Functional characterization of VIP-expressing interneurons in the hippocampal dentate gyrus

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The hippocampus is a key brain structure for learning and memory. The dentate gyrus (DG) serves as the primary gate of the hippocampus and controls information flow from the cortex. To maintain normal functions, the granule cells (GCs), the principal neurons in the DG, receive fine-tuned inhibition from local-circuit GABAergic interneurons (INs). There are various classes of GABAergic inhibitory INs with different physiological, anatomical and neurochemical features. Among them, vasoactive intestinal peptide-expressing (VIP^+) INs mainly target somatostatin-expressing INs in both the hippocampal CA1 area and the cortex. As a result, VIP^+ INs are thought of as IN-specific cells. However, the properties, function and connectivity of VIP^+ INs in the DG remain largely unknown. Here, we combined electrophysiology and single-cell biocytin staining to investigate the intrinsic properties and anatomical structures of DG VIP^+ INs using a VIP-IRES-Cre knock-in mouse line by breeding with Ai14 (Cre reporter line). Our preliminary results revealed that VIP^+ INs have small round somata (6.7 ± 0.3 μm; mean ± s.e.m.) located in all subregions of the DG and exhibit diverse electrophysiological properties, but relatively specific axonal projection patterns. VIP^+ INs show various input resistances, ranging from 200 MΩ to 2 GΩ (904.2 ± 45 MΩ; mean ± s.e.m.) and different discharge patterns, including regularly spiking, fast-adapting, and irregularly spiking phenotypes. In addition, approximately 80% of VIP^+ INs send their axons primarily to the hilus. Cell-attached recording from VIP+ INs demonstrated that they are preferentially recruited during the late phase of a spike series evoked at cortical input. Finally, optogenetic-circuit mapping show that VIP^+ INs preferentially form synapses with certain types of INs in the DG, suggesting that VIP^+ INs regulate GC excitability through disinhibitory circuits.