EBRAINS Data Descriptor

TITLE*

Julich-Brain Atlas, cytoarchitectonic maps (v3.0.3)

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ABSTRACT*

This dataset contains the Julich-Brain Atlas, Cytoarchitectonic maps in different coordinate spaces. The parcellation provided by the Atlas is derived from the individually released probability maps (PMs) of cytoarchitectonically defined cortical and subcortical brain regions. For the whole-brain parcellation, the available PMs are combined into a maximum probability map (MPM) by considering for each voxel the probability of all cytoarchitectonic brain regions, and determining the most probable assignment. In later versions of this dataset, gap maps complement the maximum probability map of the cytoarchitectonically defined brain regions to achieve full cortical coverage.

There are two sets of PMs with a different degree of parcellation included. The set with 157 PMs corresponds to the usual granularity of the Julich-Brain Atlas. This set was used for the calculation of the MPM. Furthermore, a set with 175 PMs is included. This dataset contains, for some regions, more detailed cytoarchitectonic parcellations. For technical reasons, this finer parcellation is only representable via individual PMs due to the spatial resolution of the reference space, i.e., the MPM for the set of 175 PMs is not available.

In addition, a set of cortical areas of the MPM is available on the FreeSurfer fsaverage surface.

Note that methodological improvements and integration of new brain structures may lead to small deviations in the parcellation between released versions of this dataset.

VERSION SPECIFICATIONS*:

Change Log:

- v3.0.1, minor changes in the XML files of version 3.0 (correction of spelling mistakes, XML tag naming, removal of forbidden white spaces).
- v3.0.2 corrects a technical error in the FreeSurfer surface that led to the misplacement of a few labels on some platforms.
- v3.0.3 corrects a technical error in the FreeSurfer surface that led to the misplacement of area 7M and area 7P labels in siibra-explorer.

We therefore strongly recommend using the most recent version of this release!

Like the previous version, this version contains two sets of probability maps (PMs) with a hemispheric subdivision of 157 and 175 cortical and subcortical regions, as well as a maximum probability map (MPM) and a surface model based on the subdivision set of 157 areas. Note that both subdivision sets contain 6 gap maps in each hemisphere to achieve full coverage of the cerebral cortex.

The PMs are stored in separate files for left and right hemisphere. The MPMs are stored additionally in a file combining both hemispheres.

PMs, gap maps and MPM are available in the following coordinate spaces:

- MNI ICBM 152 (2009c Nonlinear Asymmetric)
- Colin 27 (1998)
- FreeSurfer fsaverage surface space. The surface model is based on cortical areas of the 157 subdivision and the cortical gap maps.

Note: To open the FreeSurfer fsaverage surface gifti files, please ensure that you are using the latest version of FreeSurfer.

BACKGROUND & SUMMARY

Maps of the microstructural segregation of the human brain are a 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 (Amunts et al., 2020, 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 version 3.0 of the Julich-Brain Atlas includes for the first time a set of cortical areas of the MPM transferred onto the FreeSurfer fsaverage surface. 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 = 71 years, age range = 43-86 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 with 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 0.3 mm^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 were 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 nonlinear 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 set was saved to be applied later to the mapped cytoarchitectonic areas. In order to make the maps of the Julich-Brain Atlas also available to the community of surface-based working scientists, version 3.0 of the Julich-Brain Atlas includes for the first time a set of cortical areas of the MPM transferred onto the FreeSurfer fsaverage surface.

Individual 3D cytoarchitectonic maps

Borders between cytoarchitectonic cortical areas of the cerebral cortex were identified using image analysis and statistical criteria to make the 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 their 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 automatically manages 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 nonlinear 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 of 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 therefore 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. In order to make the maps of the Julich-Brain Atlas also available to the community of surface-based working scientists, version 3.0 of the Julich-Brain Atlas includes for the first time a set of cortical areas of the MPM transferred onto the FreeSurfer fsaverage surface. 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 MPM 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).

SPATIAL ANCHORING:

The individual probabilistic maps and the maximum probability map of the Julich Brain Atlas have been integrated into the HBP Human Brain Atlas: https://interactive-viewer.apps.hbp.eu/
It was spatially anchored to the MNI-Colin27 and MNI-ICBM152 2009c nonlinear asymmetric reference spaces (Evans et al., 2012) and the FreeSurfer fsaverage surface and is accessible as part of the Julich-Brain atlas (Amunts et al., 2020).

DATA RECORDS*

repository-root/

...**data-descriptor_9c56f019bbc8.pdf** [contains a short description of the dataset]

...**Licence-CC-BY-NC-SA.pdf**

...**fsaverage_surface** [contains a set of cortical areas of the MPM transferred onto the FreeSurfer fsaverage surface]

...**maximum_probability_maps_MPMs_157areas** [contains combined probabilistic maps into a maximum probability map (MPM) determining the most probable assignment for each voxel. Left/Right and both hemispheres version available]

...**probabilistic_maps_pmaps_157areas** [contains probabilistic maps for 157 distinct cytoarchitectonic areas]

...**probabilistic_maps_pmaps_175areas** [contains probabilistic maps for 175 distinct cytoarchitectonic areas. Some of the areas of the 157 data set are further subdivided]

...**JulichBrainAtlas_3.0_157areas_terminology.json** [contains the terminology tree for the Julich-Brain atlas 157 dataset]

...**listOfPMapFiles.csv** [contains a list of all included probabilistic maps as a unified list for the 157pmap and 175pmap data set]

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 is responsible for coordination and quality control.

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