Plasticity in the anterior cingulate cortex of mice with neuropathic pain

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Neurons undergo plastic changes to adapt to a changing environment. Among the many forms of plasticity mechanisms are plasticity of intrinsic excitability, structural plasticity and long-term potentiation (LTP) and depression (LTD) of synaptic transmission. Neuronal plasticity mechanisms are thought to be the cellular correlate of learning and memory and serve several important physiological functions, but may also be the basis for pathological conditions such as chronic pain. It is known that noxious stimuli result in increased activity in several cortical brain areas, including the anterior cingulate cortex (ACC), an area particularly important for interpreting the unpleasantness of pain. This increased activity may cause cortical neurons to undergo long-term plastic changes that are involved in the chronification of pain.

We induce neuropathic pain in mice by chronic constriction injury (CCI) of the left sciatic nerve and we use patch-clamp electrophysiology to record the electrical activity of up to four cells in the ACC simultaneously.

Our experiments show that excitatory pyramidal neurons in the ACC of mice with neuropathic pain have a significantly lower action potential threshold than neurons in control mice, indicating that neuropathic pain induces plasticity of intrinsic excitability. Also, we observe a reduced number of connections between excitatory pyramidal neurons and inhibitory interneurons under neuropathic pain conditions. Such structural plasticity would shift the excitation-inhibition ratio towards increased excitation. Furthermore, we find that excitatory synapses on pyramidal neurons do not undergo LTD in mice with neuropathic pain.

Our data indicate that chronic neuropathic pain induces long-term neuronal changes in the ACC that keep will keep the neuronal activity at an elevated level. These changes may be involved in turning pain from an occasional nuisance to an ongoing agony.