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Cytoarchitectonic mapping of five new areas in the anterior lateral prefrontal cortex

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The region from the vertical part of the intermediate frontal sulcus (infs-v) to the anterior inferior frontal gyrus (ifg) in the lateral prefrontal cortex is an extensive region that contains many functional subregions, which play essential roles in various human functions, including motor preparation (Vogt 2007), working memory (Mizuno 2008), empathy (Cui 2015), language control (Vingerhoets 2003, Abutalebi 2009), voluntary eye movement (Kleiser 2017) and music perception (Hyde 2011). However, their structural correlates are largely unknown because areal borders are not reliably associated with macroanatomical landmarks, especially in this region which exhibits a high variability in the sulcal pattern between individuals.

Five new areas were identified by analyzing the cytoarchitecture in serial sections of ten human post mortem brains, including the two BigBrains. Areal borders were detected by an observer-independent mapping approach (Schleicher 1999). The areas were named according to their anatomical localization: INFS1 (intermediate frontal sulcus area 1), IFMS1 (intermediate frontomarginal sulcus 1), MFG3 (middle frontal gyrus area 3), IFG1 and IFG2 (inferior frontal gyrus area 1-2), were arranged in a dorsal to ventral as well as rostral to caudal orientation. They were granular areas with well-developed layer IV. Area INFS1 had a detectable layer IV, without larger pyramidal cells in layer III and V. IFMS1 had larger cells in the deeper part of layer III and V than INFS1, and its layer IV was not as developed as INFS1. MFG3 was similar to IFMS1, while the cell size in the deep part of layer III and V was larger than IFMS1. IFG2 had a relatively diffuse layering with densely packed cells. Area IFG1 contained a thin layer IV with a blurry border with layer III and V, and few large pyramidal cells in the deeper layer III. A hierarchical cluster analysis was used to quantify cytoarchitectonic similarities of the newly mapped areas and neighboring cortices. INFS1 was more similar to IFMS1 and MFG3 than IFG1 and IFG2, while IFG1 was more distinct different from the other four areas. In addition, the newly defined five areas showed higher cytoarchitectonic similarity with the areas of the mfg (MFG1 and MFG2) and Broca's areas 44 and 45 than to the frontal pole (Fp1), lateral orbitofrontal cortex (Fo5 and Fo6) (Amunts 2022). The new areas have been 3D reconstructed and superimposed in reference spaces (MNI Colin27 and ICBM152casym). Additionally, the calculated 3D-probabilistic maps showed their interindividual variability. Furthermore, ultra-high resolution cytoarchitectonic maps of the areas were reconstructed in the BigBrain space (Schiffer 2021). The new maps will be implemented in the Jülich Brain Atlas and provide a reference for localizing results from functional imaging studies and linking them to cytoarchitectonic areas.

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