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3D reconstruction of 20 neurotransmitter receptor atlases from 2D autoradiographs

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We present a 3D reconstruction pipeline for 2D autoradiographs that will allow for the creation of the first ever set of ultra-high resolution (50 μ m). The 3D atlases for 20 different neurotransmitter binding sites in the human brain. This pipeline was designed to overcome significant challenges in the data, including: non-linear deformations in the brain tissue, intensity variations between autoradiographs, variability in autoradiograph acquisitions, a large number of slices lost in sectioning, and non-orthogonal brain sections. Moreover, because sections are serially sectioned for 20 different ligands, there are significant gaps between autoradiographs for a given ligand. Surface-based linear interpolation was used to interpolate ligand densities over the cortex. Surface ligand binding densities were interpolated into a 3D volume to create atlases of ligand binding densities.

Finally, the two methods have been implemented to validate the quantitative accuracy of the reconstructed ligand values. The first approach involves directly comparing the pixel intensities of sections in the reconstructed ligand volumes to the raw autoradiographs. This is done to verify that the pipeline preserves the ligand binding densities. Initial results indicate ~90% accuracy for a flumazenil binding density volume at 0.6mm resolution.

The second validation technique applies the surface-based interpolation algorithm within acquired autoradiographs. This involves identifying a random set of vertices within aligned autoradiographs and attempting to interpolate the binding densities using the surface-based interpolation algorithm.

The methods presented here provide all the necessary processing steps to reconstruct a dataset of multiple neurotransmitter receptor atlases at 50 μ m for a full human brain.

Primary author: Dr FUNCK, Thomas (Institute of Neuroscience and Medicine INM-1, Research Centre Jülich, Jülich, Germany)

Co-authors: Dr WAGSTYL, Konrad (Wellcome Center for Human Neuroimaging, University College London, London, United Kingdom); Dr OMIDYEGANEH, Mona (Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada); Dr LEPAGE, Claude (Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada); Dr TOUSSAINT, Paule-Joanne (Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada); Dr ZILLES, Karl (Institute of Neuroscience and Medicine INM-1, Research Centre Jülich, Jülich, Germany); Dr THIEL, Alexander (Lady Davis Institute, Jewish General Hospital, McGill University, Montreal, Quebec, Canada); Dr EVANS, Alan C. (Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada); Dr PALOMERO-GALLAGHER, Nicola (Institute of Neuroscience and Medicine INM-1, Research Centre Jülich, Jülich, Germany)

Presenter: Dr FUNCK, Thomas (Institute of Neuroscience and Medicine INM-1, Research Centre Jülich, Jülich, Germany)

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