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Traumatic Brain Injury (TBI): Overview of Diagnosis and Treatment

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Abstract

Objective: To provide an overview of literature on the diagnosis and rehabilitation of adults following traumatic brain injury (TBI).

Method: A comprehensive systematic search identified current literature in TBI diagnosis and rehabilitation interventions. Included studies were examined to identify current standards for diagnostic criteria for TBI in clinical and research contexts, and to present evidence for rehabilitation treatments in TBI.

Results: Strong agreement exists for a diagnosis of TBI in the presence of post traumatic amnesia (PTA) following head trauma; and that Glasgow Coma Score (GCS) of 9-12 is moderate TBI, and GCS of 3-8 is severe TBI. There is no agreement for whether GCS of 13 should be mild or moderate TBI; which GCS to use to grade TBI severity; which clinical feature (aside from PTA) indicates a diagnosis of mild TBI; and whether imaging findings should be incorporated into diagnostic criteria for TBI and for severity grading. Nomenclature for TBI type in the literature remains disorganised, which is problematic for TBI research. There is strong evidence for effectiveness of psychological interventions such as attention training and cognitive interventions after TBI; nutritional support for improved survival and disability outcomes and hyperbaric oxygen therapy for reduction of risk of death after TBI. There is moderate evidence for cognitive behaviour therapy for managing stress after mild TBI. For all other interventions the evidence is limited or insufficient due to lack of studies in the area.

Conclusion: Clear diagnostic criteria for TBI could improve management using targeted therapies. More robust trials in TBI treatments are needed to build evidence for effectiveness of rehabilitation.

Keywords: TBI; Traumatic brain injury; Diagnosis; Rehabilitation; Treatment

Introduction

Traumatic brain injury (TBI) is a common, preventable, and disabling health condition with heterogeneous aetiology, type, severity, and outcomes. Ongoing challenges in TBI care are reflected by rapidly growing literature in the prevention, assessment and treatment of TBI, especially in sports concussion and blast-related TBI. Recent advances include TBI modelling, to predict outcomes of TBI and to improve future data collection, by the International Mission on Prognosis and Analysis of randomized Controlled Trials in TBI (IMPACT) [1] and Transforming Research and Clinical Knowledge in Traumatic Brain Injury pilot (TRACK-TBI) [2], respectively. In comparison, there is a lack of clarity and standardization in the diagnostic criteria, severity grading, and nomenclature to describe TBI, which could improve many aspects of TBI care, especially in developing targeted therapies for TBI [3,4]. TBI is currently defined as 'an alteration in brain function, or other evidence of brain pathology, caused by an external force' [5].

Glasgow Coma Scale (GCS) was introduced for clinical monitoring following TBI (Teasdale et al., 1974) [6], and was subsequently used to grade TBI severity (Rimel et al., 1979) [7]. Inadequacies of GCS for this latter purpose is widely recognised [8,9], but no clear alternative exists. PTA is an excellent prognostic marker (Katz et al., 1994) [10], and was incorporated into the criteria for mild TBI by the American College of Rehabilitation Medicine (ACRM) (ACRM, 2013) [11]. However, there is no consensus in the literature for the selection of clinical features for TBI diagnosis and severity grading [3]. There is no standardized nomenclature of TBI subtype, which may be based on the history, clinical features and imaging findings [12].

Treatments for TBI patients are varied and complex. Evidence to support early rehabilitation interventions for definable stages of recovery for patients' emerging from traumatic coma (such as, early application of awareness stimulation techniques), and management of PTA (reducing agitation by environmental modification) is unclear. Treatments for TBI address cardiovascular disorders (e.g. hypertension); respiratory issues; fever; bladder and bowel dysfunction; swallowing and nutrition; and spasticity management. Others target thrombophlebitis; contractures; fractures; peripheral nerve injuries; and heterotopic ossification. Despite a range of cognitive remediative therapies that are cornerstone of rehabilitation, and specific interventions for movement disorders in TBI (such as tremors, rigidity, dystonia, chorea, or tics), the evidence to support these interventions needs clarification.

The objectives of this overview are [1] to critically examine the literature for diagnostic criteria, severity grading, and types of TBI, [2] to present existing evidence for treatment in TBI, and [3] to consider future direction in TBI diagnosis and management.

Methods

Search strategy

Firstly, a comprehensive electronic search of Medline, Allied and Complementary Medicine (AMED), Biological Abstracts, Health and Psychosocial Instruments, Cochrane Central Register of Controlled Trials (CENTRAL), and PsycINFO identified studies in TBI diagnosis. Secondly, a further targeted search of the CENTRAL identified studies

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		Systematic review of the diagnostic criteria in TBI	Systematic review of the rehabilitation in TBI
Electronic database searched		Ovid Medline Allied and Complementary Medicine (AMED) Biological Abstracts Health and Psychosocial Instruments Cochrane Central Register of Controlled Trials (CENTRAL) PsycINFO	Cochrane Central Register of Controlled Trials (CENTRAL)
Search strategy	Health Condition	**Traumatic brain injury:** "brain injuries" [MeSH with automatic explosion], or "trauma*", "TBI", "mTBI" "concussion", "blast", "military", or "head injury" [title/abstract]	**Traumatic brain injury:** "craniocerebral trauma", "cerebrovascular trauma", "brain edema", "Glasgow Coma Scale", "Glasgow Outcome Scale", "unconsciousness" explode all trees [MeSH with automatic explosion], or Glasgow near3 scale*, or "unconscious*", "coma*", "concuss*", "persistent vegetative state", "Rancho Los Amigos Scale", or (head or crani* or cerebr* or capitis or brain* or forebrain* or skull* or hemispher* or intra-ran* or inter-cran*) near3 (injur*or trauma* or damag* or wound* or fracture* or contusion*), or Diffuse axonal injur*
	Area of interest	**Diagnosis and classification:** "diagnos*", "defini*", "classif*", "nomenclature", "grad", "severity", or "type" [title/abstract]	**Rehabilitation and treatment:** "brain injuries" [MeSH with automatic explosion], or "ambulatory care", "rehabilitation", "hospitalization", "physical therapy modalities", "exercise therapy", "orthotics", "acupuncture", "cognitive therapy", "social work", "occupational therapy", "behavior", "message therapy", "dietetics", "outpatients", "inpatient", "patient care team" [MeSH with automatic explosion], or "multidisciplinary", "integrated", "rehabilitat*", "physiotherap*","physical therap*", "occupation*", "acupuncture", "social work","orthotics", "cognitive therap*", "behavio?r therap*", "counsel?ing", "nutrition", "diet*", "food", "outpatient*", "inpatient*", "hospital*", "home"
Limits		English studies and adults (≥18 years) Published 1999-2013, inclusive (15 years)	English studies and adults (≥18 years) Published 2004-2013, inclusive (10 years)
Additional sources		References of included studies	None
Inclusion criteria		Examination of the current or alternative diagnostic and classification systems in TBI including concussion, *and, or* Examination of any outcome measure designed to diagnose or grade TBI severity	All current and updated systematic reviews in TBI rehabilitation
Exclusion criteria		Diagnostic criteria for postconcession syndrome (PCS)/post-traumatic stress disorder (PTSD) TBI in children and adolescents (under 18 years of age) Animal models Non-validated or experimental diagnostic techniques and instruments Prognostic factors as surrogate measures of TBI severity	None

Table 1: Search strategy, inclusion and exclusion criteria for the systematic review in traumatic brain injury (TBI) diagnostic criteria and rehabilitation.

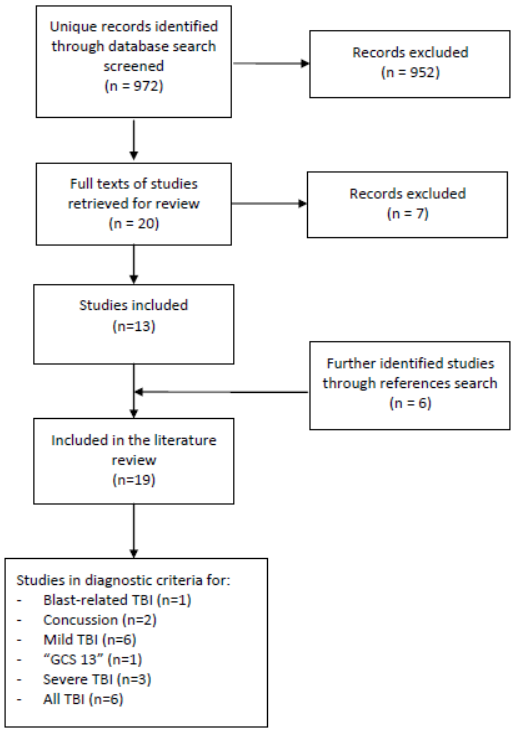

Figure 1: PRISMA outlining search process for studies in TBI diagnostic criteria [36].

for TBI rehabilitation interventions. Comprehensive search strategy; and inclusion and exclusion criteria are outlined in Table 1. No restrictions were applied with respect to research design. Medical subject headings (MeSH) search terms were used for all databases. A key word search was used if the medical subject heading was unavailable.

Study selection

Screening of all titles and abstracts from the search strategy identified studies for closer examination. Full texts of included studies were obtained for further assessment to determine whether the study met the inclusion or exclusion criteria inclusion into the evidence synthesis. For the rehabilitation treatment section all current and updated systematic reviews in CENTRAL were included. Wherever comprehensive updated systematic review were identified, search for individual studies within those reviews was not conducted.

Data extraction

Data extraction was conducted for all included studies for TBI diagnosis using a standard proform a consisting of:author; publication year; study location; study design; sample size; TBI type and severity; key findings; recommended outcome measures or criteria for TBI; and key sources for recommendations. The pro forma for TBI rehabilitation consisted of: author; publication year; injury type; intervention; key findings; and level of evidence. For the rehabilitation treatments, all interventions, type of injury, study year and key findings were examined.

Data synthesis

A wide range of terminologies described similar clinical problems in TBI in the literature, and therefore, similar concepts were grouped together for convenience: 'altered conscious state' to include 'disordered consciousness', 'dazed', 'disorientated', 'confused states'; and 'PTA' to include 'amnesia of blow'.

Quality assessment and analysis of the included studies

Quantitative analysis of included studies was not possible due to the heterogeneity of studies in terms of intervention and outcomes measured. Therefore results were presented qualitatively. To determine level of evidence for treatment in TBI, the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades for Recommendations for Developers of Guidelines 2009 [13] was used. All detailed information from the included studies was tabulated.

Results

Systematic search

For TBI diagnosis, from the initial search (n=972), thirteen studies were included, and a further five studies were identified for inclusion into the evidence synthesis based on the inclusion and exclusion criteria (Figure 1) to a total of nineteen studies in the areas of blast-related TBI (n=1); concussion (n=2); mild TBI (n=6); 'GCS 13' (n=1); severe TBI (n=3); and all TBI (n=6). Data synthesis based on the pro forma is presented in Table 2.

For TBI treatment, the targeted search strategy identified 32 reviews, of which 25 systematic reviews evaluated various rehabilitation interventions in the TBI population, and are tabulated in Table 3.

Characteristics of included studies

TBI diagnosis

Consensus for the lowest threshold for TBI diagnosis: The concept of a lowest threshold for diagnosing TBI is significant, firstly, due to a lack of clear consensus in the diagnostic criteria for mild TBI, and secondly, to avoid over-diagnosis in TBI given increasingly sensitive methods for identifying brain dysfunction following head trauma. Ambiguity in TBI diagnosis could also contribute to under-diagnosis of TBI due to lowered community awareness; presentations to hospitals; and accurate documentation of cases [14]. Four of the included studies in TBI diagnosis specifically addressed this issue: two systematic reviews (Carroll et al., 2004; Rees, 2003) [3,15]; a consensus statement (Menon et al., 2010) [5]; and a database analysis (Malec et al., 2007) [16] (Table 4).

There is general agreement that a clear mechanism and suspicion of injury, plus a minimum of one significant clinical feature of TBI comprise this lowest threshold. PTA was the only agreed and emphasised criteria for the lowest threshold for diagnosing TBI by all four studies [3,5,15,16]. As expected, GCS was not criteria for the lowest threshold, being a specific but not a sensitive marker of TBI [15]. There was no consensus over the significance of other clinical features, which were proposed as a diagnostic criteria for TBI, and these were: on history – loss of consciousness [3,5,16], or seizure [3]; on examination – altered consciousness [3,5,15], focal neurological deficit [3,5]; and on imaging – intracranial lesion [3,5,16] or skull fracture [5,16].

Consensus for severity grading in TBI: Accurately diagnosing TBI severity has widespread implications for public health, clinical research, and clinical care of persons with TBI. Eleven studies specifically discussed severity grading system for TBI based on narrative reviews (n=2) (Van Baalen et al., 2003; DeCuypere and Klimo Jr 2012) [4,17]; systematic reviews (n=2) (Servadei et al., 2001; Carroll et al., 2004) [3,18]; consensus (n=1) (Menon et al., 2010) [5]; survey of clinicians (n=1) (Chieregato et al., 2010) [8]; and clinical studies including retrospective data reviews (n=5) (Ruff and Jurica, 1999; Stein, 2001; Firsching et al., 2001; Grote et al., 2011; Malec et al., 2007) [16,19-22].

For the purpose of evidence synthesis for TBI grading, we considered their comments but did not explicitly incorporate studies with: no clear alternative grading system [4,8]; recommendations for sub classification within mild TBI [18,19] or severe TBI [21] – which were beyond the scope of this study. Recommendations by the remaining six studies are presented in Table 5.

In the included studies, GCS was the most common basis for TBI severity grading [3,17,18,20]. However, there was no consensus for GCS 13, whether this is mild or moderate TBI, despite a metanalysis demonstrating poor outcomes in GCS 13 [20]. Duration of loss of consciousness (LOC) and PTA were included for severity grading by two studies citing the same ACRM position statement [3,16]. There was no agreement over the role of: radiological findings of skull fractures or intracranial lesions [3,16]; Abbreviated Injury Score for head (AIS_{head}) [22]; or neurological abnormality [3], for determining TBI severity. There was no agreement for timing of GCS assessment for severity grading.

Consensus for nomenclature for TBI types: The vast range of potential mechanism of injury and the resulting TBI makes nomenclature for describing types of TBI a challenge, and a potential barrier to developing targeted therapies for TBI [12]. Six studies were included for the nomenclature in TBI: in concussion – a consensus statement (McCrory et al., 2013) [23] and a narrative review (Almasi and Wilson, 2012) [24]; in blast-related TBI – a narrative review (Rosenfeld, 2013) [25]; and in TBI, two consensus papers (Menon et al., 2010; Saatman et al., 2008) [5,12], and one narrative review (Nolan, 2005) [26]. Nomenclatures for TBI in the studies are presented in Table 6.

TBI types and severity	Study design, sample size	Author, publication year, study location	Key findings in relation to TBI definition	Recommended outcome measures or criteria for TBI (in addition to a credible mechanism of injury and, or evidence of head trauma)	Key sources cited for recommendations
Blast-related TBI	Narrative review	Rosenfeld et al., 2013, international [25]	Discusses definition, diagnosis, and pathophysiology of blast-related TBI	TBI type None recommended	Various
Concussion	Narrative review	Almasi and Wilson, 2012, USA [24]	Discusses diagnosis and management of concussion	None recommended	McCrory et al., 2008 [37]
Concussion	Consensus	McCrory et al., 2012, international [23]	Discusses definition of concussion, risk stratification, and management.	TBI type Concussion is a brain injury and is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces.	Previous consensus statements by the same committee
Mild head injury	Systematic review (n=42)	Servadei et al., 2001 [18]	Recommends acute management based on calculations of risks of developing an ICH requiring surgical evacuation	TBI severity GCS 14-15 defines mild head injury Low risk: GCS 15 and no LOC, amnesia, vomiting, or diffuse headache (risk <0.1:100) Medium risk: GCS 15 and ≥1 of LOC, amnesia, vomiting, or diffuse headache (risk 1-3:100) High risk: GCS 14; GCS 15 and skull fracture, and/or neurological deficits (risk 6-10:100); or GCS 15 with risk factors of coagulopathy, drug or alcohol consumption, previous neurosurgical procedures, pre-trauma epilepsy, age >60 years.	Various
Mild TBI	Systematic review (n=313)	Carroll et al., 2004, Canada [3]	62% of studies used GCS for case definition. No agreed GCS. Recommends a revised definition for mild TBI.	Lowest threshold for TBI/TBI severity Operational definition for mild TBI *includes*: 1 of confusion or disorientation; LOC (≤30min); PTA (<24h); transient neurological abnormalities (focal signs, seizures, or intracranial lesion not requiring surgery); GCS 13-15 at ≥30 min (not from other causes)	ACRM, 1993 [11] and CDC, 2003 [38]
Mild TBI	Narrative review	de Kruijk et al., 2001, the Netherlands [39]	Mild TBI definition lacks uniformity in the literature. Clear case definition for mild TBI is needed.	None recommended	Various
Mild TBI	Systematic review	Rees, 2003, Canada [15]	Minimum criteria in adults for clinical diagnosis of TBI	Lowest threshold for TBI Minimum criteria for diffuse mild TBI: [A] Obligatory criteria A credible mechanism of injury Craniofacial impact [B] Major criteria Amnesia for blow Disordered awareness, not necessarily LOC Finite PTA	Wrightson and Gronwall, 1999 [40]
Mild TBI	Clinical study (n=76)	Ruff and Jurica, 1999, USA [19]	Proposes a new classification system for mild TBI based on the diagnostic criteria by ACRM and DSM-IV for concussion	TBI severity Classification for mild TBI [Type I] Altered state or transient LOC; PTA 1-60 seconds; ≥1 neurological symptoms [Type II] Definite LOC unknown – 5 min duration; ≥1 neurological symptoms [Type III] LOC 5-30 min; PTA >12 h; ≥1 neurological symptoms	ACRM, 1993 [11] and DSM-IV [41]
Mild TBI	Clinical study (n=125)	Tellier et al., 2009, Canada [42]	Symptoms or CT results did not differ between subgroups (GCS 15 cf. GCS 13-14). PTA duration is a better predictor of outcomes.	None recommended	Various
TBI with GCS 13	Metanalysis (n=1,047)	Stein, 2001, USA [20]	Intracranial lesions on CT (33.8%) and emergency surgery (10.8%) in GCS 13 are comparable to GCS 9-12, and should be treated as moderate TBI.	TBI severity GCS 13 (in addition to 9-12) is moderate TBI.	Various
Severe TBI	Pre-course survey of anaesthetists in 2005 (n=843)	Chieregato et al., 2010, Italy [8]	40% believed that classification of TBI severity would be improved by adding pupil reactivity to light, and CT findings, to GCS scores.	TBI severity Severe TBI definition should incorporate: GCS; Pupil reactivity to light; *and* CT findings	Saatman et al., 2008 [12]
Severe TBI with coma for ≥24h	Prospective clinical study (n=102)	Firsching et al., 2001, Germany [21]	Diagnostic groups of lesions based on MRI are predictive of mortality, coma duration, and GOS.	TBI severity Grades based on MRI: [I] Supratentorial lesion only [II] Unilateral lesion of brain stem at any level [III] Bilateral lesion of mesencephalon [IV] Bilateral pontine lesion	Various
Severe TBI (AIS_{head}≥3)	Retrospective analysis of registry (n=8,746)	Grote et al., 2011, Germany [22]	GCS ≤ 8 in patients with multiple injuries (ISS >16) has a low sensitivity (56.1%) for severe TBI compared with AIS	TBI severity Recommend defining severe TBI as AIS_{head}≥3 in multiple injuries	Various

TBI types and severity	Study design, sample size	Author, publication year, study location	Key findings in relation to TBI definition	Recommended outcome measures or criteria for TBI (in addition to a credible mechanism of injury and, or evidence of head trauma)	Key sources cited for recommendations
All severity TBI	Narrative review	DeCuypere and Klimo Jr, 2012, USA [17]	TBI is graded based on GCS. Duration of LOC and PTA are indices of severity of TBI.	TBI severity Defines GCS of: 13-15 as mild TBI 9-12 as moderate TBI 3-8 as severe TBI	Bullock et al., 2007 [43]
All severity TBI	Analysis of epidemiological dataset n=1,501)	Malec et al., 2007, USA [16]	Despite missing information, the Mayo Classification System for TBI Severity allowed classification of TBI	Lowest threshold for TBI/TBI severity [a] Classify as Moderate-Severe (Definite) TBI if ≥1 of: Death; LOC ≥ 30 min; PTA ≥ 24h; worst GCS in 24h <13; ICH; SDH; EDH; cerebral contusion; haemorrhagic contusion; dura penetrated; SAH; or brain stem injury; and if none of the above apply, [b] Classify as Mild (Probable) TBI if ≥1 of: LOC momentary to <30min; PTA momentary to <24h; or depressed, basilar or linear skull fracture; and if none of the above apply, [c] Classify as Symptomatic (Possible) TBI if ≥1 of: Blurred vision; confusion; dazed; dizziness; focal neurological symptoms; headache; or nausea.	ACRM, 1993 [11] and Rimel et al., 1982 [44]
All severity TBI	Consensus	Menon et al., 2010, international [5]	TBI defined as an alteration in brain function, or other evidence of brain pathology, caused by an external force.	Lowest threshold for TBI/TBI severity/TBI type [a] Alteration in brain function: Any period of LOC Any duration of PTA Neurologic deficits Any alteration in mental state [b] Or other evidence of brain pathology: Visual, Neuroradiologic, or Laboratory confirmation of damage to the brain [c] Caused by an external force Head being struck/striking an object Acceleration/deceleration without direct external trauma Penetrating foreign body Forces from blasts/explosion, or Other force yet to be defined	ACRM, 1993 [11] and VA/DoD, 2009 [45]
All severity TBI	Narrative review	Nolan, 2005, USA [26]	Discusses diagnosis and management of TBI	TBI type Mechanism of injury Blunt, penetrating or blast Types of injury Focal: contusions, EDH, SDH, SAH, ICH Diffuse: cerebral concussion, DAI	Brain Trauma Foundation, 2000
All severity TBI	Consensus	Saatman et al., 2008 [12]	Multidimensional classification system incorporating pathoanatomical and severity indices will improve TBI clinical trial design	TBI type None recommended	Various
All severity TBI	Narrative review	Van Baalen et al., 2003, the Netherlands [4]	Initial severity can be based on CT or clinical condition	TBI severity None recommended	Various

Abbreviations: ACRM: American College of Rehabilitation Medicine; AIS: Abbreviated Injury Scores; BIAA: Brain Injury Association of America; BTF: Brain Trauma Foundation; CDC: Centre for Disease Control and Prevention; CT: computerised tomography; GCS: Glasgow Coma Scale; h: hours; GOS: Glasgow Outcome score; ICH: intracranial haematoma; ISS: Injury Severity Score; LOC: loss of consciousness; min: minutes; NINDS: National Institute of Neurological Disorders and Stroke; PTA: post traumatic amnesia; TBI: traumatic brain injury; TRISS: Trauma Score and Injury Severity Score; UK: United Kingdom; USA: United States of America; Va/DoD: The United States Department of Veterans Affairs and Department of Defense.

Table 2: Summary of the studies in the diagnostic criteria for traumatic brain injury (TBI).

There was no single comprehensive nomenclature system for TBI types in the literature. Each study emphasized different aspects of the injury mechanism or outcomes to describe the TBI type, which were: the context of injury – being sports in concussion [23]; the type of force – being blast-related [25], acceleration-deceleration, or blunt [5]; the distribution of force – being focal or diffuse [17]; the impact of the force – being closed or open, or penetrating [26]; or the pathoanatomical diagnosis – such as skull fractures of intracranial lesions [12]. No study provided clinical correlations of their classification system to support the clinical relevance or superiority of their proposed classification structures.

Rehabilitation interventions in TBI: The current evidence for various rehabilitation interventions in TBI were categorized according to study design using evidence defined by the National Health and Medical Research Council (NHMRC) programme for intervention studies[13] (see Table 3).

A rehabilitation approach to TBI includes a wide spectrum of treatment and use of different interventions. However, many interventions have not yet been carried into comprehensive programmes and are provided often as individual interventions. Based on the NHMRC levels of evidence there is strong evidence for the effectiveness of psychological interventions such as attention training and cognitive interventions after TBI (Rohling et al., 2009) [27]; for nutritional support for improved survival and disability outcomes (Wang et al.,

Interventions	Injury type	Study, year	Key findings	Level of evidence
Acupuncture	TBI	Wong et al., 2013 [46]	Insufficient evidence for effectiveness and safety of acupuncture in the acute treatment and/or rehabilitation of TBI.	I
Physical therap	TBI	Bland et al., 2011 [47]	Limited evidence to support the effectiveness of PT in improving balance and gait in functionally mild-to-moderate individuals with TBI.	I
	TBI	Hassett et al., 2008 (edited 2009) [48]	Insufficient evidence to support the effectiveness of fitness training in improving cardio-respiratory fitness in persons with TBI.	I
Psychological interventions	TBI	Lane-Brown and Tate, 2009 [49]	No evidence for use of interventions for apathy such as cranial electrotherapy stimulation in persons with TBI.	I
	TBI	Soo and Tate, 2007 (edited 2009) [30]	Moderate evidence for effectiveness of CBT for treatment of acute stress disorder following mild TBI; and combination of CBT and neurorehabilitation for treatment of general anxiety symptoms for mild to moderate TBI.	I
	TBI	Snell et al., 2009 [50]	Limited evidence to support the selection of active treatments for mild TBI, although patient education approaches may be beneficial in the early stages.	I
	Traumatic physical injuries: fracture/crush injuries	De Silva et al., 2009 [51]	Insufficient evidence for psychological interventions for prevention of disability following traumatic physical injury.	I
	TBI	Rohling et al., 2009 [27]	Strong evidence for effectiveness of attention training after TBI, and for language and visuospatial training for aphasia and neglect syndromes after stroke.	I
	TBI	Fann et al., 2009 [52]	Insufficient evidence to support practice recommendations regarding any of the psychotherapeutic or rehabilitation interventions for depression following TBI.	I
	TBI	Kennedy et al., 2008 [53]	Strong evidence that meta cognitive strategy instruction should be used in adults with TBI. Insufficient evidence for trained verbal reasoning and multi-tasking in improved function.	I
Hyperbaric oxygen therapy (HBOT)	TBI	Bennett et al., 2012 [29]	Strong evidence for HBOT as adjunctive therapy in reduction of risk of death in TBI, but insufficient evidence that HBOT improves outcomes (QoL) in survivors.	I
Hyperventilation therapy	TBI	Roberts and Schierhout, 1997 (updated 2009) [54]	Limited evidence for any potential benefits or harm that might result from hyperventilation therapy in improving patient outcomes in persons with TBI.	I
Sensory stimulation programmes	Head injury	Lombardi et al., 2002 (edited 2009) [55]	Limited evidence to support, or refute the effectiveness of multisensory programmes in patients with coma and vegetative state.	I
Hypothermia therapy	TBI	Georgiou and Manara, 2013 [56]	No evidence of benefit of primary therapeutic hypothermia on mortality or neurological morbidity. Hypothermia was associated with cerebrovascular disturbances on rewarming and possibly with pneumonia in adult patients.	I
	TBI/stroke	Harris et al., 2012 [57]	Insufficient evidence non-invasive head cooling may be beneficial for improving functional outcomes.	I
	TBI	Sadaka and Veremakis, 2012 [58]	Therapeutic hypothermia (32–34°C) is shown to have beneficial effect in controlling intracranial hypertension in patients with severe TBI.	I
	TBI	Sydenham et al., 2009 [59]	No evidence that hypothermia is beneficial in the treatment of head injury.	I
	TBI	Saxena et al., 2008 [60]	No evidence to support the use of moderate cooling (35°C-37.5°) therapies after TBI in improving patient outcomes.	I
Nutritional support	TBI	Wang et al., 2013 [28]	Early initiation of nutrition showed significant reduction in the rate of mortality, poor outcome, and infectious complications. It appears that parenteral nutrition is superior to enteral nutrition in improving outcomes.	I
	Head injury	Perel et al., 2008 [61]	Strong evidence that early nutritional support associated with fewer infections and a trend towards better outcomes in terms of survival and disability.	I
Vocational rehabilitation	TBI	Fadyl and McPherson, 2009 [62]	Limited evidence to suggest what should be considered the best practice approach to vocational rehabilitation in people with TBI	I
Educational intervention	ATLS training for ambulance crews	Jayaraman and Sethi, 2010 [63]	No evidence that ATLS for ambulance crews cuts death rates or decreases disability in injured people.	I
	ATLS for hospital staff	Jayaraman and Sethi, 2009 [64]	Insufficient evidence that ATLS programmes improve knowledge of hospital staff, and no evidence that ALTS for hospital staff reduces death and disability of injured patients.	I
Speech and language therapy	TBI/stroke	Sellars et al., 2005 (edited 2009) [65]	No evidence that speech and language therapy in improving dysarthria following non-progressive brain injury (TBI/stroke).	I

Abbreviations: ATLS: Advanced Trauma Life Support; CBT: Cognitive Behavioural Therapy; HBOT: Hyperbaric Oxygen Therapy; PT: Physical Therapy; QoL: Quality of Life; TBI: Traumatic Brain Injury.

Reference:National Health and Medical Research Council (NHMRC) (2009) NHMRC Levels of Evidence and Grades for Recommendations for Developers of Guidelines. Accessed in October 2013, from http://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf.

Table 3: Summary of the systematic reviews in the Cochrane Central Register for the treatment of traumatic brain injury (TBI).

2013) [28]; and hyperbaric oxygen therapy for reduction of risk of death after TBI (Bennett et al., 2012) [29]. There is moderate evidence for cognitive behavior therapy for managing stress after mild TBI (Soo and Tate, 2007; edited 2009) [30]. For all other interventions the evidence is limited or insufficient due to lack of studies in the area. These include: speech therapy for dysarthria; vocational rehabilitation; hypothermia treatment; sensory stimulation programmes; hyperventilation therapy; and use of acupuncture in TBI.

Discussion

This review provides an overview of literature on the diagnosis and rehabilitation interventions in TBI. Current approach to diagnosing TBI

		Clinical features						
		Seizure	Focal neurological deficit	Intracranial lesion	Loss of consciousness	Altered consciousness (including disordered consciousness, confused, disoriented, or dazed)	Post traumatic amnesia (including amnesia of blow)	Depressed, basilar or linear skull fracture
Study methodology to support the recommendations	Systematic review [Rees, 2003] [15]					≥1 are required for TBI diagnosis		
	Systematic review [Carroll et al, 2004] [3]	≥1 are required for TBI diagnosis						
	Analysis of dataset [Malec et al, 2007] [16]*			Either ≥1 of these, or…			…≥1 are required for TBI diagnosis	
	Consensus [Menon et al, 2010] [5]		≥1 are required for TBI diagnosis					

*The minimumcriteria for Mayo Classification for mild (probable) TBI were applied, rather than symptomatic (possible) TBI, since the latter category allows a degree of uncertainty of a TBI diagnosis.

Table 4: Summary of lowest thresholds for diagnosingtraumatic brain injury (TBI) in the literature.

			Clinical features					
		TBI Severity	**Glasgow Coma Scale (GCS)**	**Loss of Consciousness (LOC)**	**Post traumatic amnesia (PTA)**	**Radiological evidence of injury**	**Abbreviated Injury Score for head (AIS_{head})**	**Neurological abnormality**
Study methodology to support the recommendation	Consensus [Servadei et al, 2001] [18]	Mild	14-15 in first 12 hours					
	Metanalysis [Stein et al, 2001] [20]		14-15					
	Narrative review [DeCuypere et al, 2012] [17]		13-15					
	Systematic review [Carroll et al., 2007] [3]		13-15 at ≥30 minutes **and, or**	Momentary to <30 minutes **and, or**	Momentary to <24 hours **and, or**	Intracranial lesion not requiring surgery **and, or**		Transient abnormality (focal sign, seizures)
	Analysis of dataset [Malec et al, 2007] [16]					Depressed, basilar or linear skull fracture (intact dura)		
	Consensus [Servadei, 2001] [18]	Moderate	9-13 in first 12 hours					
	Metanalysis [Stein et al, 2001] [20]		9-13					
	Narrative review [DeCuypere et al, 2012] [17]		9-12					
	Analysis of dataset [Malec et al, 2007] [16]	Moderate to severe	Worst score in first 24 hours is <13 or death **and, or**	≥30 minutes **and, or**	≥24 hours **and, or**	ICH, SDH, EDH, cerebral or haemorrhagic contusion, penetrating TBI, SAH, brain stem injury		
	Analysis of registry [Grote et al, 2011] [22]	Severe					≥3	
	Consensus [Servadei, 2001] [18]; Metanalysis [Stein et al, 2001] [20]; and Narrative review [DeCuypere et al, 2012] [17]		3-8					

Abbreviations: ICH: intracerebral haemorrhage; SDH: Subdural Haemorrhage; EDH: Extradural Haemorrhage; SAH: Subarachnoid Haemorrhage.

Table 5: Summary of traumatic brain injury (TBI) severity grading in the literature.

lacks clarity in its structure, and there is limited consensus for current systems in use, with its flow-on effect into the quality of epidemiological data, and acute and long term outcomes in TBI. This is a major issue which needs to be addressed with an international consensus approach, and clinical data to support the recommendations. Although a plethora of rehabilitation interventions are available for TBI population, the evidence to support many is lacking and are discussed below.

Lowest threshold for TBI

In the absence of unified diagnostic criteria for mild TBI, the lowest threshold for TBI diagnosis is useful. Following head trauma, PTA is a specific and agreed diagnostic criterion for TBI. The significance of other structural or functional changes remains unclear, and highly sensitive diagnostic approaches should be carefully correlated with clinical outcomes for their relevance. Excessive or missed diagnoses of TBI should be minimized to prevent psychosocial burden; and to avoid ambiguous outcomes of epidemiological and clinical studies.

TBI severity

The lack of a consensus for grading TBI severity remains problematic for interpreting clinical research and long term outcomes of TBI. Historical grading based on GCS [7] remains the mainstay of severe TBI diagnosis (GCS 3-8), however, there is no consensus on other relevant clinical features such as intracranial haemorrhage

Category	Type of TBI	Approach to diagnosis
Context of injury (McCrory et al., 2013) [23]	Concussion	History of biomechanical force in sports
Type of force (Menon et al., 2010; Rosenfeld et al., 2013) [5,25]	Blast-related	History of explosives, missiles, other blasts
	Blunt	History of being struck or striking a blunt object in assault, motor vehicle accident, or falls
	Acceleration-deceleration	History of acceleration-deceleration without history of external head trauma
Distribution of force (DeCuypere and Klimo Jr, 2012) [17]	Focal	History, clinical and imaging
	Diffuse	
Impact of force (Nolan, 2005) [26]	Closed	Clinical
	Open/penetrating	
Pathoanatomical diagnosis (Saatman et al., 2008) [12]	Skull fractures	Imaging
	Diffuse axonal injury	
	Cerebral contusion	
	Traumatic subarachnoid haematoma	
	Subdural haematoma	
	Extradural haematoma	
	Intraparenchymal haematoma	
	Brainstem lesion	

Table 6: Summary of nomenclature for traumatic brain injury (TBI) types in the literature.

or penetrating TBI (together with GCS>8), which potentially should also lead to the diagnosis of severe TBI [8]. Given GCS is a dynamic monitoring tool, we should also consider which GCS to use for severity grading: whether early or delayed; field or arrival; or the best or the worst score [31]. On the other hand, GCS is not sensitive or specific in mild TBI [8], and should no longer be used in isolation to diagnose mild TBI [19,22]. Further, the lack of consensus in the literature regarding GCS 13 as mild or moderate TBI remains a problem [3]. As per ACRM's position statement, PTA and LOC duration remain key aspects of mild TBI diagnosis [11]. Despite its clinical relevance impacting on the management of TBI, radiological findings and neurological changes are not widely accepted as diagnostic criteria for TBI. Risk of complications in concussion and mild head injury has been examined to identify high risk persons within milder spectrum of TBI [18,19,23].

TBI type

A standardized nomenclature to specify the type of TBI do not exist, but its potential benefits can be anticipated from clinical, research, and knowledge translation perspectives, especially for future targeted therapeutic agents [12]. In the absence of clear guidance for describing TBI, any combination of numerous words to describe the type of TBI are possible – as an example, a person could sustain *concussion* in football as a result of striking a *blunt* object (e.g. another person), with *diffuse* distribution of force, resulting in *closed* TBI with *subdural haematoma*. Each of these italicized words contains limited information, and any of these words could reasonably be used in isolation to communicate with other clinicians to describe the type of TBI sustained. A system of clear and mutually exclusive categories and definitions to classify TBI types would be beneficial, especially for clinical research designs [12]. Further, in animal modelling of TBI – especially in designing therapeutic inventions – the type of TBI that is being reproduced by the model should be carefully considered for their relevance and limitations [32].

Regarding concussion, its current definition closely resembles that of TBI, being 'a brain injury and is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces' [23]. Concussion as a subset of TBI is predominantly – but not exclusively – used in reference to blunt and low velocity impact resulting in mild injuries in the context of sports [33,34]. However, by definition, concussion could range from no pathological consequences to all severity of TBI [23], and potentially include a wide spectrum of injury mechanisms and pathophysiological processes. For blast-related TBI, the literature has extended beyond mild TBI to include severe TBI of penetrating missile injuries to the brain in military and civilian settings [25], with growing appreciation of extended impact of blast-waves on susceptible organs in close proximity to fluid and air [35]. Therefore, by definition, concussion and blast-related TBI refer to the injury mechanism, respectively, and do not allude to any associated pathoanatomical sequelae of the head trauma.

Treatments in TBI aim to stabilise the medical and rehabilitation issues; prevent secondary complications; restore functional abilities; and provide adaptive equipment to enhance functional independence and social reintegration into the community. The evidence to support psychological interventions (attention training) and cognitive interventions after TBI is strong (Table 3). Cognitive remediative therapies remain the cornerstone of TBI rehabilitation. More evidence, however, is needed for emotional and psychotherapeutic interventions in this population. Although hyperbaric oxygen therapy reduces the risk of death after TBI, there is insufficient evidence that it improves outcomes or quality of life in TBI. Parenteral nutrition is superior to enteral nutrition; and early initiation of nutrition showed reduction in mortality and sepsis in TBI with improved survival and disability outcomes. Interestingly, despite widespread use of physical therapy modalities, the evidence is 'limited' for improving balance and gait and 'insufficient' to support fitness training in TBI. There is insufficient evidence for acupuncture; hyperventilation; hypothermia therapy; and speech therapy for improving dysarthria in TBI (Table 3). Robust trials in these areas is urgently required to build evidence-based practices in rehabilitation.

Clinical relevance and future directions

The wider community of clinicians treating persons with TBI have much to benefit from a clear and comprehensive diagnostic criterion for TBI according to its severity and type. The present literature is unclear, but alludes to a combination of a etiological, clinical and radiological features to identify the injury sustained. Importantly, GCS, and duration of LOC and PTA, in addition to other clinical and radiological features remain the mainstay for TBI diagnosis. Highly sensitive and emerging diagnostic approaches need clinical correlation for their relevance as a standalone diagnostic marker of TBI. An awareness of

various approaches to diagnosing and grading TBI severity should be considered for clinical practice, and should alert clinicians to consider other clinical features suggestive of TBI in for example, isolated skull fractures or small intracranial lesions following head trauma, and guide further management including referrals for rehabilitation assessment and management. For describing the type of TBI, perhaps the most striking aspect of TBI, such as blast-wave exposure in mild TBI; or the findings of a large extradural haemorrhage should be used when communicating with other clinicians.

Limitations

This study has a number of limitations. Firstly, the systematic review was restricted by publication date for recent literature and includes only published data. Secondly, different research methods incorporated in reaching individual recommendations for TBI diagnosis in the included studies have not been weighted in the analysis. Quality assessment was not conducted for studies on diagnosis of TBI and included literature reviews. Thirdly, this review may not be reflective of the clinical pathways and approaches in use in TBI care, which have not been explicitly expressed in the examined literature. The Cochrane register was used for systematic reviews for TBI treatments – individual studies within these reviews were not included.

Conclusion

This systematic review provides an overview of diagnostic criteria and rehabilitation in TBI. Clear diagnostic criteria for TBI could improve TBI care, data collection, and the quality of future clinical trials for specific targeted therapies according to the diagnosis, the severity and the type of TBI. More studies of good methodological design are needed to establish evidence to support interventions used in rehabilitation settings.

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