Recruitment of Resting Vesicles into Functionally Recycling Pools as a Mechanism of Synaptic Potentiation at Hippocampal Synapses

Arjuna Ratnayaka[1], Vincenzo Marra[1], Daniel Bush[1], Jemima J Burden[2], Tiago Branco[3], Kevin Staras[1]

[1] School of Life Sciences, University of Sussex, Brighton, BN1 9QG, UK
[2] MRC LMCB, UCL, London WC1E 6BT, UK
[3] Wolfson Institute for Biomedical Research, UCL, London WC1E 6BT, UK

Hippocampal synapses are characterized by two functionally-distinct vesicle populations: a recycling pool, which supports action potential-driven neurotransmitter release via vesicle exocytosis and reuse, and a resting pool. The relative proportions of these two pools are highly variable between individual synapses, prompting speculation on their specific relationship, and on the possible functions of the resting pool. Using a combination of fluorescence and correlative EM-based approaches we show here that Hebbian plasticity-dependent changes in synaptic strength can increase the recycling pool fraction at the expense of the resting pool. This change, mediated by a spaced tetanic stimulation protocol (6 x 100 APs, 20 Hz), is accompanied by an increase in the probability of neurotransmitter release at individual terminals. We demonstrate that the increase in the recycling fraction is dependent on NMDA-receptor activation and is sensitive to nitric oxide signalling blockers and a calcineurin antagonist. Our results suggest that resting pool vesicles can be rapidly recruited to the recycling pool, providing a mechanism to quickly implement long-lasting changes in presynaptic strength to support synaptic potentiation.