Astrocyte Response and Transforming Growth Factor-B Localization in Acute Spinal Cord Injury

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Study Design. An experimental histologic and immunohistological investigation of acute spinal cord injury was performed in a rat model.

Objective. This study determined (1) the immediate cellular and molecular responses within the spinal cord that result from a clinically relevant compression injury; (2) the acute astrocytic response to injury using the astrocyte specific GFAP antibody; and (3) the temporal pattern of cellular and extra cellular localization of transforming growth factor B1 (TCF-B1) within the spinal cord injury zone immediately after injury.

Summary of Background Data. Ultimate neurologic outcome from spinal cord injury results from both the primary mechanical trauma and a subsequent cascade of cellular and molecular events that are termed the secondary injury. Efforts aimed at improving neurologic outcome may depend on the manipulation of cellular and molecular mechanisms that are responsible for propagating this secondary injury cascade. Astrocytes and TGF-B are two potentially key components of this secondary injury.

Methods. Twenty-one Sprague-Dawley adult rats underwent open thoracic spinal cord injuries using the Allen weight-drop technique. Spinal cord specimens were harvested at 0, 1, 2, 4, 8, 24 and 72 hours after injury for histologic and immunohistochemical evaluation. Harvesting of injured and surrounding uninjured cord was performed before sectioning in sagittal and transverse planes. These paraffin-embedded sections were stained with polyclonal antibodies against glial fibrillary acidic protein (GFAP, an astocytic cytoskeleton marker) and TGF-B1.

Results. A complex astrocytic response to the spinal cord injury was found within 24 hours of injury. Both the geographic and temporal patterns of astrocyte localization suggest a role in the regulation of spinal cord injury propagation. High concentrations of extra cellular TGF-B were seen immediately after injury within the hematoma at the zone of impact. Subsequently, intracellular TGF-B was seen in astrocytic nuclei and cytoplasm, intramedullary and extramedullary capillary endothelial cells and in motor neurons.

Conclusions. The neurologic outcome in patients with spinal cord injury results in part from a secondary injury whose cellular and molecular mechanisms are poorly understood. This study suggests that both astrocytes and TGF-B are involved in the regulation of spinal cord secondary injury. An improved understanding of their specific roles may result in novel treatments to improve the outcome from spinal cord injury.