerobic dancing and slide-and-step training improved balance and coordination in individuals with TBI, and this intervention was more effective than traditional muscular training.

Conclusions

There is level 1b evidence (Curcio et al., 2020) that aquatic therapy may not be more effective than conventional training for rehabilitation of balance impairment in individuals with severe TBI.

There is level 1b evidence (Peirone et al., 2014) that an individualized dual-task home-based rehabilitation program may improve balance in individuals with ABI.

There is level 2 evidence (Tefertiller et al., 2019; Straudi et al., 2017) that virtual reality therapy using an Xbox Kinect system may not be more effective than a home-based program for balance rehabilitation; however, it may be more effective than a balance platform.

There is level 2 evidence (Dault & Duga, 2002) that a combined program including aerobic dancing and slide and step training may be more effective for the rehabilitation of balance impairment post TBI than traditional muscular training.

There is level 4 evidence (Schmid et al., 2016) that yoga may improve balance in individuals with TBI; however, further research with larger samples is needed to confirm the effectiveness of this intervention.

KEY POINTS

- Aquatic therapy, compared to conventional training, may not improve balance in individuals with severe TBI.
- An individualized dual-task home-based rehabilitation program may improve balance in individuals with ABI.
- For the rehabilitation of balance impairment, virtual reality therapy using an Xbox Kinect system may be more effective than a balance platform; however, virtual reality therapy may not be more effective than a home-based balance program.
- A combination of aerobic dancing and slide and step training may be more effective than traditional muscular training for rehabilitation of balance post TBI.
- Yoga may be effective for rehabilitation of balance post TBI; however, more research is needed.

VESTIBULAR DYSFUNCTION

Vestibular dysfunction post ABI is a major contributor to reduced tolerance for rehabilitation and delayed recovery (Bhatnagar et al., 2019). Vestibulo-ocular function can be impacted by TBI, with symptoms including dizziness, unsteadiness, headache, blurry vision, difficulties with concentration and reading, as well as nausea (Wallace & Lifshitz, 2016); impaired vestibular function can present with vertigo. Vertigo is often described by the individual as a sensation of falling, feeling as the room spinning or the ground is suddenly moving (Wallace & Lifshitz, 2016). The most common persisting vestibular symptom after TBI is positional vertigo, or vertigo caused by head movement, which is caused by dysfunction of the vestibular nerve or the labyrinth (Shepard & Telian, 1995) and the inability of the central nervous system to effectively compensate for the dysfunction (Gurr & Moffat, 2001).

Vestibular rehabilitation is intended to promote adaptation and recovery, often facilitated with techniques such as gaze stability exercises, vestibulo-ocular reflex gain adaptation, substitution exercises, habituation techniques, as well as static and dynamic balance and gait exercises (Scherer & Schubert, 2009). The optimal recovery of vestibular dysfunction is thought to be based on selecting the appropriate vestibular exercises for a specific individual and progressing through the assigned exercises with gradually increasing difficulty and intensity (Wee, 2002), although research in this area is limited and optimal strategies or techniques is not established.

TABLE 28 | Interventions for the Treatment of Vestibular Dysfunction Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
	Betahistine	
Jafarzadeh et al. (2018) Iran RCT PEDro=4 N=20	**Population:** TBI; Mean Age=44.2yr; Gender: Not Reported; Time Post Injury=Not Reported. **Intervention:** Participants were randomly divided into two groups: one group received medical therapy with, Betaserc (betahistine) pills 8mg at least 3x/day, and the other group received vestibular rehabilitation that included gaze stability, adaptation exercises, and some substitution exercises (4-wk period) and medical therapy. **Outcome Measures:** Dizziness Handicap Inventory (DHI).	1. There was no significant difference between the two groups in DHI total score or on subtests at the beginning of the program. 2. There were no significant differences between the two groups at weeks 1 and 2 in terms of recovery status, but significant differences were observed at weeks 3 and 4. 3. After 1 month of rehabilitation, patients receiving vestibular rehabilitation and medication showed greater progress than patients receiving medication only (P=0.000). 4. Early vestibular rehabilitation within 1 month post injury can decrease vertigo symptoms, and increase stability and balance performance, thereby improving the patient's functional and physical conditions.

Author, Year Country Study Design Sample Size	Methods	Outcome
Naguib & Madian (2014) Egypt RCT PEDro=5 N=60	**Population:** TBI; Mean Age=30yr; *Group 1 (n=20):* Gender: Male=14, Female=6; Severity: Mild=8, Moderate=7, Severe=5. *Group 2 (n=20):* Gender: Male=14, Female=6; Severity: Mild=8, Moderate=8, Severe=4. *Group 3 (n=20):* Gender: Male=15, Female=5; Severity: Mild=6, Moderate=8, Severe=6. **Intervention:** Participants were randomized to receive betahistine dihydrochloride (48mg/d, Group 1), a vestibular rehabilitation program (Group 2), or both (Group 3) as treatment for a balance disorder. Outcomes were assessed via videonystagmography at baseline, 1 and 2wk, and then every month until recovery. **Outcome Measures:** Recovery time.	1. Group 3 showed the earliest recovery time: complete recovery within 2mo. 2. For Group 2, 80% had complete recovery within 2 months and 20% within 3mo. 3. For Group 1, 85% had complete recovery within 2-3mo, and 15% in more than 3mo. 4. Mean duration of recovery in patients who only received betahistine was 62.1d. That was significantly (p<.05) longer than in patients who only received early vestibular rehabilitation, 37.6d, or those who received both treatments, 34.4d.
Particle Repositioning Maneuver		
Motin et al. (2005) Israel Post-Test N=10	**Population:** Severe TBI; Mean Age=43yr; Gender: Male=8, Female=2; Mean Time Post Injury=67d. **Intervention:** Patients underwent a particle reposition maneuver. The examiner performed the Dix-Hallpike test to the affected side such that nystagmus and vertigo were elicited; this position was maintained for 1-2min. The patient's head was then rotated 90º to the opposite side and held for ~ 30sec. The participant was then asked to turn their head another 90º to the unaffected side. This position was maintained for another 1-2min and then the participant was assisted to sit-up. **Outcome Measure:** Improvements in Positional Nystagmus.	1. Six of ten participants had resolved positional nystagmus and vertigo following a single particle repositioning maneuver. 2. Nine of 14 (64%) affected ears had resolved positional nystagmus and vertigo following a single particle repositioning maneuver. 3. The other four participants needed between 3 and 6 repeated treatments until their symptoms were completely resolved.
Behavioural Exposure		
Gurr and Moffat (2001) UK Pre-Post N=41	**Population:** TBI; Mean Age=44.1yr; Gender: Male=28, Female=41; Mean Time Post Injury=78.7mo. **Intervention:** Therapy consisted of a behavioural exposure program to movements and activities that provoked vertigo and anxiety in order to assist compensation of vestibular dysfunction and habituation to physical anxiety symptoms. **Outcome Measure:** Vertigo Symptom Scale (VSS), Vertigo Rating scale (VRS), Vertigo Handicap Questionnaire (VHQ), Sway-Monitor Assessment.	1. Participants' vertigo symptoms and somatic anxiety had significantly decreased from pre-test to post-test (both p<0.01). 2. Significant reductions in VRS scores were shown from pre-test to post-test, and post-test to follow up (both p<0.01). 3. Post-test levels of postural sway on the sway monitor (ability to balance on an unstable surface with eyes open) had significantly improved compared to pre-test levels (p=0.008). 4. Vertigo handicap levels (VHQ scores) significantly decreased from pre- to post-intervention (p<0.01).

Discussion

Multiple rehabilitation strategies and techniques have been studied to address vestibular dysfunction in persons with ABI and other neurologic conditions. The use of Betahistine was examined in two RCT studies. Jafarzadeh et al. (2018) found that, while there were no significant differences between the study groups at baseline, participants who received both vestibular rehabilitation and betahistine showed greater improvements after 1 month than those who received betahistine alone. In the study by Naguib and Madian (2014), the combination of vestibular rehabilitation and betahistine resulted in the shortest recovery time, when compared to treatment with betahistine alone or vestibular rehabilitation alone.

The effectiveness of particle repositioning maneuvers was examined in a post-test study by Motin et al. (2005). The authors found that positional nystagmus was resolved for the majority of their participants following the intervention (Motin et al., 2005). In a pre-post study, Gurr and Moffat (2001) examined behavioural exposure to vestibular rehabilitation. The authors attempted to restructure the maladaptive thoughts and belief patterns associated with the symptoms of provoked vertigo. This multidimensional psychological approach was effective in improving vertigo symptoms, independence, emotional distress, physical flexibility and postural stability (Gurr & Moffat, 2001).

Conclusions

There is level 2 evidence (Naguib & Madian, 2014; Jafarzadeh et al., 2018) that betahistine in combination with vestibular rehabilitation may be more effective than betahistine or rehabilitation alone in improving vertigo and balance disorder after a TBI.

There is level 4 evidence (Motin et al., 2005) that the Particle Repositioning Maneuver may lead to improvements in positional nystagmus in individuals with severe TBI.

There is level 4 evidence (Gurr & Moffat, 2001) that a behavioural exposure program may improve symptoms of vertigo in patients after TBI.

KEY POINTS

- Betahistine in combination with vestibular rehabilitation may improve vertigo and balance in individuals with TBI.
- Particle repositioning maneuvers may be effective for the improvement of positional nystagmus post TBI.
- A behavioural exposure program may improve vertigo post TBI.

OLFACTORY DYSFUNCTION

Olfactory dysfunction, following TBI primarily, occurs as a result of damage to olfactory nerve fibers as they cross the cribriform plate, injury to the sinonasal tract, or hemorrhage within the olfactory cortex (Whitcroft & Hummel, 2019). Impairments in olfactory function can be quantitative (reduced or lack of ability to detect and perceive odors) and/or qualitative (distortion in the perceived quality of odor stimuli). Based on severity, quantitative olfactory impairments can be further divided into *hyposmia* (reduced olfactory function) and *functional anosmia* (inability to detect odors or absence of sense of smell) (Bratt et al., 2020; Limphaibool et al., 2020). The presence of olfactory dysfunction post TBI hinders quality of life in affected individuals and often leads to heightened risks of personal injury. Although TBI is one of the main causes of olfactory dysfunction (Limphaibool et al., 2020), the management of olfactory dysfunction in the TBI population has been largely neglected in current research and clinical practice. Several pharmacological options have been used for the treatment of olfactory dysfunction due to various conditions, such as intranasal insulin, minocycline, zinc gluconate, vitamin A, and corticosteroids (Whitcroft & Hummel, 2019). Olfactory training has also shown to be effective in improving olfactory function in persons without ABI (Sorokowska et al., 2017).

TABLE 29 | Interventions for the Treatment of Olfactory Dysfunction Post ABI

Author, Year Country Study Design Sample Size	Methods	Outcome
Jiang et al. (2019) Taiwan RCT PEDro=5 $N_{Initial}$=111, N_{Final}=90	**Population:** TBI; 4-Odorant (n=45); Mean Age=43.07yr; Gender: Male=20, Female=25, Mean Time Post Injury=16.27mo; PEA (n=45); Mean Age=39.71yr; Gender: Male=18, Female=27; Mean Time Post Injury=9.64mo. **Intervention:** 90 participants were randomized into two groups and completed 6 months of olfactory training: 1) 4-Odorant Group – individuals were given 4 bottles containing PEA, lemon, eucalyptus, and clove oils, 2) Phenyl ethyl alcohol (PEA) group – individuals were given a bottle of PEA. **Outcome Measures:** Traditional Chinese Version of the University of Pennsylvania Smell Identification Test (UPSIT-TC), MRI.	1. There were no significant differences in olfactory bulb (OB) volumes between the 4-Odorant and PEA groups at baseline. 2. The UPSIT-TC score increased significantly in the PEA group but not in the 4-Odorant group. OB volumes were not significantly different between these 2 groups. 3. Results showed that olfactory training can slightly improve odor threshold levels in patients with traumatic anosmia, but did not improve odor identification ability.
Langdon et al. (2018) Spain RCT PEDro=6 N=42	**Population:** Olfactory Training (n=21); Mean Age=36.7yr; Gender: Male=14, Female=7; Mean Time Post Injury=11.4mo; Control (n=21); Mean Age=34.3yr; Gender: Male=15, Female=6; Mean Time Post Injury= 11.4mo. **Intervention:** Participants were randomized into an experimental group with olfactory training (OT) and a control group without	1. After 12 weeks of OT, participants showed a significant improvement in the n-BTt compared with those who received no training. 2. Significant differences were also observed in BAST-24 outcomes and smell loss by VAS. 3. Results indicated that OT induced a mild and transient improvement in smell threshold

Author, Year Country Study Design Sample Size	Methods	Outcome
	(nOT). OT was performed twice daily with a six odor training set for 12 weeks. Odorants used were: anise, lemon, rose, vinegar, smoked, eucalyptus. **Outcome Measures:** Subjective olfactometry (Barcelona Smell Test [BAST] 24), a visual analogue scale (VAS), and n-butanol threshold (n-BTt).	performance and that structural brain damage is strongly correlated with olfactory function.
Jiang et al. (2017) Taiwan RCT PEDro=4 N_{Inital}=83, N_{Final}=81	**Population:** TBI; PEA (n=42); Mean Age=37.7yr; Gender: Male=27, Female=15; Mineral Oil (n=39); Mean Age= 40.7yr; Gender: Male=20, Female=19. **Intervention:** Participants were randomly divided into two groups. In the phenyl ethyl alcohol (PEA) group (N=42) participants were given a bottle of pure PEA, whereas those in the mineral oil group (N=39) were given a bottle of odorless mineral oil. **Outcome Measures:** University of Pennsylvania Smell Identification Test - Chinese version (UPSIT-TC), PEA Test	1. The improvement of olfactory function with a bi- or unirhinal PEA threshold below -1.0 after olfactory training was observed in 10 patients (23.8%) who received olfactory training with PEA and in two patients (5.1%) who received olfactory training with mineral oil. 2. The UPSIT-TC score increased four or more points after olfactory training in six patients (14.3%) who had received olfactory training with PEA and in six (15.4%) who had received olfactory training with mineral oil. 3. Olfactory training with PEA could improve PEA odor threshold levels in patients with traumatic anosmia.
Bratt et al. (2020) Norway Pre-Post $N_{Initial}$=23, N_{Final}=22	**Population:** TBI=23; Mean Age=49±13yr; Gender: Male=17, Female=6; Mean Time Post Injury=62±25mo; Severity: Mean GCS=9±3. **Intervention:** Participants with posttraumatic olfactory dysfunction following TBI were treated with oral corticosteroids (30mg prednisone, once daily) for 10d, followed by olfactory training twice daily for 3mo. Outcome measures were assessed at baseline, the end of corticosteroid treatment, the end of olfactory training, and after 12mo. **Outcome Measures:** Olfaction (mean threshold, discrimination, and identification score (TDI)).	1. The TDI significantly improved from baseline to follow-up (14.4±7.3 versus 20.8±7.7, p<.001). 2. Half of the participants experienced a clinically significant improvement of >5 TDI points. 3. Improvement was not associated with any sociodemographic, trauma-related characteristics or olfactory function at baseline.

Discussion

In an RCT study, Jiang et al. (2017) examined the effect of olfactory training in individuals with traumatic anosmia. The authors reported that odor thresholds improved in those who received a bottle of phenyl ethyl alcohol (PEA), compared to those who received a bottle of mineral oil; however, no improvements in odor identification were observed. Similarly, in a subsequent RCT study, Jiang et al. (2019) examined the effectiveness of olfactory training on odor identification in individuals who had anosmia post TBI. Participants received either four bottles of PEA, lemon, eucalyptus, and clove oils, or a single bottle of PEA for six months. The authors again found that olfactory training improved odor threshold but not odor identification.

In an RCT study, Langdon et al. (2018) examined the effectiveness of olfactory training using a variety of odors, including anise, lemon, rose, vinegar, smoke, and eucalyptus. The authors found that participants who received olfactory training, compared to the control group, showed a significant improvement in odor thresholds, but not in subjective olfactometry.

In a pre-post study by Bratt et al. (2020), participants with posttraumatic olfactory dysfunction post TBI received sequential treatment of oral corticosteroids (30mg prednisone, once daily for 10 days) and olfactory training (twice daily for 3mo). At 12-month post-intervention, participants demonstrated a significant improvement in olfaction from baseline (Bratt et al., 2020).

Conclusion

There is level 1b evidence (Langdon et al., 2018) that olfactory training using a variety of odors such as anise, lemon, rose, vinegar, smoke, and eucalyptus, may improve odor thresholds, but not subjective olfactometry.

There is level 2 evidence (Jiang et al., 2017; 2019) that olfactory training with a bottle of PEA may improve odor threshold levels but not the ability to identify odors, when compared to mineral oil and bottles of PEA with lemon, eucalyptus, and clove oils.

There is level 4 evidence (Bratt et al., 2020) that corticosteroids and olfactory training may improve olfactory dysfunction in individuals with moderate to severe TBI.

KEY POINTS

- Olfactory training using odors such as anise, lemon, rose, vinegar, smoke, and eucalyptus may be effective for the improvement of odor thresholds in individuals with TBI.
- Olfactory training with a bottle of phenyl ethyl alcohol (PEA) may be more effective for the improvement of odor threshold levels when compared to mineral oil and bottles of PEA with lemon, eucalyptus, and clove oils; however, it may not lead to improvements in odor identification ability.
- Corticosteroids and olfactory training may improve olfactory dysfunction in individuals with moderate to severe TBI.

Conclusions

Overall, a wide variety of interventions exist for sensory and motor rehabilitation and to address spasticity post ABI. Selection of therapies for motor and sensory dysfunction should be individualized, patient-centered, and initiated as part of a comprehensive rehabilitation strategy. For motor impairment a variety of physical interventions may be effective for the remediation of motor deficits post ABI. For

spasticity, physical interventions as well as oral, injected, and intrathecally-administered pharmacological interventions have been shown to be effective. It is important to keep in mind that some of the pharmacological interventions discussed have a longer history of investigation than others, such as botulinum toxin injections, while studies examining newer pharmacological interventions may need to be interpreted with more care. Ultimately the course of treatment should be individualized and agreed upon by the patient and their care team and realistic expectations for recovery should be discussed. Available research indicates that few interventions are effective for vestibular and olfactory dysfunction and these areas would benefit from additional research.

References

Aida, J., Chau, B., & Dunn, J. (2018). Immersive virtual reality in traumatic brain injury rehabilitation: A literature review. *NeuroRehabilitation, 42*(4), 441-448. https://doi.org/10.3233/nre-172361

Alashram, A. R., Annino, G., Raju, M., & Padua, E. (2020). Effects of physical therapy interventions on balance ability in people with traumatic brain injury: A systematic review. *NeuroRehabilitation, 46*(4), 455-466. https://doi.org/10.3233/nre-203047

Anggelis, E., Powell, E. S., Westgate, P. M., Glueck, A. C., & Sawaki, L. (2019). Impact of motor therapy with dynamic body-weight support on Functional Independence Measures in traumatic brain injury: An exploratory study. *NeuroRehabiltiation, 45*(4), 519-524.

Anwar, F., Antiga, S., Mee, H., & Al Khayer, A. (2019). Management of spasticity with intrathecal phenol injections: The past and the present. *The Journal of the International Society of Physical and Rehabilitation Medicine, 2*(2), 94.

Armstrong, R. A. (2018). Visual problems associated with traumatic brain injury. *Clinical and Experimental Optometry, 101*(6), 716-726.

Baagoe, S. K., Kofoed-Hansen, M., & Poulsen, I. (2018, April-May). Occurrence of dystonia, spasticity and contractures in patients with severe acquired brain injury a prospective cohort study. *Neurorehabilitation and neural repair, 32 (4-5)*, 430-431. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emexa&AN=622759679

http://vr2pk9sx9w.search.serialssolutions.com/?url_ver=Z39.88-2004&rft_val_fmt=info:ofi/fmt:kev:mtx:journal&rfr_id=info:sid/Ovid:emexa&rft.genre=article&rft_id=info:doi/10.1177%2F1545968318765498&rft_id=info:pmid/&rft.issn=1552-6844&rft.volume=32&rft.issue=4-5&rft.spage=430&rft.pages=430-431&rft.date=2018&rft.jtitle=Neurorehabilitation+and+Neural+Repair&rft.atitle=Occurrence+of+dystonia%2C+spasticity+and+contractures+in+patients+with+severe+acquired+brain+injury+a+prospective+cohort+study&rft.aulast=Baagoe

Bateman, A., Culpan, F. J., Pickering, A. D., Powell, J. H., Scott, O. M., & Greenwood, R. J. (2001, Feb). The effect of aerobic training on rehabilitation outcomes after recent severe brain injury: a randomized controlled evaluation. *Arch Phys Med Rehabil, 82*(2), 174-182. https://doi.org/10.1053/apmr.2001.19744

Becker, B. E. (2009, Sep). Aquatic therapy: scientific foundations and clinical rehabilitation applications. *Pm r, 1*(9), 859-872. https://doi.org/10.1016/j.pmrj.2009.05.017

Becker, R., Alberti, O., & Bauer, B. L. (1997). Continuous intrathecal baclofen infusion in severe spasticity after traumatic or hypoxic brain injury. *Journal of neurology, 244*(3), 160-166.

Berryman, A., Rasavage, K., Politzer, T., & Gerber, D. (2020). Oculomotor Treatment in Traumatic Brain Injury Rehabilitation: A Randomized Controlled Pilot Trial. *The American Journal of Occupational Therapy, 74*(1), 7401185050p7401185051–7401185050p7401185057.

Bhambhani, Y., Rowland, G., & Farag, M. (2005, Feb). Effects of circuit training on body composition and peak cardiorespiratory responses in patients with moderate to severe traumatic brain injury. *Arch Phys Med Rehabil, 86*(2), 268-276. https://doi.org/10.1016/j.apmr.2004.04.022

Bhatnagar, S., Anderson, M., Chu, M., Kuo, D., & Azuh, O. (2019). Rehabilitation Assessment and Management of Neurosensory Deficits After Traumatic Brain Injury in the Polytrauma Veteran. *Physical Medicine and Rehabilitation Clinics of North America, 30*(1), 155-170. https://doi.org/http://dx.doi.org/10.1016/j.pmr.2018.08.014

Boake, C., Francisco, G. E., Ivanhoe, C. B., & Kothari, S. (2000). Brain injury rehabilitation. In B. RL (Ed.), *Physical medicine and rehabilitation* (pp. 1073-1116). Saunders Company.

Brassel, S., Power, E., Campbell, A., Brunner, M., & Togher, L. (2021, Jul 30). Recommendations for the Design and Implementation of Virtual Reality for Acquired Brain Injury Rehabilitation: Systematic Review. *J Med Internet Res, 23*(7), e26344. https://doi.org/10.2196/26344

Bratt, M., Moen, K. G., Nordgard, S., Helvik, A. S., & Skandsen, T. (2020). Treatment of posttraumatic olfactory dysfunction with corticosteroids and olfactory training. *Acta oto-laryngologica, 140*(9), 761-767. https://doi.org/http://dx.doi.org/10.1080/00016489.2020.1767301

Brown, T. H., Mount, J., Rouland, B. L., Kautz, K. A., Barnes, R. M., & Kim, J. (2005, Sep-Oct). Body weight-supported treadmill training versus conventional gait training for people with chronic traumatic brain injury. *J Head Trauma Rehabil, 20*(5), 402-415. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCFBDGGLEO00/fs047/ovft/live/gv024/00001199/00001199-200509000-00002.pdf

Burr, P., & Choudhury, P. (2022). Fine Motor Disability. In *StatPearls*. StatPearls Publishing

Copyright © 2022, StatPearls Publishing LLC.

Bushbacher, R. M., & Porter, C. D. (2000). Deconditioning, conditioning, and the benefits of exercise. In Braddom RL (Ed.), *Physical Medicine and Rehabilitation* (pp. 702-726). Saunders Company.

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

Canning, C. G., Shepherd, R. B., Carr, J. H., Alison, J. A., Wade, L., & White, A. (2003, Jul). A randomized controlled trial of the effects of intensive sit-to-stand training after recent traumatic brain injury on sit-to-stand performance. *Clin Rehabil, 17*(4), 355-362.

Charrette, A. L., Lorenz, L. S., Fong, J., O'Neil-Pirozzi, T. M., Lamson, K., Demore-Taber, M., & Lilley, R. (2016, Jul 28). Pilot study of intensive exercise on endurance, advanced mobility and gait speed in adults with chronic severe acquired brain injury. *Brain Inj*, 1-7. https://doi.org/10.1080/02699052.2016.1187766

Chin, L. M., Chan, L., Woolstenhulme, J. G., Christensen, E. J., Shenouda, C. N., & Keyser, R. E. (2015, Nov-Dec). Improved Cardiorespiratory Fitness With Aerobic Exercise Training in Individuals With Traumatic Brain Injury. *J Head Trauma Rehabil, 30*(6), 382-390. https://doi.org/10.1097/htr.0000000000000062

Chow, J. W., Yablon, S. A., & Stokic, D. S. (2015, Feb). Effect of intrathecal baclofen bolus injection on ankle muscle activation during gait in patients with acquired brain injury. *Neurorehabil Neural Repair, 29*(2), 163-173. https://doi.org/10.1177/1545968314533615

Ciuffreda, K. J., Han, Y., Kapoor, N., & Ficarra, A. P. (2006). Oculomotor rehabilitation for reading in acquired brain injury. *NeuroRehabilitation, 21*(1), 9-21. http://iospress.metapress.com/content/83386nv4yvplc9hb/?genre=article&issn=1053-8135&volume=21&issue=1&spage=9

Clark, R. A., Williams, G., Fini, N., Moore, L., & Bryant, A. L. (2012). Coordination of dynamic balance during gait training in people with acquired brain injury. *Arch Phys Med Rehabil, 93*(4), 636-640. https://doi.org/10.1016/j.apmr.2011.11.002

Clemenzi, A., Formisano, R., Matteis, M., Gallinacci, L., Cochi, G., Savina, P., & Cicinelli, P. (2012). Care management of spasticity with botulinum toxin-A in patients with severe acquired brain injury: A 1-year follow-up prospective study. *Brain Injury, 26*(7-8), 979-983. https://doi.org/10.3109/02699052.2012.660512

Conrad, J. S., Mitchell, G. L., & Kulp, M. T. (2017, Jul 23). Vision Therapy for Binocular Dysfunction Post Brain Injury. *Optom Vis Sci*. https://doi.org/10.1097/opx.0000000000000937

Corral, L., Javierre, C., Blasi, J., Viscor, G., Ricart, A., & Ventura, J. L. (2014). Combined intermittent hypobaric hypoxia and muscle electro-stimulation: a method to increase circulating progenitor cell concentration? *Journal of translational medicine, 12*(1), 174.

Curcio, A., Temperoni, G., Tramontano, M., De Angelis, S., Iosa, M., Mommo, F., Cochi, G., & Formisano, R. (2020). The effects of aquatic therapy during post-acute neurorehabilitation in patients with severe traumatic brain injury: a preliminary randomized controlled trial. *Brain Injury, 34*(12), 1630-1635.

Cuthbert, J. P., Staniszewski, K., Hays, K., Gerber, D., Natale, A., & O'Dell, D. (2014). Virtual reality-based therapy for the treatment of balance deficits in patients receiving inpatient rehabilitation for traumatic brain injury. *Brain Injury, 28*(2), 181-188. https://doi.org/10.3109/02699052.2013.860475

Damiano, D., Zampieri, C., Ge, J., Acevedo, A., & Dsurney, J. (2016, 03/30). Effects of a rapid-resisted elliptical training program on motor, cognitive and neurobehavioral functioning in adults with chronic traumatic brain injury. *Experimental brain research, 234*(8), 2245-2252. https://doi.org/10.1007/s00221-016-4630-8

Dario, A., Di Stefano, M. G., Grossi, A., Casagrande, F., & Bono, G. (2002, Feb). Long-term intrathecal Baclofen infusion in supraspinal spasticity of adulthood. *Acta Neurol Scand, 105*(2), 83-87. http://onlinelibrary.wiley.com/doi/10.1034/j.1600-0404.2002.1o042.x/abstract

Dault, M. C., & Dugas, C. (2002, Mar). Evaluation of a specific balance and coordination programme for individuals with a traumatic brain injury. *Brain Inj, 16*(3), 231-244.

Dettmers, C., Teske, U., Hamzei, F., Uswatte, G., Taub, E., & Weiller, C. (2005, Feb). Distributed form of constraint-induced movement therapy improves functional outcome and quality of life after stroke. *Arch Phys Med Rehabil, 86*(2), 204-209. https://doi.org/10.1016/j.apmr.2004.05.007

Ding, K., Juengst, S. B., Neaves, S., Turki, A., Wang, C., Huang, M., Pham, T., Behbehani, K., Li, M., Hynan, L., Driver, S., Zhang, R., & Bell, K. R. (2022). Usability of a two-way personalized mobile trainer system in a community-based exercise program for adults with chronic traumatic brain injury. *Brain Injury, 36*(3), 359-367.

Dougherty, A. L., MacGregor, A. J., Han, P. P., Heltemes, K. J., & Galarneau, M. R. (2011). Visual dysfunction following blast-related traumatic brain injury from the battlefield. *Brain Injury, 25*(1), 8-13.

Dragunas, A. C., & Gordon, K. E. (2016, Sep 6). Body weight support impacts lateral stability during treadmill walking. *J Biomech, 49*(13), 2662-2668. https://doi.org/10.1016/j.jbiomech.2016.05.026

Driver, S., Rees, K., O'Connor, J., & Lox, C. (2006, Feb). Aquatics, health-promoting self-care behaviours and adults with brain injuries. *Brain Inj, 20*(2), 133-141. https://doi.org/10.1080/02699050500443822

Ertzgaard, P., Campo, C., & Calabrese, A. (2017). Efficacy and safety of oral baclofen in the management of spasticity: A rationale for intrathecal baclofen. *J Rehabil Med, 49*(3), 193-203.

Esquenazi, A., Lee, S., Packel, A. T., & Braitman, L. (2013). A Randomized Comparative Study of Manually Assisted Versus Robotic-Assisted Body Weight Supported Treadmill Training in Persons With a Traumatic Brain Injury. *PM and R, 5*(4), 280-290. https://doi.org/10.1016/j.pmrj.2012.10.009

Fan, M. C., Li, S. F., Sun, P., Bai, G. T., Wang, N., Han, C., Sun, J., Li, Y., & Li, H. T. (2020). Early Intensive Rehabilitation for Patients with Traumatic Brain Injury: A Prospective Pilot Trial. *World Neurosurgery, 137*, e183-e188. https://doi.org/http://dx.doi.org/10.1016/j.wneu.2020.01.113

Farag, J., Reebye, R., Ganzert, C., & Mills, P. (2020). Does casting after botulinum toxin injection improve outcomes in adults with limb spasticity? A systematic review. *J Rehabil Med, 52*(1), 1-7.

Foo, J., Paterson, K., Williams, G., & Clark, R. (2013). Low-cost evaluation and real-time feedback of static and dynamic weight bearing asymmetry in patients undergoing in-patient physiotherapy rehabilitation for neurological conditions. *Journal of NeuroEngineering and Rehabilitation, 10*(1), Article 74. https://doi.org/10.1186/1743-0003-10-74

[Record #90 is using a reference type undefined in this output style.]

Francisco, G. E., Hu, M. M., Boake, C., & Ivanhoe, C. B. (2005, May). Efficacy of early use of intrathecal baclofen therapy for treating spastic hypertonia due to acquired brain injury. *Brain Inj, 19*(5), 359-364.

Francois, B., Vacher, P., Roustan, J., Salle, J. Y., Vidal, J., Moreau, J. J., & Vignon, P. (2001, Jan). Intrathecal baclofen after traumatic brain injury: early treatment using a new technique to prevent spasticity. *J Trauma, 50*(1), 158-161.

Fusco, A., Giovannini, S., Castelli, L., Coraci, D., Gatto, D. M., Reale, G., Pastorino, R., & Padua, L. (2022, Apr 20). Virtual Reality and Lower Limb Rehabilitation: Effects on Motor and Cognitive Outcome-A Crossover Pilot Study. *J Clin Med, 11*(9). https://doi.org/10.3390/jcm11092300

Gaid, M. (2012). Phenol nerve block for the management of lower limb spasticity. *ACNR, 12*(3), 23-25.

Garland, D. E., Lilling, M., & Keenan, M. A. (1984, May). Percutaneous phenol blocks to motor points of spastic forearm muscles in head-injured adults. *Arch Phys Med Rehabil, 65*(5), 243-245.

Gormley, M. E., Jr., O'Brien, C. F., & Yablon, S. A. (1997). A clinical overview of treatment decisions in the management of spasticity. *Muscle Nerve Suppl, 6*, S14-20.

Gracies, Nance, P., Elovic, E., McGuire, J., & Simpson, D. M. (1997). Traditional pharmacological treatments for spasticity. Part II: General and regional treatments. *Muscle Nerve Suppl, 6*, S92-120.

Green, E., Huynh, A., Broussard, L., Zunker, B., Matthews, J., Hilton, C. L., & Aranha, K. (2019, Jan/Feb). Systematic Review of Yoga and Balance: Effect on Adults With Neuromuscular Impairment. *Am J Occup Ther, 73*(1), 7301205150p7301205151-7301205150p7301205111. https://doi.org/10.5014/ajot.2019.028944

Gregory, C. M., & Bickel, C. S. (2005, Apr). Recruitment patterns in human skeletal muscle during electrical stimulation. *Phys Ther, 85*(4), 358-364. http://ptjournal.apta.org/content/85/4/358.full.pdf

Grotta, J. C., Noser, E. A., Ro, T., Boake, C., Levin, H., Aronowski, J., & Schallert, T. (2004, Nov). Constraint-induced movement therapy. *Stroke, 35*(11 Suppl 1), 2699-2701. https://doi.org/10.1161/01.STR.0000143320.64953.c4

Gurr, B., & Moffat, N. (2001, May). Psychological consequences of vertigo and the effectiveness of vestibular rehabilitation for brain injury patients. *Brain Inj, 15*(5), 387-400. https://doi.org/10.1080/02699050010005904

Han, C., Wang, Q., Meng, P. P., & Qi, M. Z. (2013, Jan). Effects of intensity of arm training on hemiplegic upper extremity motor recovery in stroke patients: a randomized controlled trial. *Clin Rehabil, 27*(1), 75-81. https://doi.org/10.1177/0269215512447223

Hassett, L. M., Moseley, A. M., Tate, R. L., Harmer, A. R., Fairbairn, T. J., & Leung, J. (2009, Mar). Efficacy of a fitness centre-based exercise programme compared with a home-based exercise programme in traumatic brain injury: a randomized controlled trial. *J Rehabil Med, 41*(4), 247-255. https://doi.org/10.2340/16501977-0316

Hassett, L. M., Moseley, A. M., Whiteside, B., Barry, S., & Jones, T. (2012). Circuit class therapy can provide a fitness training stimulus for adults with severe traumatic brain injury: a randomised trial within an observational study. *J Physiother, 58*(2), 105-112. https://doi.org/10.1016/s1836-9553(12)70090-5

Hassett, L. M., Tate, R. L., Moseley, A. M., & Gillett, L. E. (2011). Injury severity, age and pre-injury exercise history predict adherence to a home-based exercise programme in adults with traumatic brain injury. *Brain Inj, 25*(7-8), 698-706. https://doi.org/10.3109/02699052.2011.579934

Hirose, T., Shiozaki, T., Shimizu, K., Mouri, T., Noguchi, K., Ohnishi, M., & Shimazu, T. (2013, Aug 2013

2014-03-10). The effect of electrical muscle stimulation on the prevention of disuse muscle atrophy in patients with consciousness disturbance in the intensive care unit. *Journal of Critical Care, 28*(4), 536.e531-537. https://doi.org/http://dx.doi.org/10.1016/j.jcrc.2013.02.010

Hoarau, X., Richer, E., Dehail, P., & Cuny, E. (2012a). A 10-year follow-up study of patients with severe traumatic brain injury and dysautonomia treated with intrathecal baclofen therapy. *Brain Injury, 26*(7-8), 927-940. https://doi.org/10.3109/02699052.2012.661913

Hoarau, X., Richer, E., Dehail, P., & Cuny, E. (2012b). Comparison of long-term outcomes of patients with severe traumatic or hypoxic brain injuries treated with intrathecal baclofen therapy for dysautonomia. *Brain Injury, 26*(12), 1451-1463. https://doi.org/10.3109/02699052.2012.694564

Hoffman, J. M., Bell, K. R., Powell, J. M., Behr, J., Dunn, E. C., Dikmen, S., & Bombardier, C. H. (2010, Oct). A randomized controlled trial of exercise to improve mood after traumatic brain injury. *Pm r, 2*(10), 911-919. https://doi.org/10.1016/j.pmrj.2010.06.008

Horn, T. S., Yablon, S. A., Chow, J. W., Lee, J. E., & Stokic, D. S. (2010, Jan). Effect of intrathecal baclofen bolus injection on lower extremity joint range of motion during gait in patients with acquired brain injury. *Arch Phys Med Rehabil, 91*(1), 30-34. https://doi.org/10.1016/j.apmr.2009.08.148

Horn, T. S., Yablon, S. A., & Stokic, D. S. (2005, Jun). Effect of intrathecal baclofen bolus injection on temporospatial gait characteristics in patients with acquired brain injury. *Arch Phys Med Rehabil, 86*(6), 1127-1133. https://doi.org/10.1016/j.apmr.2004.11.013

Iaccarino, M. A., Bhatnagar, S., & Zafonte, R. (2015). Rehabilitation after traumatic brain injury. *Handb Clin Neurol, 127*, 411-422. https://doi.org/10.1016/b978-0-444-52892-6.00026-x

Intiso, D., Simone, V., Di Rienzo, F., Iarossi, A., Pazienza, L., Santamato, A., Maruzzi, G., & Basciani, M. (2014). High doses of a new botulinum toxin type A (NT-201) in adult patients with severe spasticity following brain injury and cerebral palsy. *NeuroRehabilitation, 34*(3), 515-522. http://www.iospress.nl/site/html/10538135.html

http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed12&NEWS=N&AN=2014400417

http://content.iospress.com/articles/neurorehabilitation/nre1052

Jafarzadeh, S., Pourbakht, A., Bahrami, E., Jalaie, S., & Bayat, A. (2018). Effect of early vestibular rehabilitation on vertigo and unsteadiness in patients with acute and sub-acute head trauma. *Iranian Journal of Otorhinolaryngology, 30*(2), 85-90.

Jankovic, J., & Brin, M. F. (1991, Apr 25). Therapeutic uses of botulinum toxin. *N Engl J Med, 324*(17), 1186-1194. https://doi.org/10.1056/nejm199104253241707

Jiang, R.-S., Twu, C.-W., & Liang, K.-L. (2019). The effect of olfactory training on odor identification in patients with traumatic anosmia. *International forum of allergy & rhinology, 9*(11), 1244-1251.

Jiang, R. S., Twu, C. W., & Liang, K. L. (2017). The Effect of Olfactory Training on the Odor Threshold in Patients with Traumatic Anosmia. *American Journal of Rhinology & Allergy, 31*(5), 317-322.

Kasten, E., Poggel, D. A., & Sabel, B. A. (2000, Nov). Computer-based training of stimulus detection improves color and simple pattern recognition in the defective field of hemianopic subjects. *J Cogn Neurosci, 12*(6), 1001-1012.

Kasten, E., Wust, S., Behrens-Baumann, W., & Sabel, B. A. (1998, Sep). Computer-based training for the treatment of partial blindness. *Nat Med, 4*(9), 1083-1087. https://doi.org/10.1038/2079

Katz, Dewald, J. P., & Schmit, B. D. (2000). Spasticity. In B. RL (Ed.), *Physical medicine and rehabilitation.* (pp. 592-615). Saunders Company.

Keenan, M. A., Tomas, E. S., Stone, L., & Gersten, L. M. (1990, Mar). Percutaneous phenol block of the musculocutaneous nerve to control elbow flexor spasticity. *J Hand Surg Am, 15*(2), 340-346.

Korman, M., Shaklai, S., Cisamariu, K., Gal, C., Maaravi-Hesseg, R., Levy, I., Keren, O., Karni, A., & Sacher, Y. (2018, 2018 Jan 30

2018-03-01). Atypical within-session motor procedural learning after traumatic brain injury but well-preserved between-session procedural memory consolidation. *Frontiers in Human Neuroscience, 12*, 14. https://doi.org/http://dx.doi.org/10.3389/fnhum.2018.00010

Kriz, G., Hermsdorfer, J., Marquardt, C., & Mai, N. (1995, Jul). Feedback-based training of grip force control in patients with brain damage. *Arch Phys Med Rehabil, 76*(7), 653-659. http://www.sciencedirect.com/science/article/pii/S0003999395806350

Lance, J. W. (1980, Dec). The control of muscle tone, reflexes, and movement: Robert Wartenberg Lecture. *Neurology, 30*(12), 1303-1313.

Langdon, C., Lehrer, E., Berenguer, J., Laxe, S., Alobid, I., Quintó, L., Mariño-Sánchez, F., Bernabeu, M., Marin, C., & Mullol, J. (2018). Olfactory Training in Post-Traumatic Smell Impairment: Mild Improvement in

Threshold Performances: Results from a Randomized Controlled Trial. *Journal of neurotrauma, 35*(22), 2641-2652.

Lannin, N. A., Horsley, S. A., Herbert, R., McCluskey, A., & Cusick, A. (2003, Feb). Splinting the hand in the functional position after brain impairment: a randomized, controlled trial. *Arch Phys Med Rehabil, 84*(2), 297-302. https://doi.org/10.1053/apmr.2003.50031

Leung, J., Harvey, L. A., Moseley, A. M., Whiteside, B., Simpson, M., & Stroud, K. (2014, Dec). Standing with electrical stimulation and splinting is no better than standing alone for management of ankle plantarflexion contractures in people with traumatic brain injury: a randomised trial. *J Physiother, 60*(4), 201-208. https://doi.org/10.1016/j.jphys.2014.09.007

Leung, J., King, C., & Fereday, S. (2019). Effectiveness of a programme comprising serial casting, botulinum toxin, splinting and motor training for contracture management: a randomized controlled trial. *Clinical Rehabilitation, 33*(6), 1035-1044.

Limphaibool, N., Iwanowski, P., Kozubski, W., Swidzinski, T., Frankowska, A., Kaminska, I., Linkowska-Swidzinska, K., Sekula, A., Swidzinski, P., Maciejewska-Szaniec, Z., & Maciejewska, B. (2020). Subjective and Objective Assessments of Post-traumatic Olfactory Dysfunction. *Frontiers in Neurology, 11*, 970. https://doi.org/http://dx.doi.org/10.3389/fneur.2020.00970

Lorentzen, J., Nielsen, D., Holm, K., Baagøe, S., Grey, M. J., & Nielsen, J. B. (2012). Neural tension technique is no different from random passive movements in reducing spasticity in patients with traumatic brain injury. *Disability and rehabilitation, 34*(23), 1978-1985. https://doi.org/10.3109/09638288.2012.665132

Margetis, K., Korfias, S. I., Gatzonis, S., Boutos, N., Stranjalis, G., Boviatsis, E., & Sakas, D. E. (2014, Oct). Intrathecal baclofen associated with improvement of consciousness disorders in spasticity patients. *Neuromodulation, 17*(7), 699-704: discussion 704. https://doi.org/10.1111/ner.12147

Matsumoto-Miyazaki, J., Asano, Y., Ikegame, Y., Kawasaki, T., Nomura, Y., & Shinoda, J. (2016). Acupuncture Reduces Excitability of Spinal Motor Neurons in Patients with Spastic Muscle Overactivity and Chronic Disorder of Consciousness Following Traumatic Brain Injury. *The Journal of Alternative and Complementary Medicine, 22*(11).

Mayer. (1997). Clinicophysiologic concepts of spasticity and motor dysfunction in adults with an upper motoneuron lesion. *Muscle Nerve Suppl, 6*, S1-13.

Mayer, Esquenazi, A., & Keenan, M. A. (1996). Analysis and management of spasticity, contracture and impaired motor control. In Z. N. Horn LJ (Ed.), *Medical rehabilitation of traumatic brain injury* (pp. 411-458). Mosby.

Mayer, N. H., Whyte, J., Wannstedt, G., & Ellis, C. A. (2008, May). Comparative impact of 2 botulinum toxin injection techniques for elbow flexor hypertonia. *Arch Phys Med Rehabil, 89*(5), 982-987. https://doi.org/10.1016/j.apmr.2007.10.022

Mehrholz, J., Pohl, M., & Elsner, B. (2014, Jan 23). Treadmill training and body weight support for walking after stroke. *Cochrane Database Syst Rev, 2014*(1), Cd002840. https://doi.org/10.1002/14651858.CD002840.pub3

Meythaler, Guin-Renfroe, S., & Hadley, M. N. (1999, May-Jun). Continuously infused intrathecal baclofen for spastic/dystonic hemiplegia: a preliminary report. *Am J Phys Med Rehabil, 78*(3), 247-254.

Meythaler, J. M., Clayton, W., Davis, L. K., Guin-Renfroe, S., & Brunner, R. C. (2004, Mar-Apr). Orally delivered baclofen to control spastic hypertonia in acquired brain injury. *J Head Trauma Rehabil, 19*(2), 101-108. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCFBDGGLEO00/fs047/ovft/live/gv031/00001199/00001199-200403000-00003.pdf

Meythaler, J. M., DeVivo, M. J., & Hadley, M. (1996, May). Prospective study on the use of bolus intrathecal baclofen for spastic hypertonia due to acquired brain injury. *Arch Phys Med Rehabil, 77*(5), 461-466. http://www.sciencedirect.com/science/article/pii/S0003999396900349

Meythaler, J. M., Guin-Renfroe, S., Grabb, P., & Hadley, M. N. (1999, Jan). Long-term continuously infused intrathecal baclofen for spastic-dystonic hypertonia in traumatic brain injury: 1-year experience. *Arch Phys Med Rehabil, 80*(1), 13-19. http://www.sciencedirect.com/science/article/pii/S0003999399903015

Meythaler, J. M., McCary, A., & Hadley, M. N. (1997, Sep). Prospective assessment of continuous intrathecal infusion of baclofen for spasticity caused by acquired brain injury: a preliminary report. *J Neurosurg, 87*(3), 415-419. https://doi.org/10.3171/jns.1997.87.3.0415

Mortenson, P. A., & Eng, J. J. (2003, Jul). The use of casts in the management of joint mobility and hypertonia following brain injury in adults: a systematic review. *Phys Ther, 83*(7), 648-658. http://ptjournal.apta.org/content/83/7/648.full.pdf

Morton, R. (2004). Visual Dysfunction Following Traumatic Brain Injury. In A. MJ (Ed.), *Traumatic Brain Injury - Rehabilitative Treatment and Case Management.* (pp. 183-207). CRC Press;.

Moseley, A. M. (1997, Mar). The effect of casting combined with stretching on passive ankle dorsiflexion in adults with traumatic head injuries. *Phys Ther, 77*(3), 240-247; discussion 248-259. http://ptjournal.apta.org/content/77/3/240.full.pdf

Moseley, A. M., Hassett, L. M., Leung, J., Clare, J. S., Herbert, R. D., & Harvey, L. A. (2008, May). Serial casting versus positioning for the treatment of elbow contractures in adults with traumatic brain injury: a randomized controlled trial. *Clin Rehabil, 22*(5), 406-417. https://doi.org/10.1177/0269215507083795

Moseley, A. M., Herbert, R. D., Sherrington, C., & Maher, C. G. (2002). Evidence for physiotherapy practice: a survey of the Physiotherapy Evidence Database (PEDro). *Aust J Physiother, 48*(1), 43-49. https://doi.org/10.1016/s0004-9514(14)60281-6

Mossberg, K. A., Kuna, S., & Masel, B. (2002, Sep). Ambulatory efficiency in persons with acquired brain injury after a rehabilitation intervention. *Brain Inj, 16*(9), 789-797. https://doi.org/10.1080/02699050210131894

Motin, M., Keren, O., Groswasser, Z., & Gordon, C. R. (2005, Aug 20). Benign paroxysmal positional vertigo as the cause of dizziness in patients after severe traumatic brain injury: diagnosis and treatment. *Brain Inj, 19*(9), 693-697. https://doi.org/10.1080/02699050400013600

Mumford, N., Duckworth, J., Thomas, P. R., Shum, D., Williams, G., & Wilson, P. H. (2012). Upper-limb virtual rehabilitation for traumatic brain injury: a preliminary within-group evaluation of the elements system [Evaluation Studies

Research Support, Non-U.S. Gov't]. *Brain Injury, 26*(2), 166-176. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22360522

http://sfx.scholarsportal.info/western?sid=OVID:medline&id=pmid:22360522&id=doi:10.3109%2F02699052.2011.648706&issn=0269-9052&isbn=&volume=26&issue=2&spage=166&pages=166-76&date=2012&title=Brain+Injury&atitle=Upper-limb+virtual+rehabilitation+for+traumatic+brain+injury%3A+a+preliminary+within-group+evaluation+of+the+elements+system.&aulast=Mumford&pid=%3Cauthor%3EMumford+N%3BDuckworth+J%3BThomas+PR%3BShum+D%3BWilliams+G%3BWilson+PH%3C%2Fauthor%3E%3CAN%3E22360522%3C%2FAN%3E%3CDT%3EEvaluation+Studies%3C%2FDT%3E

http://informahealthcare.com/doi/pdfplus/10.3109/02699052.2011.648706

Naguib, M. B., & Madian, Y. T. (2014). Betahistine Dihydrochloride With and Without Early Vestibular Rehabilitation for the Management of Patients With Balance Disorders Following Head Trauma: A Preliminary Randomized Clinical Trial. *Journal of Chiropractic Medicine, 13*(1), 14-20. https://doi.org/10.1016/j.jcm.2014.01.011

Narasaki-Jara, M., Wagatsuma, M., Holt, J. L., Acuña, S. M., Vrongistinos, K., & Jung, T. (2020). Aquatic treadmill walking at three depths of water in people with traumatic brain injury. *Physiotherapy Research International : the Journal for Researchers and Clinicians in Physical Therapy, 25*(2), e1817.

Neistadt, M. E. (1994, Oct). The effects of different treatment activities on functional fine motor coordination in adults with brain injury. *Am J Occup Ther, 48*(10), 877-882.

Padula, W. V., Argyris, S., & Ray, J. (1994, Feb-Mar). Visual evoked potentials (VEP) evaluating treatment for post-trauma vision syndrome (PTVS) in patients with traumatic brain injuries (TBI). *Brain Inj, 8*(2), 125-133.

Page, S., & Levine, P. (2003, Aug). Forced use after TBI: promoting plasticity and function through practice. *Brain Inj, 17*(8), 675-684. https://doi.org/10.1080/0269905031000107160

Parfitt, R., Hensman, M. Y., & Lucas, S. J. E. (2017, Jul). Cerebral Blood Flow Responses to Aquatic Treadmill Exercise. *Med Sci Sports Exerc, 49*(7), 1305-1312. https://doi.org/10.1249/mss.0000000000001230

Peirone, E., Goria, P. F., & Anselmino, A. (2014). A dual-task home-based rehabilitation programme for improving balance control in patients with acquired brain injury: a single-blind, randomized controlled pilot study. *Clin Rehabil, 28*(4), 329-338. https://doi.org/10.1177/0269215513501527

Peters, D. M., Jain, S., Liuzzo, D. M., Middleton, A., Greene, J., Blanck, E., Sun, S., Raman, R., & Fritz, S. L. (2014). Individuals with chronic traumatic brain injury improve walking speed and mobility with intensive mobility training. *Arch Phys Med Rehabil, 95*(8), 1454-1460. https://doi.org/10.1016/j.apmr.2014.04.006

Pohl, M., Ruckriem, S., Mehrholz, J., Ritschel, C., Strik, H., & Pause, M. R. (2002, Jun). Effectiveness of serial casting in patients with severe cerebral spasticity: a comparison study. *Arch Phys Med Rehabil, 83*(6), 784-790. http://www.sciencedirect.com/science/article/pii/S0003999302603016

Posteraro, F., Calandriello, B., Galli, R., Logi, F., Iardella, L., & Bordi, L. (2013). Timing of intrathecal baclofen therapy in persons with acquired brain injury: influence on outcome. *Brain Inj, 27*(13-14), 1671-1675. https://doi.org/10.3109/02699052.2013.828852

Riggs, R. V., Andrews, K., Roberts, P., & Gilewski, M. (2007, Oct). Visual deficit interventions in adult stroke and brain injury: a systematic review. *Am J Phys Med Rehabil, 86*(10), 853-860. https://doi.org/10.1097/PHM.0b013e318151f907

Sackett, D. L., Richardson, W. S., Rosenberg, W., & Hayes, R. B. (2000). *Evidence-based medicine: how to practice and teach EBM*.

Schafer, A. Y., & Ustinova, K. I. (2013). Does use of a virtual environment change reaching while standing in patients with traumatic brain injury? *Journal of NeuroEngineering and Rehabilitation, 10*(1), Article 76. https://doi.org/10.1186/1743-0003-10-76

Scherer, M. R., & Schubert, M. C. (2009, Sep). Traumatic brain injury and vestibular pathology as a comorbidity after blast exposure. *Phys Ther, 89*(9), 980-992. https://doi.org/10.2522/ptj.20080353

Schiess, M. C., Eldabe, S., Konrad, P., Molus, L., Spencer, R., Stromberg, K., Weaver, T., & Plunkett, R. (2020). Intrathecal baclofen for severe spasticity: longitudinal data from the product surveillance registry. *Neuromodulation: Technology at the Neural Interface, 23*(7), 996-1002.

Schmid, A. A., Miller, K. K., Van Puymbroeck, M., & Schalk, N. (2016). Feasibility and results of a case study of yoga to improve physical functioning in people with chronic traumatic brain injury. *Disability and rehabilitation, 38*(9), 914-920.

Segal, M. (2018, Aug). Muscle Overactivity in the Upper Motor Neuron Syndrome: Pathophysiology. *Phys Med Rehabil Clin N Am, 29*(3), 427-436. https://doi.org/10.1016/j.pmr.2018.04.005

Seib, T. P., Price, R., Reyes, M. R., & Lehmann, J. F. (1994, Jul). The quantitative measurement of spasticity: effect of cutaneous electrical stimulation. *Arch Phys Med Rehabil, 75*(7), 746-750.

Shaw, S. E., Morris, D. M., Uswatte, G., McKay, S., Meythaler, J. M., & Taub, E. (2005, Nov-Dec). Constraint-induced movement therapy for recovery of upper-limb function following traumatic brain injury. *J Rehabil Res Dev, 42*(6), 769-778.

Shepard, N. T., & Telian, S. A. (1995, Jan). Programmatic vestibular rehabilitation. *Otolaryngol Head Neck Surg, 112*(1), 173-182.

Sietsema, J. M., Nelson, D. L., Mulder, R. M., Mervau-Scheidel, D., & White, B. E. (1993, Jan). The use of a game to promote arm reach in persons with traumatic brain injury. *Am J Occup Ther, 47*(1), 19-24.

Singer, B. J., Singer, K. P., & Allison, G. T. (2003, Apr). Evaluation of extensibility, passive torque and stretch reflex responses in triceps surae muscles following serial casting to correct spastic equinovarus deformity. *Brain Inj, 17*(4), 309-324.

Sorokowska, A., Drechsler, E., Karwowski, M., & Hummel, T. (2017, Mar 1). Effects of olfactory training: a meta-analysis. *Rhinology, 55*(1), 17-26. https://doi.org/10.4193/Rhin16.195

Stevenson, V. (2010). Rehabilitation in practice: spasticity management. *Clinical Rehabilitation, 24*(4), 293-304.

Stokic, D. S., Yablon, S. A., & Hayes, A. (2005, Sep). Comparison of clinical and neurophysiologic responses to intrathecal baclofen bolus administration in moderate-to-severe spasticity after acquired brain injury. *Arch Phys Med Rehabil, 86*(9), 1801-1806. https://doi.org/10.1016/j.apmr.2005.03.027

Straudi, S., Severini, G., Sabbagh Charabati, A., Pavarelli, C., Gamberini, G., Scotti, A., & Basaglia, N. (2017). The effects of video game therapy on balance and attention in chronic ambulatory traumatic brain injury: an exploratory study. *BMC Neurology, 17*(1), 86-86.

Subramanian, S. K., Fountain, M. K., Hood, A. F., & Verduzco-Gutierrez, M. (2022, Jan). Upper Limb Motor Improvement after Traumatic Brain Injury: Systematic Review of Interventions. *Neurorehabil Neural Repair, 36*(1), 17-37. https://doi.org/10.1177/15459683211056662

Tefertiller, C., Hays, K., Natale, A., O'Dell, D., Ketchum, J., Sevigny, M., Eagye, C. B., Philippus, A., & Harrison-Felix, C. (2019). Results From a Randomized Controlled Trial to Address Balance Deficits After Traumatic Brain Injury. *Archives of Physical Medicine and Rehabilitation, 100*(8), 1409-1416.

Thibaut, A., Deltombe, T., Wannez, S., Gosseries, O., Ziegler, E., Dieni, C., Deroy, M., & Laureys, S. (2015). Impact of soft splints on upper limb spasticity in chronic patients with disorders of consciousness: A randomized, single-blind, controlled trial. *Brain Inj, 29*(7-8), 830-836. https://doi.org/10.3109/02699052.2015.1005132

Thibaut, A., Wannez, S., Deltombe, T., Martens, G., Laureys, S., & Chatelle, C. (2018). Physical therapy in patients with disorders of consciousness: Impact on spasticity and muscle contracture. *NeuroRehabilitation, 42*(2), 199-205. https://doi.org/10.3233/NRE-172229

Ustinova, K. I., Chernikova, L. A., Dull, A., & Perkins, J. (2015, Jan). Physical therapy for correcting postural and coordination deficits in patients with mild-to-moderate traumatic brain injury. *Physiother Theory Pract, 31*(1), 1-7. https://doi.org/10.3109/09593985.2014.945674

Ustinova, K. I., Perkins, J., Leonard, W. A., & Hausbeck, C. J. (2014). Virtual reality game-based therapy for treatment of postural and co-ordination abnormalities secondary to TBI: A pilot study. *Brain Injury, 28*(4), 486-495. https://doi.org/10.3109/02699052.2014.888593

Verplancke, D., Snape, S., Salisbury, C. F., Jones, P. W., & Ward, A. B. (2005). A randomized controlled trial of botulinum toxin on lower limb spasticity following acute acquired severe brain injury. *Clinical Rehabilitation, 19*(2), 117-125.

Wallace, B., & Lifshitz, J. (2016). Traumatic brain injury and vestibulo-ocular function: current challenges and future prospects. *Eye Brain, 8*, 153-164. https://doi.org/10.2147/eb.S82670

Wang, Z. M., Law, J. H., King, N. K., Rajeswaran, D. K., Soh, S., Rao, J. P., Ng, W. H., & Chua, K. S. (2016, Jan). Treatment of severe, disabling spasticity with continuous intrathecal baclofen therapy following acquired brain injury: the experience of a tertiary institution in Singapore. *Singapore Med J, 57*(1), 8-12. https://doi.org/10.11622/smedj.2016005

Warburton, D. E. R., & Bredin, S. S. D. (2017, Sep). Health benefits of physical activity: a systematic review of current systematic reviews. *Curr Opin Cardiol, 32*(5), 541-556. https://doi.org/10.1097/hco.0000000000000437

Wee, S. K. (2002). Vestibular rehabilitation for a patient with severe traumatic brain injury: a case study. *Physiotherapy Singapore, 5*, 59-65.

Wen, P. S., Herrin, I., & Pittman, A. (2022, Jan). Feasibility of Yoga to Improve Symptoms in Individuals With Severe, Chronic Traumatic Brain Injury: A Mixed-Methods Case Series. *Altern Ther Health Med, 28*(1), 32-37.

Whitcroft, K. L., & Hummel, T. (2019). Clinical Diagnosis and Current Management Strategies for Olfactory Dysfunction: A Review. *JAMA Otolaryngology–Head & Neck Surgery, 145*(9), 846-853. https://doi.org/10.1001/jamaoto.2019.1728

Williams, G., & Schache, A. G. (2019). Impaired ankle joint mechanics during running can be resolved in people with traumatic brain injury. *Brain Injury, 33*(5), 670-678. https://doi.org/http://dx.doi.org/10.1080/02699052.2019.1567940

Wilson, D. J., Powell, M., Gorham, J. L., & Childers, M. K. (2006, Jan). Ambulation training with and without partial weightbearing after traumatic brain injury: results of a randomized, controlled trial. *Am J Phys Med Rehabil, 85*(1), 68-74. http://graphics.tx.ovid.com/ovftpdfs/FPDDNCFBDGGLEO00/fs047/ovft/live/gv024/00002060/00002060-200601000-00010.pdf

Yablon, S. A., Agana, B. T., Ivanhoe, C. B., & Boake, C. (1996, Oct). Botulinum toxin in severe upper extremity spasticity among patients with traumatic brain injury: an open-labeled trial. *Neurology, 47*(4), 939-944.

Yungher, D., & Craelius, W. (2012). Improving fine motor function after brain injury using gesture recognition biofeedback. *Disability and Rehabilitation: Assistive Technology, 7*(6), 464-468. https://doi.org/10.3109/17483107.2011.650782

Zhu, Y., Yang, Y., & Li, J. (2019). Does acupuncture help patients with spasticity? A narrative review. *Annals of Physical and Rehabilitation Medicine, 62*(4), 297-301.