EBRAINS Data Descriptor

TITLE*

Julich-Brain Atlas - whole-brain collections of cytoarchitectonic probabilistic maps (v2.9)

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ABSTRACT*

This dataset provides a complete collection of all published probability maps of the Julich-Brain Cytoarchitectonic Atlas in the MNI Colin 27 and / or the MNI ICBM 152 (2009c Nonlinear Asymmetric) coordinate space. The probability maps were combined into four-dimensional NIfTI files, one per reference space. This way, the entire Julich-Brain Atlas is offered in a bundled format and still retains the probability information of the individual probability maps. Each NIfTI file is accompanied by a text file, which provides the mapping of the index in the fourth dimension to the respective brain region. Each probabilistic map is defined by histological analysis of ten individual postmortem brains. Thus they are capturing human intersubject variability and therefore describe how likely a particular structure is found at each voxel position of the reference spaces. Details for each particular probabilistic map can be found in the original data and journal publications.

BACKGROUND & SUMMARY

Maps of the microstructural segregation of the human brain are the key to understand the biological substrates of brain functions, dysfunctions, and behavior. Cytoarchitecture, i.e., the arrangement of cells, their distribution, composition and layering, is a major principle of microstructural brain organization. It is closely linked to the connectivity pattern of a region and its function (Goulas et al., 2018). Furthermore,

cytoarchitecture allows referencing multiple aspects of brain organization such as myeloarchitecture, molecular architecture, gene expression, but also activation or resting state networks and many more to a common ground, serving as the interface to represent and integrate the different aspects of brain organization (Amunts et al., 2015). It is widely accepted that a multifaceted but integrated approach is mandatory to explore brain organization (Van Essen et al., 2019; Fischl et al., 2018). To capture the variable cytoarchitecture of areas and nuclei in a cytoarchitectonic map with sufficient spatial resolution, the analysis and processing of thousands of histological sections per brain, with consistently high quality, is required (Zilles and Amunts, 2010). We created the Julich-Brain Atlas in our labs in Jülich and Düsseldorf. It is a cytoarchitectonic atlas containing probabilistic maps of cortical areas and subcortical nuclei. The preparation of human brain tissue, microstructural mapping, analysis and complex data processing is data-, time- and labor-intensive, in particular with increasing sample sizes and higher spatial resolution. It is thus impossible to provide whole-brain maps with sufficient detail by single researchers or small teams in an acceptable time frame. Increased computing power and storage capacities, as well as improved algorithms and workflows for data processing, now enable much faster and more robust processing at a high spatial resolution.

METHODS*

The Julich-Brain Atlas is based on a modular, flexible and adaptive framework to create probabilistic cytoarchitectonic maps resulting from the analysis of post-mortem human brains. Maps, each relying on 10 brains, have been aligned to two widely used stereotaxic spaces, MNI-Colin27 and ICBM152asym2009c space. Individual maps were superimposed to compute the probabilistic cytoarchitectonic Julich-Brain Atlas. The framework relies on a long-standing expertise for handling whole human post-mortem brains, cytoarchitectonic mapping of a variety of cortical and subcortical regions, and computational expertise to develop robust and adaptive tools, employing both local clusters and supercomputers. To ensure accuracy, reproducibility and consistency of data and processing steps over the entire data life-cycle, automated and reproducible workflows governed by provenance tracking were applied. All aspects have undergone significant changes during time (and are still subject to change), but have to converge to form a uniform, reproducible, probabilistic cytoarchitectonic human brain atlas. The main components of the framework are described in more detail below. For an overview going beyond this, see Amunts et al. 2020.

Histological processing

The Julich-Brain Atlas relies on histological sections of 23 post-mortem brains (11 female, mean age = 72 years, age range = 61-77 years, mean postmortem delay = 12 hours, from 8 to 18 hours), acquired from the body donor programs of the Anatomical Institute of the University of Düsseldorf, Germany in accordance to local legal and ethical requirements. The brains were fixed in formalin, MR-imaged, embedded in paraffin, and serially cut with a microtome into 20µm thick sections. Coronal (n=16), sagittal (n=1) and horizontal (n=6) section series of whole brains were aggregated. Among them, two brains form complete coronal series (the “BigBrain data sets”), where every single section has been stained and digitized, resulted in 7404 (BigBrain 1) and 7676 (BigBrain 2) sections. The other brains were stained with larger gaps between neighboring sections (intervals of up to 15 sections). Silver staining for cell bodies was performed using a modified Merker method, which is robust and gives a high contrast between cell bodies and neuropil. Histological sections were digitized with flatbed scanners at an optical resolution of 2400 dpi, reduced to an isotropic resolution of 20µm and framed to a unique picture size. Unavoidable local deformations, damages, and staining inhomogeneities were semi-automatically corrected.

3D reconstruction of post-mortem brains

To recover the original 3D shape and topology of the brain volume a multi-step procedure starting from an initially 3D data set at a resolution of $0.3mm^3$ was computed. The spatial resolution was then incrementally increased, which is computationally challenging in terms of CPU hours and data storage. The workflow includes the semi-automatic elimination of artifacts, intensity correction, optical balancing, linear and nonlinear 2D alignment of histological sections at different scale levels to corresponding sections of the MR images, volume-to-volume registration of MR images to stacked histological sections, and section-to-section alignment of histological sections to each other or to MR images; most steps were executed one after the other whereas some are carried out in an iterative way. The initial 3D reconstruction resulted in a first, coarse approximation of the 3D volume of the histological images. Hereby, histological artifacts were ignored. In general, however, the higher the desired spatial resolution of the 3D reconstruction, the more artifacts have to be corrected, since smaller artifacts would become more prominent and increasingly hinder the registration. Thereto, the coarse 3D reconstruction was then improved by successively replacing corrupted sections by repaired ones. A dataflow management system ensured automatically that only those data sets were re-processed, which had been modified, and included all subsequent data sets dependent on them. In addition, data processing strategies for quality control were established.

3D Registration to stereotaxic reference space

The 3D reconstructed histological data sets were initially transferred to the stereotaxic standard space of the T1-weighted, single subject template of the MNI (”Colin27”). In contrast to “smoother” templates, e.g. the MNI305 template, the individual reference brain shows a detailed (but not representative) anatomy thus allowing a precise registration of the gross anatomy of the post-mortem brains to that space. Additionally, a non-linear transformation into the ICBM2009c Nonlinear Asymmetric space has been computed. This template represents a compromise between the detailed, but specific anatomical structure of the MNI-Colin27 brain and the more generic, but smoother MNI305 template. In order to develop an atlas with both cortical areas and subcortical nuclei, a volume-based approach was chosen, which provides a consistent registration framework for both cortical and subcortical structures. An elastic 3D registration was applied with a well–matched parameter set that was also used for the 2D registrations. The method showed high reliability in both post-mortem and in vivo data sets. The 3D vector field transformation of each 3D-reconstructed histological data sets was saved to be applied later to the mapped cytoarchitectonic areas.

Individual 3D cytoarchitectonic maps

Borders between cytoarchitectonic, cortical areas of the cerebral cortex were identified using image analysis and statistical criteria to make mapping reproducible (Amunts et al., 2015). Cytoarchitectonic profiles were extracted along the cortical ribbon and orthogonally to the surface and analyzed using a multivariate distance measure. The positions of borders were labeled in the original digitized sections, and a closed polygon line marked its extent in the section. The outer boundaries of nuclei were identified in histological sections and labeled as closed polygonal lines. Contour stacks with borders data sets were managed using a revision control system that manages automatically files and directories and the complete history of how the localization of an areal border might have changed over its life cycle is documented. Using the computed linear and non-linear 2D transformations, the contour lines of structures in every histological section were 3D reconstructed and topologically checked and, where necessary, corrected. In order to create a 3D voxel representation of the contour stack each polygon was down-sampled to an in-plane resolution 0.3x0.3 mm using a box filter (each pixel in the resulting image was set to a value equal to the areal fraction occupied by the polygon in a subfield of 15x15 pixel in the original image) and the areal fractions were resampled from 0 (=no coverage) to 255 (=full coverage). Finally, the computed transformations for the 3D reconstruction were applied and a volume file was

generated for each cytoarchitectonic area, per hemisphere and post-mortem brain. These 3D probability maps form the basis for the calculation of the maximum probability map and therefor also form the data basis of the Julich-Brain Atlas.

Julich-Brain Atlas

The 3D reconstructed areas were transformed to the stereotaxic MNI-Colin27 and ICBM152asym2009c reference space, using the previously computed whole brain transformations. They were spatially smoothed by a Gaussian filter with a FWHM of 3 mm. In order to correct for interpolation artifacts, a global normalization that normalized the fraction values was computed incorporating all areas in the stereotaxic reference space. Individual areas and nuclei were superimposed in the reference spaces and probabilistic, cytoarchitectonic maps were generated and stored as volume data files with values ranging from 0.0 to 1.0. This encodes for the probability of an area or nuclei (0% to 100% overlap) being localized at the specific spatial position.

For the complete representation of the Julich-Brain Atlas, all probability maps were combined into a four-dimensional NIfTI file for the data set provided here. This way, the entire Julich-Brain Atlas can be offered in a bundled format and still retain the probability information of the individual probability maps. Due to the considerable amount of time required, not all cytoarchitectonic areas have yet been mapped. As a consequence, there are still areas that have not been mapped, but represent mapping projects for future research. Due to the projection of the already mapped cortical areas onto the surface of the reference brains, any remaining gaps on the cortical surface can be identified and anatomically classified. They have been combined into “gap maps”, lumping together the uncharted cortical areas in a certain brain region. Gap maps are being gradually replaced by new maps while mapping is progressing, while care is taken about detailed provenance tracking.

TECHNICAL VALIDATION*

The delineations of all individual underlying areas were compared across all ten brains by experts to verify anatomical plausibility with regards to topography and neighboring anatomical structures.

USAGE NOTES*

As part of the Julich-Brain Atlas, the individual probabilistic maps and the MPM allow for a comparison of functional activations, networks, genetic expression patterns, anatomical structures, and other data obtained across different studies in a common stereotaxic reference space (Amunts et al., 2020). The different areas contained in the four-dimensional NIfTI file can be addressed by their specific index. A list with the assignment of the index values to the corresponding areas is included in the attached text file.

An easy visualization software is mricron (https://www.nitrc.org/projects/mricron). If you load the NIfTI file, it will already ask you to select an index in order to select an individual probabilistic map of the four-dimensional NIfTI file.

In Python, the file can be loaded using standard tools, we recommend the nibabel module:

```
from nibabel import NIfTI1Image

pmaps_4d = NIfTI1Image.from_filename(

    ‘JULICH_BRAIN_CYTOARCHITECTONIC_MAPS_2_9_MNI_COLIN_27.pmaps.nii.gz’)

# access the 4th map:

pmaps_4d[:,:,:,3]
```

When using Python however, we recommend to use the siibra library which facilitates access to EBRAINS atlases and provides many ways to work with them. To retrieve the same 4D array in siibra (Version 0.2a5 or higher), you would use:

```
import siibra

atlas = siibra.atlases['human']

pmaps = atlas.get_map(parcellation='julich 2.9', space="colin27", maptype="continuous")

pmaps_4d = pmaps.fetch_all()

# find the region object for index 3

region = pmaps.decode_label(mapindex=3)
```

In Matlab, the file can be loaded using standard tools, we recommend the Statistical Parametric Mapping Toolbox (SPM):

```
julich_brain_colin27_v2_9=spm_vol('JULICH_BRAIN_CYTOARCHITECTONIC_MAPS_2_9_MNI152_2009C_NONL_ASYM.pmaps.nii');

% find/display the region object for index 3

spm_image('Display',julich_brain_colin27_v2_9(3));
```

A more detailed example (matlab_read_and_display_julich_brain_atlas.pdf) and an executable Matlab script (matlab_read_and_display_julich_brain_atlas.mlx) are included in the data package.

SPATIAL ANCHORING:

The individual probabilistic maps and the maximum probability map of the Julich Brain Atlas has been integrated into the HBP Human Brain Atlas (https://interactive-viewer.apps.hbp.eu/?templateSelected=MNI+Colin+27&parcellationSelected=JuBrain+Cytoarchitectonic+Atlas). It was spatially anchored to the MNI-Colin27 and MNI-ICBM152 2009c nonlinear asymmetric reference spaces (Evans et al., 2012) and is accessible as part of the Julich-Brain atlas (Amunts et al., 2020).

DATA RECORDS*

hbp-d000001-jubrain-cytoatlas_pub/
29.1/
julichbrain-2.9-pmaps-4d/
JULICH_BRAIN_CYTOARCHITECTONIC_MAPS_2_9_MNI152_2009C_NONL_ASYM.pmaps.nii.gz [Contains maps in the MNI ICBM 152 reference space, left and right hemisphere]
JULICH_BRAIN_CYTOARCHITECTONIC_MAPS_2_9_MNI152_2009C_NONL_ASYM.txt [Assignment of the different areas and the corresponding index of the volume file]
JULICH_BRAIN_CYTOARCHITECTONIC_MAPS_2_9_MNI_COLIN_27.pmaps.nii.gz [Contains maps in the MNI Colin 27 reference space, left and right hemisphere]
JULICH_BRAIN_CYTOARCHITECTONIC_MAPS_2_9_MNI_COLIN_27.txt [Assignment of the different areas and the corresponding index of the volume file]
EBRAINS-DataDescriptor_Julich_Brain.pdf [contains a short description of the dataset, this file.]

matlab_read_and_display_julich_brain_atlas.mlx [Includes an executable Matlab script to read and display the Julich-Brain Atlas.]

matlab_read_and_display_julich_brain_atlas.pdf [Output of executable Matlab script matlab_read_and_display_julich_brain_atlas.mlx.]

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CODE AVAILABILITY*

All available code regarding the computation of the Julich-Brain Atlas can be retrieved from the original publication (Amunts et al., 2020).

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Author contributions

The study was designed and supervised by Katrin Amunts. Probabilistic maps and MPMs were calculated by Hartmut Mohlberg. Sebastian Bludau and Andrea Brandstetter are responsible for coordination and quality control. Timo Dickscheid created the 4D NIfTI file.

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