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The hippocampal formation in the BigBrain: The deep-learning supported high-resolution mapping and 3D reconstruction

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The hippocampal formation (HF) plays a pivotal role in different aspects of memory, with its subdivisions having various functional implications. The hippocampus has been parcellated in different ways both in histological and MRI studies [1, 2]. In the BigBrain, 3D rendering of the hippocampus was performed with its subdivisions being revealed through unfolding and unsupervised clustering of laminar and morphological features [3]. However, this parcellation was not detailed enough, e.g. in the field of the subicular complex (subiculum).

We cytoarchitectonically identified and mapped in 10 postmortem brains and generated probabilistic maps of CA1, CA2, CA3, CA4, Fascia dentata (FD), prosubiculum (ProS), subiculum (Sub), presubiculum (PreS), parasubiculum (PaS), transsubiculum (TrS), hippocampal-amygdaloid transition area (HATA) and entorhinal cortex (EC) [4]. Based on this research, we generate the 3D maps of HF in the BigBrain template to study the extent, topography and neighborhood relationships of the structures.

Cytoarchitectonic mapping of 12 structures was performed in at least each 15th serial histological sections in the web-based annotation tool MicroDraw at 1-micron resolution in-plane in the BigBrain. Subsequently, a Deep Learning Workflow was applied to 3D-reconstruct the structures. Convolutional Neural Networks were used for image segmentation in the sections lying between those manually mapped [5]. The annotations of each structure were non-linearly transformed to the sections of the 3D reconstructed BigBrain space at 20-micron isotropic resolution [6], and was further visualized using the ATLaSUI.

We have identified 12 cytoarchitectonic structures of HF in the BigBrain and analyzed their macroanatomy (Fig. 1). Fasciola cinerea (FD in its mediocaudal extension) was larger in the left hemisphere, while it was minuscule on the right (Fig.1A). Left ProS extended onto dorsomedial surface of the parahippocampal gyrus (PHG), while the right ProS almost does not appear on the surface (Fig.1B). Caudally, PreS occupied medial surface of the PHG. TrS abutted on PreS ventrally. Caudal TrS bordered the temporo-parieto-occipital proisocortex laterally (Fig.1A), while rostral TrS abutted upon area 35. PaS replaced TrS rostrally. The detailed mapping of HF reflected a transition from the allocortex (ProS and Sub) to the periallocortex (PreS, PaS) within the subicular complex that traditionally was considered as a cytoarchitectonic unit. Rostrally, both hemispheres had three Digitationes hippocampi respectively (Fig.1C).

The high-resolution (20 µm) whole-brain histological references of HF are generated on the basis of the BigBrain. They will be publicly available on the EBRAINS platform and integrated with the BigBrain model. The maps of HF can extend those of the piriform cortex in the BigBrain, being two hubs of limbic system [7]. The references can serve for high-resolution MR imaging, and be basis for brain simulation and data integration.

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