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ORIGINAL PAPER

Decreased GFAP Expression and Improved Functional Recovery in Contused Spinal Cord of Rats Following Valproic Acid Therapy

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Abstract Many studies have illustrated that much of the post-traumatic degeneration of the spinal cord cells is caused by the secondary mechanism. The aim of this study is to evaluate the effect of the anti-inflammatory property of valproic acid (VPA) on injured spinal cords (SC). The rats with the contused SC received intraperitoneal single injection of VPA (150, 200, 300, 400 or 500 mg/kg) at 2, 6, 12 and 24 h post-injury. Basso–Beattie–Bresnahan (BBB) test and H-reflex evaluated the functional outcome for 12 weeks. The SC were investigated 3 months post-injury using morphometry and glial fibrillary acid protein (GFAP) expression. Reduction in cavitation, H/M ratio, BBB scores and GFAP expression in the treatment groups were significantly more than that of the untreated one ($P < 0.05$). The optimal improvement in the condition of the contused rats was in the ones treated at the acute phase of injury with 300 mg/kg of VPA at 12 h post-injury, they had the highest increase in BBB score and decrease in astrogliosis and axonal loss. We conclude that treating the contused rats with 300 mg/kg of VPA at 12 h post-injury improves the functional outcome and reduces the traumatized SC gliosis.

Keywords Astrocytes · Gliosis · Spinal injury · Inflammation · Valproic acid · GFAP

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Introduction

Spinal cord injury is one of the major causes of disability [1], traumatic insult on the spinal cord could immediately damage the cellularity of the spinal tissue by primary traumatic events [2]. The secondary events cause more losses in the spinal cells [3]. The mechanisms involved in cell death during SCI are complex, including excitotoxicity, calcium-mediated secondary injury and inflammation. It is recognized that inflammatory responses play a pivotal role in the pathogenesis of SCI leading to neuronal death, glial scar formation and eventual loss of neuronal functions [4]. Following inflammation, accumulation of intrinsic (microglia) and extrinsic (macrophages, lymphocytes, neutrophils and natural killer cells) inflammatory cells [5] and release of cytokines were documented [6]. Pro-inflammatory cytokines were reported to recruit astrocytes and microglia to the injury site [7]. While interleukin (IL)-1, a tumor necrosis factor (TNF), and IL-6 have been reported to be mitogens for neonatal astrocytes in culture, Li et al. [8] confirmed that the TNF promoted proliferation of adult human astrocytes. Thus, cytokines from inflammatory mediators can lead to glial scar formation [9], an obstacle for growth and maturation of neural progenitors, axonal regeneration and vascularization, and cause subsequent inhibition of axonal growth [10]. So far, only high

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