Contribution ID: **25** Type: **Poster**

BigBrain: High-resolution mapping and 3D reconstruction of the amygdala, supported by deep learning

Wednesday 26 October 2022 16:00 (1 hour)

The human amygdala constitute a heterogeneous complex in the anterior temporal lobe. Ten structures have been recently identified in high-resolution images (1 µm in-plane) [Kedo et al. 2018], and registered to a common reference space with 1 mm isotropic resolution. Probabilistic cytoarchitectonic maps have been computed, and are part of the openly available Julich-Brain atlas [Amunts et al. 2020]. However, the spatial resolution of the MRI reference space was not sufficient to visualize all structures. We overcome this limitation by creating the amygdala maps in the BigBrain model, a 3D reconstructed data set of 7404 images of histological sections (20 µm isotropic) [Amunts et al 2013] by using multi-scale Convolutional Neural Networks (CNNs), as proposed in [Schiffer et al 2021].
Nineteen structures were identified and delineated based on [Kedo et al 2018] in at least every 15th section (1 µm resolution in-plane) of the 'BigBrain'(57 sections in the right, 59 sections in the left hemisphere) using the web-based annotation tool MicroDraw (Institute Pasteur, Paris, France, https://github.com/r03ert0/microdraw). The mappings of the unlabelled sections were created by training and subsequent prediction, and performed on the supercomputer JURECA-DC at Jülich Supercomputer Centre [Krause and Thörnig 2018]. Multi-scale CNNs were based on a U-Net architecture [Ronneberger et al 2015]. Predictions were checked for quality, and low quality results were replaced by interpolation between nearest neighboring sections. Automatic mappings were transformed to the 3D reconstructed BigBrain space, and were used to assemble the 3D volumes of all structures. Surfaces were computed, and structures were visualized using the Neuroglancer software (fig. 1 A,B).
Extending our previous work, thirteen subdivisions (anterior amygdaloid area (AAA), central (Ce), medial (Me) of the centromedial group, amygdalopiriform transition area (APir), amygdalohippocampal transition area (AHi dorsal and ventral), ventral cortical nucleus (VCo dorsal and ventral) of the superficial group, lateral (La), basolateral (Bl), basomedial (Bm) and paralaminar (Pl) nuclei of the laterobasal group, amygdalostriatal transition zone (AStr)) and six fiber bundles (internal (icm, lm; ld, ice, iol) and external (vtm)) were identified in the BigBrain model and mapped with a spatial resolution of 20 µm isotropic. The CNNs reliably identified the structures in the unlabelled sections. They helped in verifying the border between the subdivisions of VCo and AHi, and the border between the rostrodorsal part of the lateral nucleus and the claustrum. The 3D reconstruction demonstrates a complex relationship between the structures and the fiber bundles on the caudoventral surface of the amygdala (fig. 1A).
These new maps show the microscopical details of the shape of all subdivisions and their spatial relationship to surrounding fiber bundles in full 3D. These maps are a part of the EBRAINS multi-level human brain atlas, publicly available through the EBRAINS platform and integrated with the BigBrain model at https://atlases.ebrains.eu/viewer/go/bigbrain. They can serve as a histological reference data for high-resolution MR imaging as well as the basis for brain simulation and data integration, e.g. in epilepsy research by targeting epileptogenic networks including the amygdala [Cota et al. 2016].

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Session Classification: Poster Session