



Presentation Abstract

Program#/Poster#: 615.25/F14

Presentation Title: Subcellular cooperativity and ectopic spiking in demyelinated axon models and thalamocortical circuits

Location: Halls B-H

Presentation time: Tuesday, Nov 12, 2013, 1:00 PM - 2:00 PM

Topic: ++B.10.a. Neural oscillators and activity-dependent plasticity of intrinsic membrane properties

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Abstract: Axons undergoing demyelination can produce a wide variety of firing patterns from conduction failure to afterdischarge (AD) and spontaneous spiking. AD requires slow positive feedback, represented in our model by a persistent Na conductance (gnap) and can be terminated by rundown of the Na reversal potential. Ectopic spiking initiated in the demyelinated region (phase 1) can shift to the soma (phase 2) by an interplay of these processes. This transition occurs because the soma, although less inclined to produce ectopic spikes, is more robust against intracellular sodium accumulation and can thus sustain AD longer. The distance of the lesion from the soma has no effect. The surface area-to-volume ratio of the axon is one of the determinants of the duration of phase I AD, whereas the density of Nap channels in the soma determines the number of phase 1 spikes required to trigger phase 2 AD; together these factors determine if and when the transition from phase 1 to phase 2 AD occurs. These results suggest that distant sites of ectopic spike generation can act cooperatively. Beyond cooperativity, competition is seen when both regions can independently sustain AD. In an animal model of chronic demyelination, single-unit recordings and imaging with voltage-sensitive dyes (RH795) in the thalamocortical network allow us to detect signal intensity, propagation time course, spreading and back propagation to the

thalamus. Complementing these functional analyses, we have examined the mRNA expression patterns for relevant ion channels. Initial findings confirm our ability to measure signals in cortical areas of demyelinated brain slices and suggest the up-regulation of message coding for Nap. Our results suggest new interpretations of clinical and electrophysiological observations of demyelination diseases and suggest directions for future directions.

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Keyword(s): DEMYELINATION

AXON

EXCITABILITY

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