#227 Laura Melissa Rodriguez Valencia Advisor(s): Panayiotis Tsokas

Weak high-frequency synaptic stimulation induces persistent long-term potentiation in rat hippocampal slices if preceded or followed by a brief application of 4% sevoflurane

Studies have shown that PKMζ--a brain-specific protein kinase--also serves a neuroprotective role. Specifically, sevoflurane preconditioning is associated with a de novo increase in PKMζ protein in hippocampal slices that confers neuroprotection by mitigating the aversive effects of hypoxia. However, postsynaptic whole-cell infusion of PKMζ in CA1 neurons has been shown to cause potentiation of postsynaptic responses throughout the neuron. Such wide-spread increases in synaptic strength throughout the neuron would be expected to introduce noise that could corrupt memory traces, but interestingly no LTP is observed with sevoflurane. This suggests that the sevoflurane-induced newly synthesized PKMζ exerts its neuroprotective effects without affecting pre-existing synaptic pools of PKMζ, and that the integrity of pre-existing engrams in the hippocampus may be achieved via compartmentalization of PKMζ.
To study the mechanisms that control compartmentalization of PKMζ we examined whether there is communication between different pools of neuronal PKMζ.
Results: A 20 min application of 4% sevoflurane transforms a transient LTP induced by weak HFS into persistent LTP that lasts several hours, if the weak HFS is delivered 15, 45, or 75 min after sevoflurane washout, but not at 180 min post-sevoflurane. Remarkably, 4% sevoflurane can also transform transient into persistent LTP if the weak HFS precedes sevoflurane application by 15 or 45 min (but not 75 min).
Conclusion: The underlying mechanism of this phenomenon could involve “synaptic capture” by the weakly tetanized synapses of new PKMζ synthesized in the dendrite in response to sevoflurane. Under normal physiological conditions PKMζ synthesized in response to sevoflurane is excluded from synapses and plays a role in neuroprotection without directly affecting synaptic output. This compartmentalization could break down due to pathological conditions contributing to post-operative cognitive dysfunction.

Additional contributors to this project:
Panayiotis Tsokas
Maya Desai
Changchi Hsieh
Ira S. Kass
Todd C. Sacktor
James E. Cottrell