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Review

A systematic review of fatigue in patients with traumatic brain injury: The course, predictors and consequences

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ABSTRACT

Background: Fatigue is common after traumatic brain injury (TBI). Its risk factors, natural history and consequences are uncertain. Best-evidence synthesis was used to address the gaps.
Methods: Five databases were searched for relevant peer-reviewed studies. Of the 33 articles appraised, 22 longitudinal studies were selected. Results were reported separately based on their timing of baseline assessment.
Results: All studies document changes in fatigue frequency and severity with time, irrespective of setting or TBI severity. There is limited evidence for certain clinical and psychosocial variables as predictors of fatigue severity at follow-up. Early fatigue severity predicted persistent post-concussive symptoms and Glasgow outcome score at follow-up.
Conclusions: Fatigue is present before and immediately following injury, and can persist long term. The variation in findings supports the idea of fatigue in TBI as a nonhomogeneous entity, with different factors influencing the course of new onset or chronic fatigue. To decrease the heterogeneity, we emphasize the need for agreement on a core set of relevant fatigue predictors, definitions and outcome criteria.
PROSPERO registry number: CRD42013004262.

Abbreviations: APOE-ε4, apolipoprotein-ε4; BDI, Beck depression inventory; BFS, Barosso fatigue scale; CHART, Craig handicap assessment and reporting technique; CNS, central nervous system; DRS, disability rating scale; FSS, fatigue severity scale; GCS, Glasgow coma scale; GOSE, Glasgow outcome scale-extended; GFI, global fatigue inventory; HADS, hospital anxiety and depression scale; MFIS, modified fatigue impact scale; MFI, multidimentional fatigue inventory; mTBI, mild traumatic brain injury; PRISMA, preferred reporting items for systematic reviews and meta-analyses; PCSC, post-concussion syndrome checklist; POMS, profile of moods scale; RCT, randomized controlled trial; RPQ, Rivermead post-concussive questionnaire; SIGN, Scottish intercollegiate guidelines network; SF-36, 36-item short form health survey (from medical outcomes study); TBI, traumatic brain injury; VAS, visual analog scale.

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Contents

1. Background

Traumatic brain injury (TBI), defined as "an alteration in brain function, or other evidence of brain pathology, caused by an external force" (Brain Injury Association of America, 2013), is among the most serious, disabling neurological disorders in all societies and expected to rank as the major cause of death and disability by the year 2020 (World Health Organization, 2002). Over the past decades, evidence has emerged citing fatigue as a common, long-lasting problem after TBI (Belmont et al., 2006; Ponsford et al., 2011; Middleboe et al., 1992). It is burdensome to patients, and is associated with poor outcomes (Belmont et al., 2006; Ponsford et al., 2011). In a number of studies, over half of the patients making up the TBI samples reported fatigue's negative effect on social, physical and cognitive functioning (Ziino and Ponsford, 2006) and participation in everyday activities (Cantor et al., 2008), and role in increased work-related and other disabilities (McCrimmon and Oddy, 2006). Estimates of the incidence of fatigue after TBI vary from 21% to 73%, depending on the characteristics of the studied population (e.g. severity of injury, time since injury, sampling of patients, etc.) and the method used to identify fatigue (e.g. single item or fatigue scales) (Belmont et al., 2006; Ponsford et al., 2011; Middleboe et al., 1992; Borgaro et al., 2005; Lidvall et al., 1974).

The term "fatigue" has several meanings. It is recognized when performance of an activity results in diminished capacity for carrying out a function (Chaudhuri and Behan, 2004). Within this, 'physiological fatigue' refers to the state of general tiredness due to physical or mental exertion, which can be ameliorated by rest (Schillings et al., 2007). A state that refers to a weariness unrelated to previous exertion level, and not ameliorated by rest, is termed 'pathological fatigue' (Jason et al., 2010). Despite such characterization, fatigue in the TBI population is difficult to elucidate. This is partly due to the numerous plausible biological causes of fatigue (i.e. neuroanatomical, functional, psychological/psychiatric, biochemical, endocrine, sleep-related), independently or combined, through which this symptom can evolve after brain injury (Fig. 1) (Prins et al., 2006). To date, several narrative reviews have been published to provide insight into the topic of post-traumatic fatigue (PTF) (Belmont et al., 2006; Borgaro et al., 2005; Ponsford et al., 2012; Levine and Greenwald, 2009). Nevertheless, there is still little known about which specific clinical, behavioral and physiological factors are associated with its occurrence after brain injury; nor whether fatigue remains the same in its frequency/intensity, or changes over time. Finally, the overall health burden of this symptom in the TBI population remains uncertain. Understanding the facets of fatigue in TBI can guide in differential diagnosis