

# Abstract

J Am Coll Nutr. 2004 Oct;23(5):529S-533S.

## **Magnesium attenuates post-traumatic depression/anxiety following diffuse traumatic brain injury in rats.**

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**OBJECTIVE:** Magnesium (Mg) declines after traumatic brain injury (TBI), a decline believed associated with ensuing neuronal cell death and subsequent functional impairment. While Mg's effects on motor and cognitive deficits following TBI have been well studied, few studies have addressed post-traumatic depression as an outcome parameter, despite its being a major clinical problem with an incidence of between 6 and 77%. We investigated the incidence of post-traumatic depression/anxiety in an animal model of diffuse TBI, and explored the use of magnesium sulfate (MgSO<sub>4</sub>) as an interventional treatment.

**METHODS:** Diffuse TBI was induced in 32 anesthetized, adult, male Sprague-Dawley rats, using the 2 m impact-acceleration model of injury. At 30 min after injury, half of the rats received 250 micromol/kg i.v. MgSO<sub>4</sub>; the other half served as non-treated controls. Before and for 6 weeks after injury, the open-field, spontaneous activity test was used to determine post-traumatic depression/anxiety relative to pre-injury. In this test, animals are placed in a 1-meter square box with 100 squares marked on the base. The number of squares entered in a 5-min period is recorded. Incidence of post-traumatic depression/anxiety was defined as the number of animals demonstrating a reduction in spontaneous activity to less than 100 squares in 5 min. Prior to injury, rats typically entered a mean of 201 +/- 12 (SEM) squares over a 5 min observation period.

**RESULTS:** At 1 week after injury, non-treated animals had a mean score of 62 +/- 13. The incidence of post-traumatic depression/anxiety in these animals was 61%, which is similar to that observed clinically. In contrast, animals treated with MgSO<sub>4</sub> had a mean activity score of 144 +/- 23 at 1 week after TBI and an incidence of depression/anxiety of less than 30%. The significant difference between groups persisted for the entire 6-week observation period.

**CONCLUSIONS:** The improvement in post-traumatic depression/anxiety conferred by Mg adds further weight to available evidence of Mg's benefit as a neuroprotective agent after TBI.

PMID: 15466958

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