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HippoMaps: structural and functional mapping of the hippocampus follows a 2D organization

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The hippocampus, a critical hub in both cognition and numerous neurological diseases, consists of a folded archicortex which can be digitally unfolded and aligned between individuals using the recently developed HippUnfold software. This enables the application of a wealth of bioinformatics methods to the hippocampus, including the use of spatial correlation between measures in a common space. For example, histology data pertaining to the prevalence of interneurons at the microscale can be directly compared to the temporal characteristics of fMRI or intracranial encephalography at the mesoscale.

Here, we present HippoMaps: a common-space and open source repository for comparing and sharing hippocampal data across scales, datasets, and labs. This work massively scales multimodal, multicontrast, and multiscale imaging of the hippocampus, such that thousands of individual histology slices from different sources are reconstructed in a unified space. Presently we include histology data spanning popular stains sensitive to cell bodies, neural fibers, interneuron cell types, and various others, as well as in-vivo and ex-vivo quantitative MRI pertaining to myelination, blood flow, water diffusivity, functional imaging characteristics, and functional connectivity from the hippocampus to the rest of the brain. Alongside careful considerations of interindividual alignment and statistical rigour, we feel this approach can usher in a new branch of methods for hippocampal research.

From the present data we show that much of hippocampal organization is well described by the intrinsic 2D topology of the hippocampus: structural features vary primarily across the proximal-distal (or subfield-related) axis of the hippocampus while connectivity to the rest of the brain varies primarily across the anterior-posterior (or long-axis) of the hippocampus. Though there is further nuance to explore within hippocampal structure and function, we feel that this is an important consideration for new labs given the growing literature and, in some cases, divergence in understanding about hippocampal structure across labs. In particular, issues like out-of-plane slicing or imperfect modeling of 3D folding of the hippocampus have led to misunderstanding of hippocampal structure in the field. Here, we show that a simple 2D topology provides a powerful explanation for several notable observations in recent literature, and should be considered prior to making novel claims about unique hippocampal features in the future.

To illustrate and facilitate the uses of HippoMaps in new labs, we provide open source tools and tutorials for fetching, visualizing, and statistically comparing hippocampal data. With this framework in place, hippocampal researchers can not only view normative, healthy spatial distributions of hippocampal tissue properties, but they can also download and statistically compare them to ongoing data collection and can even opt to share their results, expanding the availability of hippocampal data prospectively and maintaining open and reproducible research standards within the field.

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