Late Switch for Post-Tetanic Potentiation: Once Again It’s Ca$^{2+}$. Focus on “An Increase in Calcium Influx Contributes to Post-Tetanic Potentiation at the Rat Calyx of Held Synapse”

Felix Felmy$^1$ and Henrique von Gersdorff$^{1,2}$

$^1$Ludwig-Maximilians-Universität, Neurobiologie, Martinsried, Germany; and $^2$The Vollum Institute, Oregon Health and Science University, Portland, Oregon

Many prior studies have documented the role of calcium in the induction of posttetanic potentiation (PTP). In this issue of the Journal of Neurophysiology (p. 2868–2876), Habets and Borst now elucidate the effect of Ca$^{2+}$ during the expression of PTP. Ingenious fine tuning of the Ca$^{2+}$ imaging allowed them to measure Ca$^{2+}$ in a largely unperturbed system: the calyx of Held nerve terminal. They first loaded fluorescent Ca$^{2+}$ indicator dyes via a whole cell patch pipette for a few minutes and then removed the pipette. These nerve terminals preloaded with Ca$^{2+}$ indicators were then stimulated via their afferent axons and imaged. By using a very sensitive, cooled, and low-noise photon-multiplier tube (PMT), a judicious choice of low-noise Ca$^{2+}$ indicators to increase the signal-to-noise ratio, and a pinhole imaging only the focal plane to reduce the background even further, they resolve the time course of the Ca$^{2+}$ rise during a single presynaptic action potential (AP). Due to this technical improvement they found that after PTP induction a presynaptic AP triggers a 15% larger Ca$^{2+}$ influx added onto an increased basal Ca$^{2+}$ level. Assuming an increased vesicle pool size and a 3.5 power-law between Ca$^{2+}$ and a pinhole imaging only the focal plane to reduce the background even further, they resolve the time course of the Ca$^{2+}$ rise during a single presynaptic action potential (AP).

PTP of synaptic inputs is a long studied form of synaptic plasticity, entailing an increase of synaptic strength for up to several minutes after prolonged tetanic stimulation. PTP was first reported in 1941 by Feng in a series of pioneering experiments on the frog neuromuscular junction (NMJ) (Feng 1941). Remarkably, this solitary scientist carried out this work in his Peking lab while war raged at his doorstep. Subsequent studies of the NMJ revealed that the magnitude of PTP was due to an increased release probability. And Jonas 2000). Habets and Borst (2006) suggest that AP-broadening may play a role in PTP. However, several key questions remain unresolved. At other synapses, AP-broadening is a powerful mechanism for increasing transmitter release (Geiger and Jonas 2000). Habets and Borst (2006) suggest that AP-broadening may play a role in PTP. However, substantial AP broadening was not observed before at the calyx, at least for short stimulus trains (Korogod et al. 2005). In this respect, it would be of interest to know how much AP-broadening is...
necessary to increase the Ca\(^{2+}\) influx by 15% and if such AP-broadening would be detectable. Alternatively, Ca\(^{2+}\) currents could be increased by a Ca\(^{2+}\)-dependent facilitation without substantially altering the AP-half-width. Other unexplained observations are the increases in two distinct transmission delays. The time between stimulation and arrival of the AP is apparently prolonged due to a change in membrane excitability. In addition, the synaptic delay itself is increased. The authors speculate that AP broadening could lead to longer synaptic delays by altering the kinetics of Ca\(^{2+}\) influx. However, it remains possible that the increase in delay is independent of AP broadening. Clearly, more studies are needed to elucidate these results, especially because PTP at the avian ciliary ganglion calyx synapse does not involve presynaptic AP broadening (Martin and Pilar 1964).

Habets and Borst (2006) also found that Ca\(^{2+}\) buffering affects the strength of PTP because PTP was nearly an order of magnitude weaker when Oregon Green bis-(o-aminophenoxy)-N,N,N',N'-tetraacetic acid (OGB) was used than when the lower affinity buffer Fluo-4 was employed. The affinity of the buffer will also affect the Ca\(^{2+}\) signal during the tetanic induction period of PTP. So it may be important to separate the effects of the Ca\(^{2+}\) signals during tetanic induction leading to PTP from the elevated basal Ca\(^{2+}\) signal that remains during the PTP itself. Fluo-4, a fast buffer, is supposed to extend the time course of PTP, so it might become saturated during the induction period leading to an overshoot of the Ca\(^{2+}\) concentration, whereas OGB might be more effective in buffering the Ca\(^{2+}\) signal during tetanic stimulation. This putative overshoot of Ca\(^{2+}\) during tetanic induction might trigger intracellular signaling cascades leading to PTP. If so, OGB or EGTA-like buffers might reduce PTP via a more efficient buffering during the tetanus. This might indicate that the Ca\(^{2+}\) signal during tetanic stimulation is probably more relevant than has been recognized so far and the slow decay of elevated Ca\(^{2+}\) may only be necessary for PTP’s maintenance. Nevertheless, in spite of all these caveats, the work by Habets and Borst (2006) leads to a new direction for tackling the problem of PTP by using improved Ca\(^{2+}\) measurements in a mostly unperturbed synaptic terminal.

REFERENCES


