

POSTER PRESENTATION

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IK_{Ca}-Ca_v3 complex creates a high pass filter for parallel fiber input in cerebellar Purkinje cells

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Cerebellar Purkinje cells are contacted by up to ~150,000 parallel fibers from granule cells, of which only a subset will convey sensory information at any given time. Purkinje cells must then possess the means to respond effectively to meaningful parallel fiber input over background noise. Previous work has shown that parallel fiber excitatory postsynaptic potential (EPSP) summation can be shaped by feedforward synaptic inhibition and the hyperpolarization-activated current I_H [1,2]. We now report that parallel fiber EPSPs activate T-type calcium channels that are linked to intermediate conductance calcium-activated potassium (IK_{Ca}) channels in Purkinje cells. This novel complex exerts a frequency-dependent suppression of temporal summation, such that only high frequency parallel fiber inputs undergoing presynaptic facilitation can elicit spike output from Purkinje cells.

Cerebellar slices were prepared from P18-30 rats and patch recordings obtained from PC somata at 32-35°C. PFs were activated using a monopolar stimulating electrode in the molecular layer or granule cell layer. Alternatively, the role of postsynaptic PC ion channels were selectively tested by injecting simulated EPSCs to evoke PF simulated EPSPs (simEPSPs) at the soma.

PF EPSPs below threshold for spike discharge were followed by an after hyperpolarization (AHP) of up to 2.5 mV and 250 ms. Application of blockers against high voltage activated Ca²⁺ channels (Cd²⁺, Agatoxin IVA), SK channels (apamin), or BK channels (TEA, iberiotoxin, paxilline) did not significantly affect the rate of simEPSP decay. However, T-type Ca²⁺ channel blockers (Ni²⁺, Mibefradil, kurtoxin) caused a ~35% decrease in the rate of simEPSP decay. Moreover, these effects were

reproduced by application of IK_{Ca} channel blockers (TRAM-34, charybdotoxin). Immunofluorescent labeling for IK_{Ca} protein confirmed its expression in Purkinje cells somata and dendrites. Ni²⁺ and TRAM-34 sensitive outward currents were found in outside-out patches from PC somata, confirming current clamp data showing a functional link between Ca_v3 and IK_{Ca} channels. The outward current was further blocked by BAPTA (10 mM) but not EGTA (10 mM) in the internal patch solution, indicating that the Ca²⁺-IK_{Ca} channel interaction resides within a nanodomain. To examine the effect of this interaction on temporal summation, PFs were stimulated at varying frequencies. For frequencies up to 25 Hz, no temporal summation was observed in control conditions. However, blocking either Ca_v3 or IK_{Ca} channels caused significant summation for 25 Hz stimulations. This effect was seen in both the presence and absence of feedforward-inhibition. Application of TRAM-34 greatly altered the frequency response of PC to 50 and 100 Hz PF stimulation during tonic firing. Finally, the Ca_v3-IK_{Ca} complex selectively suppresses non-facilitating inputs while allowing smaller-amplitude, facilitating inputs to generate output.

Our current work is the first to demonstrate the expression of IK_{Ca} channels in central neurons, its association with Cav3 channels and the role of this Cav3-IKCa complex in controlling the response of PCs to PF inputs. The Cav3-IKCa complex creates a high pass filter that reduces the effectiveness of background activity and allows Purkinje cells to respond preferentially to parallel fiber input indicative of sensory input carried by mossy fibers.

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