This Week in The Journal

Dopamine Release by Tuberoinfundibular Neurons

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(see pages 4009–4022)

Release of hormones from the anterior pituitary is regulated by signaling factors secreted by hypothalamic neurons into blood vessels of the median eminence. Most of these factors are peptides that induce hormone release. A notable exception is dopamine, which is secreted by tuberoinfundibular dopamine (TIDA) neurons and inhibits the release of prolactin. This regulatory system also differs from other dopaminergic pathways in which the neurotransmitter is released into a narrow synaptic cleft and binds to nearby receptors. Because dopamine secreted by TIDA neurons diffuses into a much larger space, unique mechanisms of release and reuptake might be required. Stagkourakis et al. investigated these mechanisms by stimulating TIDA neurons in mouse brain slices and measuring dopamine levels in the median eminence using fast-scan cyclic voltammetry.

Light-mediated activation of channelrhodopsin-expressing TIDA axon terminals induced dopamine release in the median eminence. The amount of dopamine increased with stimulation frequency up to 10 Hz, after which dopamine release declined, because depolarization block prevented neurons from firing at higher frequencies. With prolonged stimulation (150 s), the maximum spike rate of TIDA neurons dropped to 5 Hz. Notably, dopamine release was greatest at spike rates similar to those exhibited by spontaneously active TIDA neurons, which fired in bursts at ~10 Hz or tonically at ~5 Hz.

Although TIDA neurons express the dopamine transporter (DAT), whether this transporter takes up dopamine released at the median eminence has been questioned, because the neuromodulator is expected to diffuse quickly away from terminals. To test DAT function, Stagkourakis et al. applied an inhibitor. The inhibitor slowed the decay and increased the half-width of the dopamine signal in the

median eminence after TIDA neuron stimulation, suggesting that DAT does in fact take up dopamine at this site.

Altogether, the results suggest that dopamine release by TIDA neurons is similar to that of other dopaminergic neurons in the maximum spike rate achievable without depolarization block, the amount of dopamine released during a burst, and the reuptake of the molecule by terminals. These experiments were performed only in male mice, however. Given that TIDA neurons regulate the release of prolactin, the predominant function of which is to stimulate lactation, future studies should explore the dynamics of dopamine release by these neurons in females.

Depolarization of myelin (during blue bar) leads to a gradual increase in the amplitude of compound action potentials (CAPs) elicited by CA1 axon stimulation. See Yamazaki et al. for details.

Synaptic Effects of Myelin Depolarization

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(see pages 4036–4050)

Processing of information in the nervous system relies on the ability of neurons to integrate inputs from multiple sources. This integration depends on the arrival time of various inputs, which is influenced by presynaptic axon length, diameter, and myelination. Neurons work with oligodendrocytes to regulate the length and thickness of their myelin sheaths, thus fine-tuning action potential conduction speed to optimize spike timing at postsynaptic cells.

Because spike timing is a key determinant of synaptic plasticity, Yamazaki et al. asked whether myelin-induced changes in axonal conduction speed influence plasticity. Previous work had indicated that myelin of CA1 axons in the alveus of mouse hippocampus was depolarized during high-frequency neuronal spiking and that this depolarization sped action potential propagation in underlying axons. Therefore, the authors expressed channelrhodopsin or halorhodopsin selectively in mature oligodendrocytes, used light to depolarize or prevent depolarization of myelin, and examined the effects of these manipulations on synapses between CA1 pyramidal cells and postsynaptic neurons in the subiculum.

Brief depolarization of oligodendrocytes in the alveus transiently narrowed the width and led to a gradual increase in the amplitude of compound action potentials recorded in CA1 axons at the border of the subiculum. The depolarization also increased the conduction speed of the longest CA1 axons (those that projected to the middle and distal subiculum) and increased the amplitude of evoked EPSCs in one class of pyramidal cells in the areas targeted by these axons. The effect on EPSC amplitude was apparent 1–3 min after oligodendrocyte depolarization and persisted for at least 30 min. Oligodendrocyte depolarization also lowered the threshold (the number of theta-frequency bursts) required to induce long-term potentiation (LTP) at CA1 synapses in the middle and distal subiculum. Conversely, inhibiting oligodendrocyte depolarization during theta-burst stimulation reduced LTP. Conduction speeds and EPSC amplitude were not affected for CA1 axons projecting to the proximal subiculum.

These results suggest that myelin depolarization contributes to LTP induced by theta-burst stimulation at some synapses. This effect might stem from the speeding of action potentials and the synchronization of spikes across axons. How myelin depolarization induces these effects and how it leads to persistent increases in synaptic transmission remain to be tested.

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