

ERABI

EVIDENCE-BASED REVIEW
of moderate to severe
ACQUIRED BRAIN INJURY

1. Introduction and Methodology

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Abbreviations

ABI	Acquired Brain Injury
ERABI	Evidence-Based Review of Moderate to Severe Acquired Brain Injury
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Score
LOC	Loss of Consciousness
PCT	Prospective Controlled Trial
PEDro	Physiotherapy Evidence Database
PTA	Post-Traumatic Amnesia
RCT	Randomized Controlled Trial
TBI	Traumatic Brain Injury

1. Introduction and Methodology

1.1 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 in the acute and post-acute phase of recovery. ERABI aims to identify all currently described rehabilitation interventions with their associated evidence, while identifying gaps in the literature deserving further research, where appropriate.

ERABI aspires to descriptively report and compare existing rehabilitation interventions such that the evidence can be used to inform and change practice in a way that benefits the patient and the caregiving team. As of 2017, ERABI was primarily used by individuals in the United States of America, and most users were physicians. Though this is a Canadian based project, it has a large international audience.

ERABI is the first step in a larger process known as knowledge translation, which ultimately seeks to incorporate new evidence into evidence-based practice. Evidence-based practice as a model, facilitates flow between the most current research and encourages its application to patient care. The primary goals of evidence-based practice are to increase knowledge and awareness of new interventions, and integrate them into practice in a clinically meaningful and significant way.

1.2 Objective of the Evidence Based Review of Acquired Brain Injury

The aim of this project was to conduct a comprehensive, evidence-based review of the research literature regarding rehabilitation interventions for moderate to severe ABI. The authors systematically reviewed the research evidence to create a review that had direct benefit and relevance to both clinicians and researchers. Clinicians are able to objectively evaluate the current body of evidence for a given intervention, and use that to guide their practice if they so choose. The conclusions made in ERABI regarding the efficacy of interventions help both clinicians and patients be more informed about which interventions are supported by scientific evidence, and at what strength. From this review, we have developed a mechanism for continued collection and dissemination of the research evidence for moderate to severe brain injury. This allows for the incorporation of new evidence regarding a specific intervention as well as provides a mechanism for the introduction of new interventions altogether.

Evidence-based practice, because of its potential to improve patient care, has become a priority in the healthcare system. Medicine has a long history of relying on anecdotal experiences, which runs the danger of promoting practices that are ineffective, inefficient, and in some cases, produce less than optimal outcomes. Evidence-based practice is therefore an increasingly important element of clinical care.

The delivery of rehabilitation is typically done by a rehabilitation clinician/team on a one-on-one basis. The chronic and ever-evolving nature of many patients' conditions makes it difficult to decide the optimum amount of therapy at the outset of treatment (Purtillo, 1992). Further, ABI rehabilitation outcomes reflect a process in which various decisions are made by different stakeholders. These stakeholders consider what is desirable, acceptable, reasonable, and appropriate, and how these decisions produce an outcome to which subjective assessments of worth or value will be attached (Banja, 1997). While evidence-based reviews may focus on the evidence existing for different interventions, the importance of the rehabilitation team cannot be underestimated when the results are

being interpreted. It is the objective of this evidence-based review to provide information and support for clinicians at all levels of ABI rehabilitation.

1.3 Defining Acquired Brain Injury

1.3.1 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 ABI 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 focal brain lesions, anoxia, tumours, aneurysm, vascular malformations, and infections of the brain (Toronto Acquired Brain Injury Network, 2005).

Depending on the severity of the ABI, an individual can be left with physical, cognitive, sensory, and/or social impairments. Eighteen module topics have been developed to address each of these specific issues. Module 6, for example, focuses on the challenges of cognitive impairments, which can result in memory or learning deficits that make it difficult for individuals to return to activities of daily living post ABI. These impairments can also make it difficult for individuals to establish the independence necessary to either return to work or reintegrate to community life. Related to that, Module 13 has been established to focus specifically on the challenges of vocational and community reintegration post ABI. By providing the evidentiary support for these interventions clinicians can apply them in the appropriate context to benefit each of their patients on an individual level.

Given that 'ABI' is a loosely defined term, studies with an 'ABI' population can be equally vague 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). Most 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.

1.3.2 Defining Severity of Injury

ABI severity is usually classified according to the level of altered consciousness experienced by the patient following injury (Table 1.2). 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).

1.3.2.1 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 1.1). 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). Module 17 provides more in depth information regarding the reliability and validity of this test.

1.3.2.2 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).

1.3.2.3 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).

Table 1.1 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

Table 1.2 Definitions of Injury Severity

Mild:	Moderate:	Severe:	Very Severe:
<ul style="list-style-type: none"> PTA <1 hour GCS 13-15 LOC <15 minutes 	<ul style="list-style-type: none"> PTA 1-24 hours GCS 9-12 LOC <6 hours 	<ul style="list-style-type: none"> PTA 1-7 days GCS between 3-8 LOC 6-48 hours 	<ul style="list-style-type: none"> PTA >7 days LOC >48 hours

1.4 Methodology

1.4.1 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–December 2017 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 may have been 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. These search terms were selected with the assistance of a medical staff librarian. 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 database subject headings used as search terms for CINAHL were "brain injuries" and "head injuries"; for EMBASE, "brain injury" and "head injury"; for MEDLINE, "brain injuries" and "craniocerebral trauma"; and for PsycINFO "brain injuries" and "traumatic brain injury". Additional keywords were used specific to each module.

1.4.2 Study Inclusion Criteria

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 was then reviewed; titles that appeared to involve ABI and a treatment/intervention were selected. The abstracts from these selected reference titles were then reviewed by two independent reviewers to determine if the studies met the inclusion criteria. The remaining articles were reviewed in full. To be included in ERABI, consensus must be reached by the two reviewers for each article based on the set criteria; a third independent reviewer was available to settle any discrepancies.

For inclusion in ERABI, the study population must have had $\geq 50\%$ ABI (as defined in Table 1.3) or the study independently reports on a subset of participants with ABI. The study population must also have a minimum sample size of three. Further, the focus is on the efficacy of interventions for moderate to severe ABI; consequently, any studies dealing with mild forms of ABI were excluded.

Table 1.3 Defining Acquired Brain Injury

Included in ABI definition	Excluded from ABI definition
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<p>Traumatic Causes</p> <ul style="list-style-type: none"> • Motor vehicle accidents • Falls • Assaults • Gunshot wounds • Sport Injuries <p>Non-traumatic Causes</p> <ul style="list-style-type: none"> • Tumours (benign/meningioma only) • Anoxia • Subarachnoid hemorrhage (non-focal) • Meningitis • Encephalitis/encephalopathy (viral, bacterial, drug, hepatic) • Subdural Hematoma 	<p>Vascular and Pathological Incidents</p> <ul style="list-style-type: none"> • Intracerebral hemorrhage (focal) • Cerebrovascular accident (i.e., stroke) • Vascular accidents • Malignant/metastatic tumours <p>Congenital and Developmental Problems</p> <ul style="list-style-type: none"> • Cerebral Palsy • Autism • Developmental delay • Down's syndrome • Spina bifida with hydrocephalus • Muscular dystrophy <p>Progressive Processes</p> <ul style="list-style-type: none"> • Alzheimer's disease • Pick's disease • Dementia • Amyotrophic Lateral Sclerosis • Multiple Sclerosis • Parkinson's disease • Huntington's disease
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Studies meeting the following criteria were included: (1) published in the English language, (2) at least 50% of the population included participants with ABI, (3) at least three participants, (4) 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, as were studies that used either experimental (randomized trials) or non-experimental designs (prospective and retrospective controlled trials, single group interventions, and retrospective studies). Articles which did not meet our definition of ABI (Table 1.1) were excluded.

1.4.3 Data Extraction

Once an article was selected for full review, the following data was extracted: author(s), place and date of publication, inclusion and exclusion criteria, sample size, participant characteristics (i.e., type of injury, severity, sex, age, time since injury), treatment/intervention, outcome measure(s), and results. This data was summarized using large tables. Articles evaluating similar treatments were then grouped together.

1.4.4 Quality Assessments of Methodological Designs

The methodological quality of all RCTs 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 each 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 better methodological quality.

1.4.4.1 Interpreting the Results of Individual Studies

For RCTs, studies scoring 9-10 on the PEDro scale were considered to be of "excellent" methodologically quality, 6-8 of "good" quality, 4-5 of "fair" quality, and below 4 of "poor" quality. The authors determined these descriptive terms of quality assessment to simplify the interpretation of results. Studies employing a non-experimental or uncontrolled design were used to formulate conclusions only in the absence of RCTs.

1.4.4.2 Formulating Conclusions Based on Levels of Evidence

The levels of evidence (Table 1.4) 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 the number of RCTs 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 cases 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 1.4 Levels of Evidence

Level	Research Design	Description
Level 1a	Randomized Controlled Trial (RCT)	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 .
	PCT	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.

1.5 Limitations

1.5.1 Limitations of Evidence-Based Reviews

Evidence-based practice does have limitations. One of the limitations alluded to above is its focus on the treatment of groups rather than individuals. Therefore, the evidence provided is based more on group treatment and may not accurately translate into individualized treatment. While the evidence may provide guidance on how an individual could be treated, in the end, it is an individual clinician’s decision. There are times when the evidence will need to be put aside for a specific case. The important element is that these cases should not be common but rather uncommon and the majority of patients should be managed according to the evidence. Evidence-based practice can also be problematic when the evidence is misinterpreted. The most common scenario occurs when results of a trial are generalized to a wider group than they should be. Evidence is a tool, and as such, the interpretation and implementation of it must be done carefully.

1.5.2 Limitations in Neurorehabilitation Research

Comparative research in the field of complex disability following ABI poses several major challenges (Turner-Stokes, 2004). There is marked heterogeneity with respect to the patient group, the intervention, the setting, and the outcomes that are relevant at each stage of recovery. This heterogeneity may not accurately reflect ABI populations at large and therefore may not translate to clinical practice.

There are ethical considerations that limit neurorehabilitation research. In ABI populations, many individuals lack the mental capacity to give fully informed consent. Another consideration is the expanding body of evidence for effectiveness of multidisciplinary rehabilitation in other conditions, particularly stroke, makes it increasingly unethical to randomize patients to 'no treatment' or even 'standard' care. The length of time, typically months or years, over which rehabilitation may have its effects is typically longer than the funding for research projects and hinders the use of 'wait-list' control groups. Control group interventions must be selected carefully for current neurorehabilitation research.

The application of randomized controlled trial (RCT) designs is limited by small numbers of patients at each site due to potential ethical considerations. Current trends towards the acceptance of RCTs as the gold standard source of evidence may also limit the knowledge base needed to make sound decisions about ABI rehabilitation priorities and policies. It is important to remember that rigorous observational alternatives to the RCT are still of significant value (Whyte, 2002). Given the existing literature base for ABI rehabilitation, evidence-based rehabilitation must rely on a variety of types of evidence, often in combination (Victoria et al., 2004). The inclusion of alternate study designs can provide a more complete picture of the existing evidence, particularly where RCTs are lacking, and thereby advise ABI practice, albeit not as strongly. Excluding data collected under other research designs could bias the evidence base toward interventions that are “easier” to evaluate but not necessarily more effective or cost-effective (Des Jarlais et al., 2004). As a result of the challenges explained above, there are few large experimental design studies in this field.

1.6 Reference List

References

- Banja, J. D. (1997). Values and outcomes: the ethical implications of multiple meanings. *Topics in Stroke Rehabilitation, 4*(2), 59-70.
- Campbell, M. (2000). *Rehabilitation for traumatic brain injury: physical therapy practice in context*: Churchill Livingstone.
- Des Jarlais, D. C., Lyles, C., Crepaz, N., & Group, T. (2004). Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement. *American journal of public health, 94*(3), 361.
- Greenwald, B. D., Burnett, D. M., & Miller, M. A. (2003). Congenital and acquired brain injury. 1. Brain injury: epidemiology and pathophysiology. *Archives of physical medicine and rehabilitation, 84*(3 Suppl 1), S3-7.
- Moseley, A. M., Herbert, R. D., Sherrington, C., & Maher, C. G. (2002). Evidence for physiotherapy practice: a survey of the Physiotherapy Evidence Database (PEDro). *Australian Journal of Physiotherapy, 48*(1), 43-49.
- Murdoch, B., & Theodoros, D. (2001). *Introduction: Epidemiology, neuropathophysiology and medical aspects of traumatic brain injury*. San Diego, CA: Singular/Thomson Learning.
- Purtillo. (1992). Whom to treat first, and how much is enough? Ethical dilemmas that physical therapists confront as they compare individual patients' needs for treatment. *International Journal of Technology Assessment in Health Care, 8*, 26-34.
- Russell, W. R. (1932). Cerebral Involvement in Head Injury a Study Based on the Examination of Two-hundred Cases. *Brain, 55*(4), 549-603.
- Sackett, D., Straus, S., Richardson, W., Rosenberg, W., & Haynes, R. (2000). *Evidence-Based Medicine: How to Practice and Teach EBM* Toronto, ON, CAN: Churchill Livingstone.
- Teasdale, G., & Jennett, B. (1974). Assessment of coma and impaired consciousness: a practical scale. *The Lancet, 304*(7872), 81-84.
- Teasdale, G., & Jennett, B. (1976). Assessment and prognosis of coma after head injury. *Acta neurochirurgica, 34*(1-4), 45-55.
- Toronto Acquired Brain Injury Network. (2005). Definition of acquired brain injury. Retrieved from <http://www.abinetwork.ca/downloads/binder-b3.pdf>
- Turner-Stokes, L. (2004). The evidence for the cost-effectiveness of rehabilitation following acquired brain injury. *Clinical Medicine, 4*(1), 10-12.
- Victora, C. G., Habicht, J.-P., & Bryce, J. (2004). Evidence-based public health: moving beyond randomized trials. *Journal Information, 94*(3).
- Whyte, J. (2002). Traumatic brain injury rehabilitation: Are there alternatives to randomized clinical trials? *Archives of physical medicine and rehabilitation, 83*(9), 1320-1322.