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HIGHLIGHTS

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SYNAPTIC PHYSIOLOGY

Please release me

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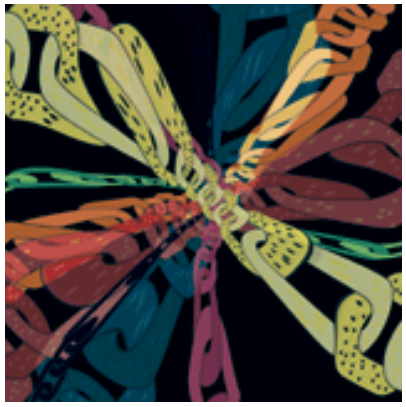
The number of 'readily releasable' synaptic vesicles shapes the postsynaptic response to presynaptic action potentials. However, new data indicate that vesicles in the readily releasable pool (RRP) are not always ready and willing to be released. Reporting in *The Journal of Neuroscience*, Moulder and Mennerick describe a population of 'reluctant' vesicles that might increase the range of potential outputs at some synapses.



The RRP contains the subset of synaptic vesicles that are on standby for release, and modulation of RRP size is a fundamental means by which synaptic strength can be altered. To estimate the size of the RRP, a stimulus is typically used to deplete the pool and the resulting postsynaptic response is measured. However, different depletion techniques have resulted in discrepancies in the RRP size estimates obtained at some synapses. Do these techniques probe the same pool of vesicles?

To address this question, Moulder and Mennerick looked at excitatory (glutamate-releasing) and inhibitory (GABA (γ-aminobutyric acid)-releasing) neurons in hippocampal cultures. They made electrophysiological recordings from single cells that had formed autaptic contacts synapses between a neuron and its own dendrites — and compared the postsynaptic response to stimulation with hypertonic sucrose or a high-frequency train of action potentials. In glutamatergic neurons, the sucrose-depleted RRP was estimated to contain 12,681 vesicles, whereas train-evoked responses gave a maximum estimate of just 1,945 vesicles.

In the case of GABA-releasing neurons, the authors found no difference between sucrose and train estimates of RRP size, which indicates that specific presynaptic or postsynaptic factors contribute to the discrepancy seen in glutamatergic cells. Postsynaptic factors that could confound estimates of RRP size, such as glutamate receptor saturation, accounted for only a small part of the difference in excitatory neurons. The authors therefore looked for presynaptic factors that could explain the discrepancy.

They found that longer trains of action potentials gave RRP estimates closer to those obtained using sucrose, and that by increasing Ca^{2+} influx during trains, they could eliminate the discrepancy. RRP size estimates made with a strong depolarizing stimulus high extracellular potassium — matched those obtained with sucrose.

These findings point to a heterogeneous population of releasable vesicles that can be differentially released with changing Ca^{2+} concentrations. The authors comment that the presence of 'reluctant' vesicles in the RRP might allow greater plasticity at hippocampal glutamatergic synapses. An interesting question that remains is whether modulators of synaptic transmission can make readily releasable vesicles more or less reluctant.

References and links

ORIGINAL RESEARCH PAPER
Moulder, K. L. & Mennerick, S. Reluctant vesicles contribute to the total readily releasable pool in glutamatergic hippocampal neurons. *J. Neurosci.* **25**, 3842–3850 (2005) | Article | PubMed | ChemPort |

FURTHER READING
Rizzoli, S. O. & Betz, W. J. Synaptic vesicle pools. *Nature Rev. Neurosci.* **6**, 57–69 (2005) | Article | PubMed | ChemPort |

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