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Abstract

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PI Title:
Project Title: PRESERVATION OF TIMING IN PLASTIC AUDITORY PATHWAYS

Abstract: DESCRIPTION: (Adapted from the Investigator's Abstract) The calyx of Held synapse is a key element in the circuitry that supposedly computes sound source localization in the mammalian auditory brain stem. Precise timing of action potential output from this synapse is central for this task but the mechanisms that modulate and preserve output is not well understood. During repetitive afferent fiber stimulation, this synapse suffers robust synaptic depression which limits its ability to sustain prolonged output of discharges. The first hypothesis to be tested is that vesicle pool depletion is the main factor behind this short-term form of plasticity. The large size of the calyx terminal allows one to simultaneously patch clamp a single calyx terminal and the postsynaptic cell, and thus, to measure presynaptic calcium currents and evoked EPSCs. Presently, this synapse is the only site in the brain where pre- and postsynaptic recordings can be made simultaneously. Voltage clamp protocols designed to elicit maximal presynaptic Ca influx will be used to fully deplete the releasable pool of vesicles, and to determine its size and recovery rate. The limit on action potential output, set by vesicle pool depletion, will thus be determined quantitatively. The second hypothesis is that glutamate transporters are critical for the synapse to maintain spikes at high frequencies. The function and locus of glutamate transporters at this synapse are unknown. To determine their function, the proposed work will examine first the effect of different transporter antagonists on presynaptic Ca currents and EPSCs. The PI plans to determine if transporters prevent glutamate "spillover" from the synaptic cleft, which in turn prevents the activation of mGluRs that inhibit Ca currents and EPSCs. Recordings of transporter mediated currents in the calyx, MNTB cell, or surrounding glia will then determine the locus of transporters and the time course of glutamate clearance. The third hypothesis is that activation of the numerous inhibitory bouton inputs onto MNTB neurons significantly alters membrane excitability, and thus, the spike output of the cell. By independently activating the bouton IPSCs and the calyceal EPSCs, they plan to determine how the interaction between excitatory and inhibitory inputs affects spike timing. The unique features of the synapse allow a systematic study of the underlying mechanisms that control spikes and may provide new insight into how synaptic properties adapt to preserve the timing of information flow through auditory pathways.

Thesaurus Terms:
auditory pathway, brain electrical activity, glutamate transporter, neural plasticity, neurotransmitter antagonist, synaptic vesicle
action potential, calcium flux, clearance rate, drug administration rate /duration, evoked potential, glia
laboratory rat, voltage /patch clamp

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