



B001 - Differential glutamate and GABA release onto hippocampal dentate cells by supramammillary nucleus neurons

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The hippocampus is a key brain structure for cognition and emotions. Among hippocampal subregions, the dentate gyrus (DG), the first information processor, receives sensory inputs from the entorhinal cortex (EC) through the perforant path (PP). Cortico-hippocampal pathways are known to be crucial for memory processing and navigation. However, little is known about the relevance of subcortical inputs to the function of hippocampus. The supramammillary nucleus (SuM), a hypothalamic structure, in which a subset of neurons project substantially to the DG and CA2/CA3a. Although the SuM-DG pathway regulates hippocampal theta oscillations, learning, REM sleep and explorative locomotor activities, its neurotransmitter signaling and synaptic properties remained elusive. By combining optogenetic tools, electrophysiological and pharmacological approaches, we found that DG-projecting SuM neurons preferentially innervate the DG granule cell layer, and form functional connections with granule cells, mossy cells and GABAergic interneurons. Optogenetic activation of channelrhodopsin-2(ChR2)-expressing SuM-DG terminals elicits monosynaptic responses in both GCs and INs. Such monosynaptic responses comprise glutamatergic and GABAergic components. Short-term plasticity of these two components are almost identical, suggesting co-release of these two transmitters. A detailed analysis of individual connections revealed that SuM-GC and SuM-fast spiking IN synapses are dominated by GABAergic transmission (inhibition (I)/excitation (E) ratio = ~4.4, n = 23) whereas SuM-non-fast spiking INs synapses are largely mediated by glutamatergic transmission (I/E ratio = 0.45, n = 5). Our findings suggest differential co-release of glutamate and GABA onto DG neurons by SuM neurons or differential innervation of DG neurons by distinct glutamatergic and GABAergic neurons within the SuM

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