Properties of Fusion-competent Mobile Synaptic Vesicles in Hippocampal Neurons

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Presynaptic terminals in hippocampal neurons house functionally-defined vesicle pools, the properties of which are major determinants of presynaptic performance. In conventional models of synaptic function, these vesicle pools are synapse-specific, but recent work has demonstrated an additional synapse-spanning pool or 'superpool' comprised of vesicles which are laterally mobile along axons. In order to contribute to activity-driven information transfer, a key feature of mobile vesicles is their capability to maintain or rapidly acquire fusion-competence upon entering a new synaptic host. Indeed evidence suggests that many trafficking vesicles retain fusion-capability during transit raising questions about the minimal molecular machinery required to permit exocytosis. Here we have used live antibody-labelling, genetically-encoded fusion constructs, FM-dye staining and timelapse fluorescence imaging to examine key properties of mobile vesicle fusion, looking at the dynamics of this process in relation to those of other synaptic components, the timing of exo-endocytosis and the relevance of extrasynaptic vesicle fusion for inter-neuron communication. We describe the relationships between trafficking dynamics and activity-driven vesicle fusion, and show that transiting vesicle packets often move to preferred axonal sites before undergoing fusion. Additionally, these packets typically show delayed-onset or slower fusion kinetics compared to recently stabilized vesicle packets or conventional presynaptic terminals, presumably corresponding to priming or maturation steps prior to fusion. Investigating mechanisms of mobile extrasynaptic fusion sheds further light on fundamental processes of vesicle exocytosis and provides insight into potentially novel aspects of neuronal signalling.