Hippocampal neurogenesis promoted by S100B after brain injury

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Evidence demonstrates that the injury-induced adult neurogenesis provides an endogenous repair mechanism following brain injury. The Ca2+ binding glial S100B protein is abundant in the brain in high concentrations and its release is boosted after an injury. However, the cellular mechanisms participating in the S100B induced adult neurogenesis and its functional consequences remain to be elucidated. Following lateral fluid percussion or sham injury in adult male rats (n=60), we infused S100B (50ng/hr) or vehicle into the lateral ventricle for 7 days. TUNEL and hematoxylin-eosin staining revealed cell death directly beneath the lesion on day 5 post-injury, but not after 5 weeks without S100B-associated differences. S100B did not affect the early and late axonal injury as assessed by APP immunostaining, but resulted in an unspecific late microglial activation (ED1 expression, p<0.01). Cell proliferation was assessed by the mitotic marker Bromodeoxyuridine (BrdU) on day 2 post-injury. BrdU-immunoreactive cells in the dentate gyrus revealed an S100B-enhanced proliferation as assessed on day 5 post-injury (p<0.05), and persisting up to 5 weeks (p<0.05). Using cell-specific markers, we determined the numbers of these progenitor cells which became neurons (NeuN) or glia (GFAP). S100B profoundly increased hippocampal neurogenesis 5 weeks after TBI (p<0.05). Furthermore, S100B induced the synaptogenesis (synaptophysin expression) in the germinative area of the hippocampus (p<0.05 on day 5 post-injury). Spatial learning, as assessed by the Morris water maze on day 30-34 post-injury, revealed an improved cognitive performance after S100B infusion (p<0.05). Collectively, S100B induces neurogenesis and synaptogenesis within the hippocampus, and enhanced cognitive function following experimental brain injury. These observations provide compelling evidence for the therapeutic potential of S100B in improving functional recovery following TBI.

Keywords: S100B, neuroprotection, synaptogenesis, cognitive function