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

INTRODUCTION AND METHODOLOGY

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Conflict of Interest

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

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Greetings from Dr. Robert Teasell,

Professor and Chair-Chief of Physical Medicine and Rehabilitation

The Collaboration of Rehabilitation Research Evidence (CORRE) team is delighted to present the Evidence-Based Review of moderate to severe Acquired Brain Injury (ERABI) *Mental Health Issues 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 Ministry of Health, 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.

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.

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. Cullen is the newly appointed Division Director for PM&R in the Department of Medicine and Chief of PM&R at HHSC and St Joseph's Healthcare. She has been the Chief of Staff and Chair of the Medical Advisory Committee at West Park Healthcare Centre for the last 10 years, actively seeking to promote system change and patient advocacy in an integrated system. Her goal is to enhance the quality of life of people with disabilities based on current best evidence.

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

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.

Mark Bayley, MD, FRCPC, is Program Medical Director & Physiatrist-in-Chief at UHN-Toronto Rehabilitation Institute. He is a Professor at the University of Toronto in the Division of Physical Medicine and Rehabilitation, Faculty of Medicine. Mark has held a number of health system leadership roles including Chair of the Canadian Stroke Best Practices committee, the Stroke Evaluation Committee at Corhealth Ontario, and the Vice Chair of the Greater Toronto Area Rehab Network.

Introduction

The Evidence-Based Review of Moderate to Severe Acquired Brain Injury (ERABI) is designed to comprehensively review current scientific literature on acquired brain injury (ABI) rehabilitation. ERABI aims to identify all currently described rehabilitation interventions with their associated evidence, with the goal of facilitating evidence-based practice. In doing so, ERABI also identifies gaps in the literature deserving further research.

Knowledge translation is an iterative process that includes synthesis, dissemination, exchange and application of knowledge/research in clinical care. ERABI aspires to descriptively report, compare and synthesize research studies to determine the effectiveness of ABI rehabilitation interventions. This is done on an annual basis. ERABI is a platform used in the earlier stages of knowledge translation to inform clinical practice guidelines and to guide clinical practice in a way that benefits the patient and the caregiving team.

Objective of the Evidence Based Review of Acquired Brain Injury

The aim of this project is to conduct a comprehensive, evidence-based review of the research literature regarding rehabilitation interventions for moderate to severe ABI. The authors have systematically reviewed the research evidence to create a review that has benefit and relevance to both clinicians and researchers.

Defining Acquired Brain Injury

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. ABI typically involves a wide range of impairments affecting physical, neurocognitive and/or psychological functioning. A person with an 'ABI' might therefore refer to an individual with a traumatic brain injury (TBI) of any severity, or a non-traumatic injury such as a person with Herpes encephalitis, viral meningitis or acute hypertensive encephalopathy. As opposed to an insidious developmental process, an 'ABI' infers that a person, previously intact from a neurological perspective, subsequently 'acquired' some form of brain pathology during their lifespan. Common traumatic causes include motor vehicle accidents, falls, assaults, gunshot wounds, and sport injuries (Greenwald et al., 2003). Non-traumatic causes of ABI include diffuse brain lesions, anoxia, tumours, aneurysm, vascular malformations, and infections of the

brain (Toronto Acquired Brain Injury Network, 2005). Although one can argue that stroke is an ABI, it is usually not included because of its focal nature; ABIs tend to be more diffuse.

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.

Defining Severity of Injury

ABI severity is usually classified according to the level of altered consciousness experienced by the individual following injury (Table 1). 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 1 | 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.).			

Glasgow Coma Scale

The GCS is one of the most widely used measures of altered consciousness. Developed by Teasdale and Jennett (1974, 1976) it is comprised of three subsections: eye opening, best motor response, and verbal response (Table 1.2). Higher scores on the GCS are indicative of an increased level of consciousness. The total score is determined by adding the three sub scores. The total score can range from 3-15, with scores of 13-15 indicating a mild injury, 9-12 indicating a moderate injury, and 3-8 indicating a severe injury (Campbell, 2000; Murdoch & Theodoros, 2001).

TABLE 2 | The Glasgow Coma Scale

Response/Item	Points
Eye Opening	
Spontaneous	4
To speech	3
To pain	2
None	1
Motor Response	
Obeys commands	6
Localizes pain	5
Withdrawal (from painful stimulus)	4
Abnormal flexion	3
Extension	2
None	1
Verbal Response	
Oriented	5
Confused	4
Inappropriate	3
Incomprehensible	2
None	1

Duration of Loss of Consciousness

For moderate to severe TBI, the duration of LOC appears to be a valid measure of injury severity. LOC of less than 15 minutes, up to 6 hours, and between 6-48 hours represents a mild, moderate, and severe injury, respectively. When LOC exceeds 48 hours, the injury is considered very severe
(Campbell, 2000).

Post-Traumatic Amnesia

PTA is the time period post trauma for which the conscious patient has no recall for events. PTA is formally defined as the period following emergence from coma in which the patient may appear confused, disoriented, or agitated (Campbell, 2000). Research indicates a dose-response relationship, with the length of PTA frequently being proportional to the severity of injury. Injury severity is defined as mild if the duration of PTA is less than 1 hour, moderate if between 1–24 hours, and severe if PTA is between 1–7 days. PTA exceeding 7 days is considered to represent a very severe injury (Campbell, 2000; Russell, 1932).

Methods

Literature Search Strategy

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–July 2021 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.

Study Inclusion Criteria

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 1.3) 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.

TABLE 3 | 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

Data Extraction

Once an article was selected for full review, the following data was extracted: author(s), country and year of publication, sample size, participant characteristics (i.e., type of injury, severity, sex, age, time since injury), treatment/intervention, outcome measure(s), and results. This data is summarized using tables presented in each module. Articles evaluating similar treatments were then grouped together under the appropriate subject headings.

Methodological Quality Assessment of Randomized Controlled Trials

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.

Formulating Conclusions Based on Levels of Evidence

The levels of evidence 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.

Using this system, conclusions were easily formed when the results of multiple studies were in agreement. However, in cases where RCTs differed in conclusions and methodological quality, the results of the study (or studies) with the higher PEDro score(s) were more heavily weighted. In rare instances the authors needed to make a judgment when the results of a single study of higher quality conflicted with those of several studies of inferior quality. In these instances, we provided rationale for our decision and made the process as transparent as possible. In the end the reader is encouraged to be a "critical consumer" of the material presented.

TABLE 4 | Levels of Evidence

Level	Research Design	Description
Level 1a	Randomized Controlled Trial	More than 1 RCT with PEDro score ≥6. Includes within subjects comparison with randomized conditions and crossover designs.
Level 1b	RCT	1 RCT with PEDro ≥6.
Level 2	RCT	RCT, PEDro <6.
	Prospective controlled trial	Prospective controlled trial (not randomized).
	Cohort	Prospective longitudinal study using at least two similar groups with one exposed to a particular condition.
Level 3	Case Control	A retrospective study comparing conditions including historical controls.
Level 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.
Level 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.

Interpretation of the Evidence

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

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