



Society for Neuroscience–Rochester Chapter Post-doc / Faculty Seminar Series

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Platelet Activating Factor Enhances Presynaptic Vesicle Release

Platelet activating factor is a potent phospholipid signaling molecule that may fuel neuroinflammation through its dual ability to alter synaptic plasticity and stimulate the immune system. Indeed PAF is elevated in the CNS with many neuroinflammatory diseases and contributes to neuronal injury as PAF receptor (PAFR) antagonism is neuroprotective in mouse models of multiple sclerosis, HIV-1 associated neurocognitive disorders, seizure, trauma, and stroke. The PAF receptor is localized to synapses and PAF exposure results in excitotoxic damage and beaded dendrites. This excitotoxic injury is likely caused by enhanced presynaptic strength. Using fluorescent reporters of presynaptic activity, we show that PAF enhances synaptic vesicle release from individual presynaptic boutons by increasing the size of the releasable pool of vesicles. PAF also activates previously silent boutons resulting in vesicle release from a larger number of terminals. The underlying mechanism involves elevated calcium within presynaptic boutons and PKC activation. Furthermore, PAF increases synapsin phosphorylation at sites 1 and 3, (both sites associated with elevated calcium) and increases dispersion of synapsin from the presynaptic compartment during stimulation, freeing synaptic vesicles for subsequent release. These experiments provide a highly plausible mechanism for PAF induced neurotoxicity via enhanced presynaptic strength and validate the PAFR signaling pathway as a viable target for reducing neuronal injury in neuroinflammatory diseases.

Thursday, July 16

4:00 pm, K-307 (3-6408)

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Refreshments will be provided

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