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Whole-Brain Spatial Organization of Hippocampal Single-Neuron Projectomes

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Mapping hippocampal single-neuron projections is essential for understanding brain-wide circuit organization. The hippocampus is a brain structure important for diverse functions including episodic memory, stress and cognition. However, how hippocampal axon projections are organized at the single-neuron level remains poorly understood. Here, we reconstructed 10,100 single-neuron projectomes of the mouse hippocampus, identified rostral and caudal axon pathways that preferentially innervated cortical vs. subcortical areas, and classified 43 projectome subtypes with distinct axon targeting patterns [1]. Notably, the soma locations along hippocampal longitudinal and transverse axes determined the number of their target areas and the spatial distribution and complexity of their axon arbors within the targets. We defined selective hippocampal subdomains based on spatial transcriptomic profiles and found that many projectome subtypes were enriched in specific subdomains. Next, we found that bi-hemispheric projecting hippocampal neurons generally projected to one pair of homologous targets with ipsilateral preference. Furthermore, we defined the wiring diagram for hippocampal neurons exclusively projecting to hippocampal formation (HPF) and those projecting to both intra- and extra-HPF targets with coordinated projection strengths. Finally, we dissected the CA1-Subiculum circuit mechanism for short-term memory maintenance [2], and developed intersectional tools to precisely label hippocampal neurons with multiple target areas [3]. Taken together, our work revealed new projection patterns of hippocampal axons and provided a new anatomical framework for analyzing the spatial organization of hippocampal axons.

References:

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