

Experimentally-induced Wernicke's encephalopathy modifies crucial rat brain parameters: the importance of Na⁺, K⁺ -ATPase and a potentially neuroprotective role for antioxidant supplementation.

[Zarros A¹](#), [Liapi C](#), [Al-Humadi H](#), [Almpani M](#), [Stolakis V](#), [Skandali N](#), [Voumvourakis K](#), [Katsouni E](#), [Tsakiris S](#).

Author information

- ¹Laboratory of Physiology, Medical School, National and Kapodistrian University of Athens, PO Box 65257, 15401, Athens, Greece.

Abstract

Wernicke's encephalopathy (WE) is a serious neuropsychiatric syndrome caused by chronic alcoholism and thiamine (T) deficiency. Our aim was to shed more light on the pathophysiology of WE, by introducing a modified in vivo experimental model of WE and by focusing on changes provoked in the total antioxidant status (TAS) and three crucial brain enzyme activities in adult rats. Rats were placed on ethanol (EtOH) consumption (20 % v/v) for a total of 5 weeks. By the end of the third week, rats were fed a T-deficient diet (TDD) and were treated with pyriethiamine (PT; 0.25 mg/kg) for the remaining 2 weeks. Following the induction of WE symptomatology, rats were treated with three consecutive (every 8 h) injections of saline or T (100 mg/kg) and were sacrificed. Brain homogenates were generated and used for spectrophotometrical evaluation of TAS and enzymatic activities. Additionally, in vitro experiments were conducted on brain homogenates or pure enzymes incubated with T or neuromodulatory antioxidants. Pre-exposure to EtOH provided a successful protocol modification that did not affect the expected time of WE symptomatology onset. Administration of T ameliorated this symptomatology. WE provoked oxidative stress that was partially limited by T administration, while T itself also caused oxidative stress to a smaller extent. Brain acetylcholinesterase (AChE) was found inhibited by WE and was further inhibited by T administration. In vitro experiments demonstrated a potential neuroprotective role for L-carnitine (Carn). Brain sodium-potassium adenosine triphosphatase (Na⁽⁺⁾,K⁽⁺⁾-ATPase) activity was found increased in WE and was reduced to control levels by in vivo T administration; this increase was also evident in groups exposed to PT or to TDD, but not to EtOH. In vitro experiments demonstrated a potential neuroprotective role for this Na⁽⁺⁾,K⁽⁺⁾-ATPase stimulation through T or L-cysteine (Cys) administration. Brain magnesium adenosine triphosphatase (Mg⁽²⁺⁾-ATPase) activity was found decreased by prolonged exposure to EtOH, but was not affected by the experimental induction of WE. Our data suggest that T administration inhibits AChE, which is also found inhibited in WE. Moreover, increased brain Na⁽⁺⁾,K⁽⁺⁾-ATPase activity could be a marker of T deficiency in WE, while combined T and antioxidant co-supplementation of Cys and/or Carn could be neuroprotective in terms of restoring the examined crucial brain enzyme activities to control levels.