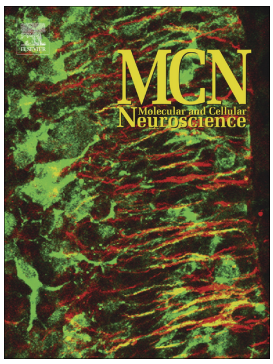

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PTEN EXPRESSION IN ASTROCYTIC PROCESSES AFTER SPINAL CORD INJURY

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Abstract

The role of the Rho/ROCK/PTEN signaling pathway in the regulation of astrocyte function for consolidation/stabilization of the synapse has not been thoroughly studied. In this study, the expression of phosphatase and tensin homolog deleted on chromosome 10 (PTEN) in GFAP-positive astrocytic processes in the ventral horns (VH) of the rat spinal cord has been evaluated in the normal condition and in a delayed period (30 days) after dosed contusion spinal cord injury (SCI) in caudal thoracic segments. In intact rats and at 30 days post-injury (dpi), semi-quantitative immunohistochemical analysis showed that there is approximately 2 folds less synaptophysin reactivity in the motoneuron perikarya than outside the perikarya, i.e., on dendritic spines, in the VH area. At 30 dpi, the square occupied by synaptophysin reactivity on the motoneuron perikarya and dendritic spines decreased ~2.4 and ~2.1 folds, respectively. Western blotting of the postsynaptic density protein 95 (PSD95) showed a decreased amount in the area of injury of ~3 folds at 30 dpi. Expression of GFAP in the astrocytic processes around the synaptophysin spots (APAS) was less than in the astrocytic processes that were located at distance from the synapses (APFS) both in the intact and SCI groups. In the APAS, the expression level of PTEN increased significantly after SCI. In these astrocytic processes, the PTEN expression level was significantly higher than in the APFS for both the intact and SCI rats. In the intact spinal cord, different PTEN expression levels were detected both in APAS and APFS. This may be due to the varying degree of integration of PTEN in the membrane compartment of astrocyte stem processes and possibly the increased delivery of PTEN from the GFAP-positive stem into fine GFAP-negative peripheral processes. The observed shifts after SCI reflect the imbalance in the mechanisms of synaptic plasticity after injury. Thus, strategies that have been developed for the deletion or knockdown of the PTEN gene are quite promising.

Keywords: spinal cord injury, PTEN, GFAP, astrocytic processes, synaptophysin.

INTRODUCTION

To recover functions after damage of the central nervous system, it is necessary to maintain survival of the neurons, to overcome the action of natural inhibitors of axon growth, to stimulate their elongation and germination through the glial barrier, and to provide formation of de novo synapses and consolidate their structure. Spinal cord injuries (SCIs) that damage sensorimotor pathways are known to cause synaptic changes in neuronal circuitry (Darian-Smith et al., 2009). Neuronal damage and axonal degeneration are accompanied by the elimination of presynaptic terminals opposing the soma and dendrites of the injured neuron. However, after SCI, in addition to atrophy or death of neurons and degeneration of part of the axons, spontaneous sprouting of preserved axons, appearance of new synapses in place of vanishing ones and the restoration of synaptic connections have been observed (Oudega, Perez, 2012). Axonal sprouting and synaptic reorganization are critical factors for neural circuit reconstruction, which may be important for optimizing therapeutic approaches.

For maintenance and recovery of synapse structures, the peripheral astrocytic processes, which regulate synaptic transmission, play an important role. Astrocytes play an active role in synaptic plasticity, promote synaptogenesis and regulate synaptic connectivity (Baldwin, Eroglu, 2017). Astrocytic processes are intimately associated with synapses by structurally enwrapping and functionally interacting with dendritic spines and synaptic terminals by responding to