

postsynaptic membrane sufficiently to open the NMDA channel. This added requirement would hinder LTP and also, in theory, learning and memory.

1 Wemmie, J.A. *et al.* (2002) The acid-activated ion channel ASIC contributes to synaptic plasticity, learning, and memory. *Neuron* 34, 463–477

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Axonal Na⁺ channels calling the shots

The neuronal action potential is one of the most important aspects of inter-neuronal communication and brain function. However, relatively little is known about the precise determinants of the action-potential threshold or its site of initiation. Using state-of-the-art electrophysiological recording techniques to study the biophysical mechanisms underlying action potentials, Colbert and Pan now shine new light onto this question [1]. It was previously thought, owing to the high density of Na⁺ channels in the axon hillock, that action potentials initiate near the neuronal soma. However, experimental evidence for this potential mechanism comes predominantly from theoretical and labeling studies rather than from functional studies. Now Colbert and Pan report direct electrophysiological recordings from neocortical axons and propose that the lowest threshold for action-potential initiation is in the axon itself rather than in the axonal hillock.

Using outside-out patch-clamp recordings from somatic, initial axon segment (<30 μm from the soma) and axonal (30–47 μm from the soma) neuronal areas, the authors observed qualitative differences in the currents evoked upon depolarization in these regions. In somatic patches, a combination of

Na⁺ and delayed-rectifier K⁺ currents, as well as fast A-type K⁺ currents, could be evoked, whereas fast A-type K⁺ currents were absent in initial segment and axonal areas. In addition, it was observed that Na⁺ channels in the axon require significantly less depolarization for activation than do those in the soma or initial segment. This shift did not decrease gradually from soma to axon, but rather, changed sharply at the initial segment. Current densities were uniform throughout the initial segment before increasing two- to threefold in the axon.

Using numerical models of neurons, and equivalent shifts in axonal Na⁺-channel activation, the authors found a decrease in axonal threshold for action-potential initiation with respect to the soma that corresponded well with the experimental data. However, modeling an increase in Na⁺-channel density in the initial segment only affected the axonal threshold at very high channel densities. In both situations, the site of initiation was biased away from the soma, although the shifted channel activation could better describe the experimental evidence for axonal action-potential initiation.

This work provides a biophysical description of the axonal ion channels that

might be involved in the initiation of action potentials. Axonal Na⁺ channels were found to require less depolarization for activation than did those in the soma or initial segment of the axon – this shift in activation kinetics could account for a lower threshold for action-potential initiation in the axon versus the soma. These data suggest that it is not the number of Na⁺ channels in the axon hillock but, rather, the properties of the Na⁺ channels in the axon that are responsible for the low axonal action-potential threshold. It is important not to overlook the role of other ion channels with respect to action-potential initiation and the diversity of neuronal physiologies; however, the data reported by Colbert and Pan in this study indicate that the likely determinants of neuronal action-potential initiation are located in the axon.

1 Colbert, C.M. and Pan, E. (2002) Ion channel properties underlying axonal action potential initiation in pyramidal neurons. *Nat. Neurosci.* 5, 533–538

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In Brief

Ouch!



A new brain scan study has confirmed what fibromyalgia patients have long been telling a skeptical medical community: the pain is real. Indeed, researchers have detected

measurable pain signals in their brains as a result of a gentle squeeze.

Fibromyalgia is a chronic disease characterized by tenderness and stiffness all

over the body, as well as by fatigue, headaches, gastrointestinal ailments and depression. Far more women (particularly those of childbearing age) are affected than men. Doubt has been cast over the biological nature of the disease, and it has often been thought of as a psychological or social problem – reflecting the failure of research to find a cause or effective treatment.

To correlate subjective pain sensation with objective views of brain signals, functional magnetic resonance imaging (fMRI) was recently used to map areas of the brain that are active during pain. The results indicated that increasing pressure activates more, and different, areas of the brain in fibromyalgia patients than in control

subjects. It seems that individuals with fibromyalgia have enhanced responses in some areas and diminished response in others, caused by some as-yet-unknown pathological process that makes patients more sensitive by amplifying pain signals several-fold. The study brings proof of the physical roots of the disease and urges future studies into the biological mechanisms that underlie it. (University of Michigan Health System, <http://www.med.umich.edu/opm/newspage/2002/fibromyalgia.htm>)

Psychic prosthetics

It might be possible to control movement of prosthetic limbs with brain waves. Monkeys