Temporal fine-tuning of synaptic efficacy

Presynaptic terminals must regulate transmission with fine-tuning of synaptic efficacy *via* reloading of their synaptic vesicle pools and controlling of the Ca^{2+} channel activity despite encountering wide variations in the number and frequency of incoming action potentials. We have addressed above issue at a model cholinergic synapse formed between superior cervical ganglion neurons. We combined genetic knockdown/overexpression and direct physiological measurements of synaptic transmission from paired neurons to show presynaptic proteins function. Dynamin, an essential endocytic protein, controls the reloading of their synaptic vesicle pools. Three isoforms of dynamin work together to match vesicle reuse-pathways having distinct rate and time constants with physiological AP frequencies. Phosphorylation of CAST, the core protein of the active zone proteins complex, controls the speed of synaptic vesicle reloading to the readily releasable pool shortly after an action potential. Ca^{2+} channel activity is temporally controlled by residual Ca^{2+} through CaMKII and Ca^{2+}-sensors which interact with Ca^{2+} channels. Thus, action potential firing conducts multiple actions of presynaptic terminal proteins that play a role in different synaptic vesicle stage, and orchestrates synaptic efficacy.