



UMEÅ UNIVERSITET

Umeå University Medical Dissertations, New Series No 2000

Fatigue after Traumatic Brain Injury

Exploring Novel Methods for Diagnosis and Treatment

Nils Berginström

Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för
avläggande av medicine doktorsexamen framläggs till offentligt
försvar i Aulan, Vårdvetarhuset

Fredagen den 8 februari, kl. 09:00.

Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Professor Jan Lexell,
Institutionen för Hälsovetenskaper, Rehabiliteringsmedicin, Lunds
Universitet, Lund, Sverige.

Department of Community Medicine and Rehabilitation,
Rehabilitation Medicine
Umeå University, Sweden 2019

Organization

Umeå University
Department of Community Medicine and Rehabilitation

Document type

Doctoral thesis

Date of publication

18 January 2019

Author

Nils Berginström

Title

Fatigue after Traumatic Brain Injury - Exploring Novel Methods for Diagnosis and Treatment.

Abstract

Background: Traumatic brain injury (TBI) is one of the most common causes of disability and mortality. While some patients recover quickly, especially at the mild side of the injury severity continuum, many will experience symptoms for years to come. In this chronic phase, patients report a wide array of symptoms, where fatigue is one the most common. This fatigue makes huge impact in several areas of these patients' lives. Despite the prevalence of fatigue after TBI, the underlying mechanisms are unclear. Further, there are no standardized way for assessment and diagnosis, and there are no treatments with satisfying empirical support. The aim of this thesis was to examine the effects of the novel compound OSU6162 on fatigue in patients with TBI, and to explore functional and structural brain imaging correlates of fatigue after TBI.

Methods: Studies I and III were based on a placebo-controlled, double-blinded clinical trial examining the effects of the monoaminergic stabilizer OSU6162 on fatigue in patients in the chronic phase of traumatic brain injury. In study I, self-assessment scales of fatigue and neuropsychological tests were used as outcomes, while functional magnetic resonance imaging (fMRI) blood-oxygen-level dependent (BOLD) signal was the primary outcome in study III. Studies II and IV used cross-sectional designs, comparing patients with TBI with age- and gender matched healthy controls. Study II examined whether fMRI BOLD signal could be used to detect and diagnose fatigue in patients with TBI, and study IV whether white matter hyperintensities (WMH) contribute to lower cognitive functioning and presence of fatigue after TBI.

Results: Study I revealed no effects of OSU6162 during 28 days of treatment at maximum doses of 15 mg twice daily on measures of fatigue or any other outcome. The results from study II indicated that fatigue after TBI is linked to alterations in striato-thalamic-cortical loops, and suggested that fMRI could be a promising technique to use in the diagnosis of fatigue after TBI. In study III the results revealed effects of treatment in the right occipitotemporal and orbitofrontal cortex. In these areas, the BOLD response was normalized in the OSU6162 group as compared to healthy controls, while the placebo group showed a steady low activity in these areas. The regional effects were located outside the network shown to be linked to fatigue in study II, which might explain why there were no effects on fatigue after treatment with OSU6162 in study I. Study IV showed that WMH lesions increased with increased TBI severity, but the presence and extent of lesions did not explain lower neuropsychological functioning or fatigue in subjects with previous TBI.

Conclusions: In summary, although no effects on fatigue after treatment with OSU6162 were seen, the results provide support to the theory that fatigue after TBI is linked to alterations in striato-thalamic-cortical loops, and on how fatigue after TBI could be assessed or diagnosed using fMRI. Structural damage within white matter was however not related to fatigue.

Keywords

Traumatic brain injury, fatigue, OSU6162, randomized clinical trials, functional magnetic resonance imaging, neuropsychology, structural magnetic resonance imaging, white matter hyperintensities

Language

English

ISBN

978-91-7601-979-5

ISSN

0346-6612

Number of pages

59 + 4 papers