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
LOC	Loss of Consciousness
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) was designed to comprehensively review current practices in acquired brain injury (ABI) rehabilitation. ERABI aims to 1) identify effective treatment intervention, 2) identify gaps in the literature deserving further research, and 3) serve as an accessible tool for clinicians in an effort to encourage evidence-based practice.

1.1.1 Defining Acquired Brain Injury

ABI is an umbrella term that encompasses traumatic and non-traumatic etiologies such as cerebral concussion, brain contusions, subarachnoid hemorrhages or other 'acquired' problems. 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, 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 his or her 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, tumors, aneurysm, vascular malformations, and infections of the brain (Toronto Acquired Brain Injury Network 2005).

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.

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 (Table 1.1). For inclusion in ERABI, the study population must have had ≥50% ABI (as defined in Table 1) or the study independently reports on a subset of participants with ABI. 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 1.1 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** • Tumors (benign/meningioma only) • Anoxia • Subarachnoid hemorrhage (non-focal) • Meningitis • Encephalitis/encephalopathy (viral, bacterial, drug, hepatic)	• 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 • Muscular dystrophy **Progressive Processes** • Alzheimer's disease • Pick's disease • Dementia • Amytrophic Lateral Sclerosis • Multiple Sclerosis • Parkinson's disease • Huntington's disease

1.2 Defining Severity of Injury

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

1.2.1 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 1.2). 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).

1.2.2 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).

1.2.3 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 1.2 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

Table 1.3 Definitions of Injury Severity

Mild:	Moderate:	Severe:	Very Severe:
• PTA <1 hour • GCS 13-15 • LOC <15 minutes	• PTA 1-24 hours • GCS 9–12 • LOC <6 hours	• PTA 1–7 days • GCS between 3-8 • LOC 6-48 hours	• PTA >7 days • LOC >48 hours

1.3 Challenges in ABI Rehabilitation 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.
- The application of randomized controlled trial (RCT) designs is limited by small numbers of patients at each site, and by ethical considerations because many patients with ABI lack the mental capacity to give fully informed consent.
- Lack of Equipoise: 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 over which rehabilitation may have its effects, often months or years, is typically longer than the funding for research projects and hinders the use of 'wait-list' control groups.

As a result of these challenges, there are few large experimental design studies in this field. Current trends towards the acceptance of RCTs as the gold standard source of evidence may limit the knowledge base needed to make sound decisions about ABI rehabilitation priorities and policies. Given the existing literature base for ABI rehabilitation, evidence-based rehabilitation must rely on a variety of types of evidence, often in combination (Victora et al. 2004) and rigorous observational alternatives to the RCT are still of significant value (Whyte 2002). 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).

1.4 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 product that had direct benefit and relevance to both clinicians and researchers. From this review, we developed a mechanism for continued collection and dissemination of the research evidence pertaining to moderate to severe brain injury.

1.5 Methodology

1.5.1 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–August 2016 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.

1.5.2 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.

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.

1.5.3 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.

1.5.4 Methodological Quality Assessments of Randomized Controlled Trials

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; http://www.pedro.fhs.usyd.edu.au/FAQs/Scale/scaleitems.htm). 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. Each RCT was assessed by two independent reviewers, with any discrepancies in scoring settled by a third reviewer.

1.6 Determining Levels of Evidence

1.6.1 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 in an effort 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.

1.6.2 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 attempted to provide a rationale for our decision and to make the process as transparent as possible. In the end the reader is encouraged to be a “critical consumer” of all 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.
	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.

1.7 The Importance of Evidence-Based Practice

Evidence-based practice, because of its potential to improve patient care, has become a priority in the healthcare system and is clearly the way of the future. 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 fact that therapy is delivered on a one-on-one basis means that there are other factors, other than the actual treatment, which will influence the outcomes (Banja 1997). 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). The experience, enthusiasm and empathy of the rehabilitation clinician still plays an extremely important role in the rehabilitation of patients with ABI but these qualities are difficult to fully capture within the structure of evidence-based practice. 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).

1.8 The Limitations of Evidence-Based Practice

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 provides guidelines as to how

patients, as a group, should be treated and in that way also provides some guidance as to how the individual patient should be treated. However, in the end, how a patient is treated 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.

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