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Promotion of brain self-repair mechanisms by stereotaxic micro-needle lesions

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Background: Long-term implantation of a fine metal electrode, even without chronic electrical stimulation may produce unwanted effects. Neuropathological examination of brain tissue from patients with deep brain stimulation (DBS) revealed activated astrocytes and microglia regardless of the underlying disease. Electrical stimulation is not required to see signs of neuro-inflammation; inflammatory changes have been observed around recording electrodes used for characterizing epileptogenic tissue and around cerebral spinal fluid (CSF) shunt catheters.

Objectives: To understand the earliest reactions to implantation of a metal electrode, we studied the cellular and cytokine responses over time to transient insertion of a fine needle (maximum diameter of 200 μm) into the dorsal hippocampus of the mouse. We tested the hypothesis that creation of a focal micro-lesion in hippocampus elicits self-repair mechanisms mediated by cytokines which activate microglia, promote astrocytosis and stimulate stem/progenitor cells to proliferate and generate new neurons.

Method: Brief stereotaxic insertion and removal of an a micro-needle into the right hippocampus resulted in a) significantly increased expression of granulocyte-colony stimulating factor (G-CSF), the chemokine MIP-1a and the pro-inflammatory cytokine IL12p40; b) pronounced activation of microglia and astrocytes, and c) increase in hippocampal neurogenesis.

Summary: This study describes immediate and early humoral and cellular mechanisms of the brain's response to micro-injury that will be useful for investigation of potential neuro-protective and deleterious effects of deep brain stimulation (DBS) in various neuro-psychiatric disorders, and eventually replace the DBS.

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