This Week in The Journal

Ephaptic Signaling in *Drosophila*

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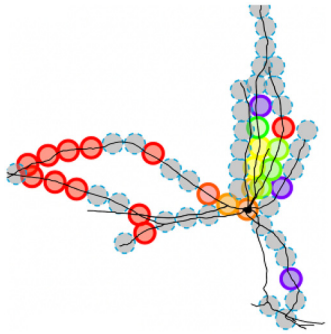
(see pages 8621–8628)

Current flowing through the plasma membrane of individual neurons causes fluctuations in the surrounding electrical field that can be detected with extracellular electrodes. Changes in the local field potential can influence the activity of all neurons within that field. For example, when two unmyelinated axons are closely apposed, an action potential in one axon alters the membrane potential of the other. This phenomenon is called ephaptic signaling. Ephaptic signaling is most prominent in layered neural structures in which numerous similarly oriented neurons are synchronously active. In fact, ephaptic signaling is thought to promote synchronous firing of cerebellar Purkinje cells and cortical and hippocampal pyramidal neurons. Ikeda et al. now show that ephaptic signaling originating in *Drosophila* eyes can influence activity in olfactory sensory neurons (OSNs) in the antennae.

Presentation of male pheromone evoked spiking in a group of OSNs located in the proximal antennae of female flies; spiking remained elevated throughout a 3 s stimulation period. If odor stimulation began in the dark, turning on a blue light halfway through the stimulation period caused a transient decrease in spike rate, followed by a gradual increase. Conversely, when odor stimulation began during blue light illumination, turning the light off caused a transient increase, followed by a decrease in spike rate. The effect of light on odor responses was prevented by covering the flies' heads (excluding the antennae) with paint, and it was absent in mutant flies lacking compound eyes. The effect persisted in flies in which chemical neurotransmission from photoreceptors was blocked, however. Moreover, the effect of light was rescued in eyeless flies by implanting a wild-type eye on top of the head, but grounding the extracellular fluid surrounding this transplanted eye blocked the effect. Finally, the effect of light was replicated by injecting current into the optic lobe.

These results suggest that activation of photoreceptors in the compound eyes of flies changes the local field potential sufficiently to affect the firing of OSNs in the proximal antennae. This might allow flies to alter behavioral responses when salient visual stimuli appear. Future work should determine whether this ephaptic signaling is direct or indirect, relying on an intermediate neuronal population that influences OSNs via synaptic transmission.



Axons of cholinergic neurons release GABA and ACh onto dendrites of SNc dopamine neurons. Synapses formed along the lateral dendrite evoke predominantly GABAergic IPSCs (indicated by red-orange circles), while synapses along the dorsal and ventral dendrites evoke predominantly cholinergic EPSCs (blue-violet circles), and synapses near the soma release both GABA and ACh (yellow-green circles). See Le Gratiet et al. for details.

Frequency-Dependent Cholinergic Effects in Substantia Nigra

Keyrian Louis Le Gratiet, Christopher K. Anderson, Nagore Puente, Pedro Grandes, Charlotte Copas, et al.

(see pages 8670–8693)

Dopamine neurons in the substantia nigra pars compacta (SNc) shape motor output, and their activity is regulated partly by cholinergic afferents from the brainstem. Notably, cholinergic fibers that innervate the medial SNc release GABA as well as acetylcholine, and they produce predominantly inhibitory effects. But Le Gratiet et al. report that the strength of GABAergic and cholinergic transmission from cholinergic afferents differs across the somatodendritic domain of dopamine neurons, and the relative influence of these transmitters shifts during sustained activity.

When channelrhodopsin was expressed selectively in cholinergic neurons, photostimulation of axons in medial SNc produced both GABAergic and cholinergic postsynaptic currents (PSCs) in a subset of dopamine neurons. But when stimulation was restricted to the area surrounding the lateral dendrites of these neurons, PSCs were predominantly GABAergic. In contrast, stimulation along dorsal and ventral dendrites often produced only cholinergic PSCs, and stimulation near the soma evoked PSCs with both cholinergic and GABAergic components. Consistent with this functional mapping, immunostaining for vesicular GABA and acetylcholine transporters suggested that cholinergic axons formed GABA-only synapses along the lateral dendrites and formed mixed GABA/acetylcholine synapses around the soma of dopamine neurons.

During photostimulation of perisomatic cholinergic fibers, IPSCs mediated by GABA receptors (GABARs) were initially much stronger than EPSCs mediated by nicotinic acetylcholine receptors (nAChRs). With continued stimulation, however, GABAR currents depressed more quickly than nAChR currents, so excitation and inhibition became more balanced. This shift rarely resulted in spiking in dopamine neurons, but by promoting the activation of voltage-gated calcium channels, it enabled otherwise subthreshold glutamatergic stimulation near the soma to elicit spikes. Finally, GABAergic input to lateral dendrites was less depressed by repeated stimulation and better able to suppress postsynaptic spiking than perisomatic GABAergic input.

These results suggest that the effect of cholinergic projections to the medial SNc varies with spike frequency. During low-frequency firing, cholinergic axons inhibit dopamine neurons by releasing GABA along lateral dendrites and around the soma. During high-frequency spiking, however, the GABAergic component of perisomatic GABA/ACh synapses is suppressed, while the excitatory ACh-mediated component is sustained. This makes dopamine neurons more responsive to glutamatergic inputs near the soma, while responses to glutamatergic input to the distal lateral dendrites continue to be suppressed.

This Week in The Journal was written by Teresa Esch, Ph.D.
https://doi.org/10.1523/JNEUROSCI.twij.42.46.2022