Heterogeneous Dynamics of Synaptic Vesicle Priming Define Synaptic Function and Plasticity

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Synaptic vesicle (SV) priming ensures reliable neurotransmission, but recent findings reveal a reversible "depriming" process that occurs even at rest. This process regulates the size and readiness of the readily releasable pool by converting Munc13-primed SVs back to the unprimed state in the absence of CAPS. Depriming fine-tunes the balance between loosely and tightly primed SVs, with synaptotagmin-1 stabilizing fusion-ready vesicles for calcium-triggered release. As a result, synaptic delay increases, release probability decreases, and short-term plasticity is reduced. Interestingly, SVs primed independently of the Munc13-1 C1 domain resist NSF/αSNAP-mediated depriming. These findings highlight depriming as a selective and reversible mechanism that regulates synaptic strength.