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A role for dopamine in value-free learning

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The CA1 pyramidal neurons are embedded in an intricate local circuitry that contains a variety of interneurons. The roles these interneurons play in the regulation of the excitatory synapticplasticity remains largely understudied. Recent experiments showed that repeated cholinergic activation of $\alpha 7$ nACh receptors expressed in oriens-lacunosum-moleculare (OLM$\alpha 2$) interneurons could induce LTP in SC-CA1 synapses. We used a biophysically realistic computational model to examine mechanistically how cholinergic activation of OLMa2 interneurons increases SC to CA1 transmission. Our results suggest that, when properly timed, activation of OLMa2 interneurons cancels the feedforward inhibition onto CA1 pyramidal cells by inhibiting fast-spiking interneurons that synapse on the same dendritic compartment as the SC, i.e., by disinhibiting the pyramidal cell dendritic compartment. Our work further describes the pairing of disinhibition with SC stimulation as a general mechanism for the induction of synaptic plasticity. We found that locally-reduced GABA release (disinhibition) paired with SC stimulation could lead to increased NMDAR activation and intracellular calcium concentration sufficient to upregulate AMPAR permeability and potentiate the excitatory synapse. Our work suggests that inhibitory synapses critically modulate excitatory neurotransmission and induction of plasticity at excitatory synapses. Our work also shows how cholinergic action on OLM interneurons, a mechanism whose disruption is associated with memory impairment, can down-regulate the GABAergic signaling into CA1 pyramidal cells and facilitate potentiation of the SC-CA1 synapse.

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