

A Toll like Receptor (TLR) 9 Antagonist Restores Astroglial Glutamate Transporter Expression in the Dorsal Horn (DH) following Spinal Cord Injury (SCI): Implications for Below-Level Neuropathic Pain

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Introduction

Astroglial glutamate aspartate transporter (GLAST) and glutamate transporter 1 (GLT-1) play important roles in the clearance of extracellular glutamate and have been implicated in glutamate-mediated hyperexcitability of dorsal horn (DH) neurons, a mechanism underlying central sensitization and neuropathic pain. We have previously reported that intrathecal treatment of mice sustaining a mid-thoracic spinal cord injury (SCI), with a toll-like receptor (TLR) 9 antagonist, CpG ODN 2088, limits the development of below-level neuropathic pain. The current study examined the effects of CpG ODN 2088 on GLAST and GLT-1 levels in the lumbar DH, a region involved in the processing of below-level chronic pain.

Methods

A severe mid-thoracic contusion injury was induced in female mice. Intrathecal CpG ODN 2088 administration started at 1 day post-injury (dpi) and was repeated at 48hr intervals until 28dpi. Thereafter, the injury epicenter and lumbar DH regions were collected. All samples were assessed for protein expression by western blot analysis. A one-way ANOVA was used for statistical analysis.

Results

A mid-thoracic SCI reduced GLAST and GLT-1 protein levels within the lumbar DH at 28dpi ($p < 0.001$). Treatment of injured mice with CpG ODN 2088 prevented the reduction in GLAST and restored GLT-1 to uninjured values. Neuronal glutamate transporter and receptor subunit levels were not affected by the antagonist. In contrast to the lumbar DH, GLAST and GLT-1 levels in the epicenter were not altered following CpG ODN 2088 treatment.

Conclusions

These findings indicate that the TLR9 antagonist affects regions remote from the injury epicenter and selectively modulates astroglial glutamate transporters following SCI, potentially, through direct effects on astrocytes.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Discuss the function of astroglial glutamate transporters and their importance in central sensitization and pain processing, and 2) Obtain an insight into the role of pattern recognition receptors in spinal cord injury.

References