Chronic Neuropathic Pain Decreases Hippocampal Neurogenesis

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Previous work from our lab has shown evidence that chronic neuropathic pain modulates hippocampus-mediated behavior and some underlying molecular properties, in particular context fear extinction and pErk expression levels. Given these results and theoretical notions about the interactions between pain and learning and memory, this current study aims to probe the impact of chronic neuropathic pain on hippocampal neurogenesis, which has been linked to learning abilities and depression and anxiety.

Spared-nerve-injury (SNI) surgery on mice was used as a model of chronic neuropathic pain with a control group consisted of sham-operated mice (DCX-EGFP mice) and tactile thresholds were measured to insure successful surgical manipulation. Starting on day 10 post-surgery and continuing for 5 days, animals were injected i.p. with 50mg/kg of the cell proliferation marker Bromodeoxyuridine (Brdu). One week after the last Brdu injection animals were perfused and tissue was stained for Brdu labeled cells in the hippocampal dentate gyrus. Brdu labeled cells were quantified as a measure of neurogenesis. SNI animals (n=5, M=15.37) show a significant decrease in labeled cells as compared to sham animals (n=5, M=24.24), $t(8)=-3.5, p=0.01$. Currently the fate and stage of these cells is being determined through NeuN and Calretinin staining co-localizing with Brdu and EGFP.

Recently it has been suggested that certain chemokines are important for adult neurogenesis in the dentate gyrus through their role in neurotransmission, in particular SDF-1/CXCR4 signaling between adult neural progenitor cells and new granule cells. We have preliminary results as to the differences in SNI versus sham animals in SDF-1/CXCR4 expression in the hippocampus, as well as MCP-1/CCR2, a chemokine known to be strongly involved in neuropathic pain.

This decrease of hippocampal neurogenesis, which may be dependent on chemokine levels of the dentate gyrus, indicates a direct influence of chronic neuropathic pain on an underlying mechanism of adult learning and memory.