Mechanics in Foreign Body Reactions to Neural Implants

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For decades, neural implants have been applied to record or trigger neural signals and to locally deliver drugs. However, even chemically inert implants often cause a foreign body reaction, which is characterized by an encapsulation of the implant by reactive microglial cells and later by reactive astrocytes. This assembly of different glial cell layers around the ‘foreign body’ results in a serious reduction of lifetime and functionality of these devices. Despite the tremendous progress in neuroscience, there is a lack of knowledge about the mechanism governing foreign body reactions.

Implants such as electrodes are orders of magnitude stiffer than healthy CNS tissue. Here we show that both neurons and glial cells, the basic building blocks of nervous tissue, respond to mechanical stimuli in their environment. Using culture substrates incorporating gradients of mechanical properties we found that neuronal axons are repelled by stiff substrates while glial cells spread more on stiffer substrates. Moreover, glial cell reactivity may be triggered by mechanical cues. An *in vitro* foreign body reaction model finally supports our hypothesis that it is the mechanical mismatch between implant and tissue that triggers the encapsulation of the implant, repelling neurons while attracting glial cells. Hence, local mechanical stimuli may lead to the reorganization of living tissue. Exploiting this knowledge may ultimately lead to the development of a new generation of implants, incorporating appropriate mechanical cues which support healthy tissue structure.