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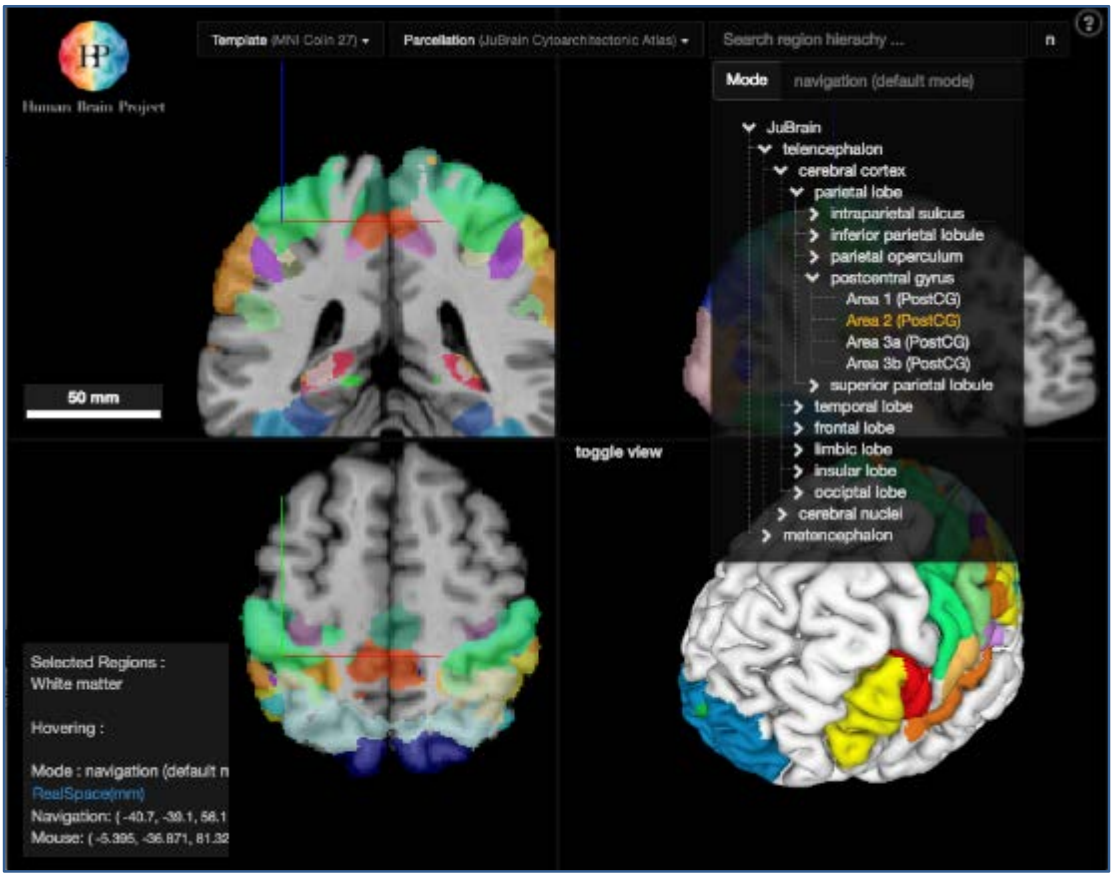
Abstract:	This deliverable is the annual compound of HBP deliveries and results (outputs and outcomes) from Sub-Project SP2 – Human Brain Organisation. The live complete catalogue of HBP deliveries is accessible online from the HBP portal. The main deliveries from April-2017 to March-2018 have been: Data sets and software in the fields of human neurogenomics, morphology and architecture of the Human Brain, function and variability, comparative computational architecture of multi-modal processing streams, integrative maps and models, and co-design/methods and Big Data analytics.
Keywords:	Cytoarchitectonic maps, Atlas Viewer, receptor densities, 3D-polarised light imaging (3D-PLI), genetic risk scores, genomic profiles, neuronal morphology, distribution, and circuits, fibre bundles, diffusion MRI, two-photon microscopy, axon imaging, electrophysiology, Individual Brain Charting (IBC), activity maps, connectivity-based parcellation, visual and auditory processing streams, ultra-high field MRI, attention, GABAergic interneurons, iEEG, HiBoP, connectivity, shape toolbox, JuBrain



The JuBrain atlas (component ID321) in a pre-release of SP5 interactive atlas viewer (component ID800).

Targeted users/readers	Neuroscientific community, clinicians and neuroinformatics
Contributing Work-Package(s):	SGA1 WPs 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7
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1. Introduction

The overall objective of SP2, the Human Brain Organisation, is to generate neuroscientific concepts, knowledge, data sets and tools contributing to a better understanding of the multi-modal and multi-level organisation of the human brain.

Multi-modality and multi-scalability are necessary to understand the complex organisation of the human brain. A major challenge is to bridge the scales and understand their connections, relationships and dependencies. To do so, SP2 provided a rich set of multi-level and multi-scale neuroscientific data ranging from the molecular to cellular level up to local neural circuits and systems network levels using state-of-the-art methods and techniques. Importantly, relationships of a level to the next spatial scale, and other aspects of brain organisation at considered scales were considered. Regarding techniques and quality, HBP is unique, e.g. in Polarised Light Imaging (3D-PLI), receptor architectonics, but also in tissue clearing, immunohistological axon staining and sub-millimetre columnar / laminar level 7+ Tesla fMRI. These data are the basis of the development and population of the HBP Human Brain Atlas with new data in close collaboration with SP5, the Neuroinformatics Platform. Workflows developed in SP2 to analyse the brain's microstructure including nerve fibres and tracts employ HPC resources (e.g. JULIA and JURON obtained in the HBP via a PCC); they are drivers for its development (SP7, High Performance Analytics and Computing Platform).

From SGA1 month 12 to month 24 (April 2016 - March 2018) SP2 provided results on six Key Results: i) human neurogenomics, ii) morphology and architecture of the human brain, iii) function and variability, iv) computational architecture of multi-modal processing streams, v) integrative maps and models and co-design/methods and vi) Big Data analytics. Details of the results and information on the data access are given in the next sections. Most of these results are already published, under revision or submitted to high-level journals. Results achieved by the co-design projects CDP3 – Multi-level Human Brain Atlas, and CDP4 – Visuo-motor Integration, can be found in separate Deliverables for these CDPs.

2. Results

2.1 Human Neurogenomics

One of the main challenges for research on brain disorders (NDD) is the lack of detailed information on the impact of genetic variation on brain structure and function. This information would improve our understanding of the biological factors (genes and gene variants) involved in proper brain structure and function in particular brain regions. This deliverable is focused on ascertaining the impact of genetic variation on brain structure and function. We have two complementary approaches that investigate the roles of both common and rare genetic variants.

In addition, we have developed a tool (JuGEx) for the scientific community that enables a precise comparison of regional gene expression data derived from the Allen Brain Atlas and cytoarchitectonic maps from the JuBrain Atlas in the same reference space (see also CDP3 Deliverable), thereby bridging the scale between the cellular organisation of the human brain and genetic underpinnings.

2.1.1 (Achieved) Impact

Regarding common variants, the laboratory of Sven Cichon (UNIBAS) has collected genetic, epigenetic, MRI, and neuropsychological data on approximately 1000 individuals from the general population. This data set was used to estimate the global impact of risk-scores derived from published SNPs associated with Late-onset Alzheimer's Disease (LOAD) on cortical atrophy. Another study is currently systematically searching for SNPs that influence the volume of three brain regions (both insulae and the dorsal anterior cingulate cortex) that show atrophy in patients with different neuropsychiatric disorders.

Further, the lab of Sven Cichon contributed to the development of the JuGEx tool (see also CDP3 Deliverable) which allows combining gene expression data and cytoarchitectonic mapping data (Bludau *et al*, 2018). This publication was downloaded 359 times during the first six days after publication, suggestive for a large interest from the community. JuGEx offers to integrate even more aspects of brain organisation (e.g. connectivity, resting state activity, structural MR morphometry), and provides the basis for capturing regional differences in gene expression in healthy subjects and different groups of patients. Due to its link to the Allen Atlas and Institute, it also reaches a new community.

The laboratory of Thomas Bourgeron is currently investigating patients with autism spectrum disorders (ASD), focused on rare and *de novo* variants. To date, more than 300 individuals have undergone whole exome sequencing (WES) or whole genome sequencing (WGS). Several *de novo* mutations, affecting known genes for ASD, were identified (for example: SHANK3, SCN2A, GRIN2B). In addition, new compelling candidate genes were also identified (for example ACTL6B, RIMS4). The brain anatomy and function of the patients carrying these mutations is currently investigated.

In a first study, we investigated 85 patients with different 22q13 rearrangements (78 deletions and 7 duplications that include the gene coding for the synaptic scaffolding protein SHANK3), and provide evidence for frequent corpus callosum abnormalities in these patients (for 10 out of 35 patients that were examined by MRI). This study was published in Npj Genomic Medicine in 2017.

Parts of this Key Result were published in 4 scientific articles (April 2017 – March 2018).

2.1.2 Component Dependencies

Component ID	Component Name	HBP Internal	Comment
859	SGA1/SGA2_T2.4.3 Genetic factors contributing to inter-individual variation on morphology and architecture	Yes	Individual genetic risk scores for 20 Alzheimer's Disease susceptibility variants in the 1000Brains sample. Genome-wide association data (phenotype: volume of a common neurobiological substrate (incl. dACC and insulae)) in the 1000Brains sample. JuGEx toolbox for combining gene expression data and cytoarchitectonic mapping data.
860	SP2 – Genetic variants and individual genomic profiles	No	Genotype/phenotype relationship of patients with Phelan-McDermid syndrome (PMS), a step towards the identification of compensatory mechanisms for a better prognosis and possibly treatments of patients with neurodevelopmental disorders.

2.2 Morphology and Architecture of the Human Brain: A multi-level and multi-modal approach

We obtained comprehensive data sets related to morphology and architecture of the human brain. The data were obtained using different techniques, thus providing multiple perspectives to look at the same organ. This integrated and multi-modal approach is a strength of the HBP consortium, as outside it is quite difficult to provide a global view since most laboratories can provide only a partial portrait of the sample under analysis. Going into detail, we have created and are further developing a cytoarchitectonic atlas of the human brain, comprehensive of inter-subject variability in cell densities. This atlas is unique and essential for revealing the structural organisation of the human brain. We have also quantified the densities of multiple receptors for classical neurotransmitters across the cortex, demonstrating differences in their distributions between iso- and allocortical areas, as well as in subcortical nuclei. To date, no layer-specific multiple receptor data for the human cerebral cortex exist, and particularly not for cytoarchitectonically and functionally defined areas of different neural systems. Our approach fills this gap and is clearly beyond the current state of the knowledge. Furthermore, we analysed the functional dimension of microstructurally defined areas, e.g. using meta-analytic approaches, functional imaging and behavioural analyses, resulting in high-level publications (e.g. Gomez *et al.*, Science, 2017). These results, obtained with wide-field light microscopy and autoradiography in combination with sophisticated image analysis for quantification, were complemented with novel approaches based on clearing and immunolabelling of large tissue blocks. We developed IHC procedures compatible with tissue clearing to map the 3D distribution of standard receptors as well as of whole neurons in samples of human brain cortex. Raw images of neurons were processed with a segmentation pipeline developed in T2.6.4 to quantify neuronal density and shape in different regions of the cortical ribbon. This approach is largely beyond the current state of the art, as optical IHC imaging is usually performed on small tissue slices rather than in 3D.

Quantitative data from different regions of the human brain were obtained using high-resolution fine-scale electron microscopy (surface area, volume and percentage of myelinated fibres). These data can be used for realistic simulations of various parameters of information processing in different fibre tracts of the normal and pathologically altered brain.

Connectivity was explored using 3D-Polarised Light Imaging (3D-PLI) at two different in-plane resolutions (1,3 µm and 64 µm, respectively). In particular, we focused on the hippocampal region, a key region for learning and memory, that is also addressed in SP1, Mouse Brain Organisation. Presently, there are no large-volume fibre architectural data of the human hippocampus at a few micron resolution. The application of 3D-PLI is unique and so are the resulting reconstructions, which disclose new features of fibre architecture, such as new components of the performant pathways (Zeihneh *et al.* Cereb Cortex, 2016). Our approach opens new avenues to approach the human connectome. We also coupled 3D-PLI with two-photon fluorescence imaging, to afford mapping at even higher resolution in relevant regions of interest. We discovered a new protocol to boost myelin autofluorescence, thus allowing fibre imaging without external staining across the spatial scales.

Finally, we complemented all architectonic data with morphofunctional characterisations. We extensively characterised human L2/3 pyramidal neurons in acute brain slices, using both morphological and electrophysiological data. The data sets have been shared with other consortium members (teams of Segev (SP4) and DeFelipe (SP1)) for realistic computational modelling. Thus far, no data existed on layer-specific synaptic connectivity and cellular properties for the human cerebral cortex and, particularly not for cytoarchitectonically and functionally defined areas of the different neural systems. Our data fill this gap.

2.2.1 (Achieved) Impact

- Cytoarchitectonic data, receptoarchitectonic data, 3D IHC neuronal maps and fibre architecture data are available through the Neuroinformatic Platform (SP5) for further internal and external use.
- All these data will serve as scaffold for realistic modelling of the human brain. More generally, our multi-modal collection is unique and essential to reveal the structural organisation of the human brain and to understand its implications for cognition and behaviour.
- The cytoarchitectonic atlas is used as a reference to localise neuroscientific findings, e.g. functional activations, to study the organisation principles of the brain, to investigate the topography of pathological changes, and to better understand regional differences in gene expression.
- The SPM anatomy toolbox contains the cytoarchitectonically defined areas and provides user-friendly tools to analyse data from neuroimaging experiments, but also large cohort studies.
- The tissue preparation protocol developed (3D IHC, myelin autofluorescence boosting) will be a valuable tool for the neuroscientific community.
- The multi-modal investigation of fibre architecture is important for a better understanding of the fine architecture of fibre tracts. It can inform on biologically meaningful constraints for diffusion MRI tractography.
- Morpho-functional single-neuron data have been shared with SP1, SP4 and SP6 participants DeFelipe (Madrid), Segev (Jerusalem), Giugliano (Antwerp) and Schürmann (EPFL). New data will be distributed through the Neuroinformatics Platform (SP5).
- Although technically challenging and labour-intensive, high-resolution electron microscopy can open a new window for the analysis of structural determinants that underlie the 'behaviour' of our brain.
- Importance for a further understanding of the human brain organisation and function of microcircuits.
- Provides data for future comparative studies and/or simulation and modelling approaches.
- This Key Result contributes to CDP6 (see CDP6 Deliverable)

- Parts of this Key Result were published in 28 scientific articles (April 2017 – March 2018)

2.2.2 Component Dependencies

Component ID	Component Name	HBP Internal	Comment
325	SP2 - Cytoarchitectonic probability maps	No	Probabilistic maps of cytoarchitectonically mapped areas – JuBrain Atlas
1582	SP2 - Preliminary investigation and characterisation of axon imaging by two-photon microscopy	Yes	Protocol for axon imaging by two-photon microscopy based on myelin autofluorescence in *ex vivo* mouse and rat samples
326	SP2 - Maps of different human neuronal circuits	*Yes*	3D tiff maps of neurons labelled with a different antibody: SMI32
770	SP2 - Multilevel maps of quantitative cell distributions and morphologies	Yes	3D tiff Maps of neurons labelled with different antibodies: NeuN, PV
772	SP2 - Multilevel maps of quantitative cell distributions and morphologies	Yes	3D tiff images of spatial distribution of different types of receptors together with celltypes, ultra-resolution imaging of receptors and sub-cellular structures.
249	SP2 - Quantification of multiple receptor distributions for selected areas	No	Receptor densities (fmol/mg protein) of up to 19 different receptor binding sites for glutamate, GABA, acetylcholine, serotonin, noradrenaline, dopamine, and adenosine in primary sensory and motor cortical areas, in hippocampus, cingulate and entorhinal cortex, as well as in the basal ganglia, selected thalamic and brainstem nuclei using receptor autoradiography.
339	SGA1/SGA2_T2.1.3 Map of human fibre bundles and their microstructure	partially	Maps of bundle localisation and microstructure in MNI space
302	SP2 - 3D-PLI data for selected human anatomical structures	Yes	3D-PLI modalities: blockface images, transmittance maps
808	SP2 – 3D models of fibre tracts	Yes	3-D reconstruction and models of fibre tracts in the human brain
328	SP2 - Morphological cortical connectivity profiles of neocortical pyramidal neurons	No	Connections of L2/L3 pyramidal neurons and interneurons
327	SP2 - Morphological data of human neocortical pyramidal neurons	No	Matching morphologies and physiologies of human pyramidal neurons

2.3 Function and Variability

Work on multi-modal functional mapping of the human brain has substantially progressed with respect to methods, applications and theory. In particular, we have implemented a first working version of a comprehensive pipeline for multi-modal connectivity based parcellation that can be run on HPC environments provided by SP7, e.g. the JURECA supercomputer. This software will be further developed in SGA2 and it should provide a novel feature for regional mapping to be widely used within and beyond the HBP. This large availability and use will be critical to assess the effect of slight variations in data processing choices on the robustness of the results. Beyond its contribution to the examination of methodological issues, our open pipeline provides a tool for the functional mapping of brain regions in large samples of thousands of subjects, as well as for quantification of inter-individual variability and its relation to behavioural function, thus contributing to a new field of research.

We have recently applied *in vivo* mapping based on structural and functional connectivity on three different regions of the brain: the left and right dorsal premotor cortex and the right hippocampus. These maps are openly shared through the ANIMA website (anima.fz-juelich.de) and frequently used by the neuroimaging community (download numbers: 17 right PMd, 11 left PMd). Comparison of the results of the functional parcellations in WP 2.3 with histological maps developed in WP 2.2 revealed that the relationship between cytoarchitectonic and connectivity-defined territories may differ across different parts of the brain. On the one hand, the organisation of the dorsal premotor cortex was largely replicated when mapped independently on histological sections and by multi-modal functional parcellation. On the other hand, the hippocampal formation is primarily differentiated along a medial-to-lateral-axe in terms of its cytoarchitecture, while connectivity patterns and functional activation differences both suggested a clear differentiation between the anterior and posterior parts of this structure. Based upon these findings, theoretical models for topographic brain organisation and multi-modal parcellation as well as brain-behaviour associations have been developed and published (Eickhoff *et al. in press*; Genon *et al. in press*). Within SGA2, we will build on the tools and knowledge developed in SGA1 to further provide empirical data on one of the key aspects of brain organisation, i.e. topographic differentiation.

Additionally, we put together an unprecedented collection of maps from the 12 subjects of the Individual Brain Charting (IBC) Project. This collection provides high-resolution (1.5mm) system-level information on the functional organisation of the brain. More specifically, it makes it possible to shift the focus from traditional contrast-based studies to cognitive level studies, where cognitive functions can be characterised according to their occurrence in various functional tasks, and mapped to brain activity. The data and analysis scripts are made freely available to the HBP consortium and the entire neuroscientific community through OpenfMRI (raw data) and NeuroVault (about 1800 maps of brain activity).

Parts of this Key Result were published in 11 scientific articles (April 2017 – March 2018)

2.3.1 (Achieved) Impact

Our work is at the forefront of the development of methods and concepts for multi-modal brain parcellation, in particular for the regional focus and the integration of parcellation and subsequent characterisation of the ensuing modules. Providing the community with multi-modal maps of multiple brain regions, including detailed characterisation of the respective areas, has resulted in an intensive usage from the neuroimaging community as *a priori* information for future analyses.

Our brain mapping work adds a dimension to brain imaging datasets that has been neglected so far: system-level cognitive mapping. Several labs use these data to characterise and simulate brain function. We also use it as a test set to study cognition-to-activation relationships, learned through existing datasets and the neuroimaging literature.

2.3.2 Component Dependencies

Component ID	Component Name	HBP Internal	Comment
365	SGA1/SGA2 _T2.1.1 Full human brain activity maps (volumes)	No	Fifty maps of brain activity spanning various cognitive contrasts at 1.5mm resolution, recorded from 12 subjects (Individual Brain Charting Project). The images are sampled in the volume.
773	SP2 - Selected multimodal regional maps with cognitive features	partially	Functional parcellation and characterisation of 3 regions of interest (ROIs): 1. right dorsal premotor cortex, 2. left dorsal premotor cortex, and 3. Hippocampus. The subregions were evidenced by multimodal connectivity-based parcellation and large-scale functional connectivity by a multi-modal approach.

2.4 Comparative Computational Architecture of Multi-Modal Processing Streams

We obtained strategic NHP data sets and human data sets using state-of-the-art methods unravelling coding principles in the visual and multi-sensory cortex. Combined with existing theories, these novel data sets were used to create detailed comparative computational architectures of visual and multi-sensory (visual-auditory) processing streams that contributed to the implementation of the visuo-motor integration neural network model (CDP4, see separate deliverable). The multi-species studies in this WP are chosen to provide critically needed, novel information to constrain the visuo-motor integration model.

We extended our knowledge of the early visual cortex by revealing the first non-invasive (*in vivo*) visualisation of all 3 stripe compartments (thin, thick and interstripes) in area V2 of the nonhuman primate (Li, Zhu, Janssens, Arsenault and Vanduffel, (2017), “In Vivo Identification of Thick, Thin, and Pale Stripes of Macaque Area V2 Using Submillimeter Resolution (f)MRI at 3 T” Cerebral Cortex). For more complex cognitive functions, we revealed that shifts of spatial attention activate homologous areas in the human and monkey superior parietal lobe (Arsenault, Caspari, Vandenberghe and Vanduffel, (2018), “Attention Shifts Recruit the Monkey Default Mode Network”, Journal of Neuroscience). This is an important finding for HBP modelling, since it supports the use of detailed NHP data to constrain the operation of the human dorsal “where” pathway of the visuo-motor integration model (CDP4). We also revealed a causal role of the primate ventral tegmental area in cortical plasticity and perceptual learning (manuscript *in preparation*), which will be important for further development and integration of biological learning rules in the CDP4 model.

We use innovative functional MRI (fMRI) at 7+ Tesla, combined with novel data analysis methods (also provided to SP3) to study non-invasively the active living human brain at the sub-millimetre level of cortical layers and cortical columns inside identified brain areas. This “mesoscopic” functional spatial scale is crucial for HBP, because it provides essential data for brain simulations, and because it bridges macroscopic and microscopic scales across species (especially NHP electrophysiological / fMRI data with human data). In collaboration with SP5, we also developed new methods to integrate regional sub-millimetre human fMRI data in the HBP brain atlas by registering cortical depth data from measured brains into corresponding cortical patches in the atlas brain.

We have continued to reveal coding principles in the human cortex and related 7 Tesla auditory data to newly acquired NHP data using the same stimuli (manuscript submitted “Homology and specificity of natural sound-encoding in human and monkey auditory cortex”). We also

investigated the coding principles in the multi-sensory cortex of the human brain. We revealed the organisation of the bimodal superior temporal cortex (bSTC) in the human brain, this region plays a crucial role in the integration of visual and auditory inputs (Gentile F, van Atteveldt N, De Martino F and Goebel R, (2017), "Approaching the Ground Truth: Revealing the Functional Organization of Human Multisensory STC Using Ultra-High Field fMRI", The Journal of Neuroscience, 37, 10104-13). We measured 7T fMRI responses at conventional and at very high spatial resolution to visual, auditory and combined multi-sensory stimuli, revealing a fine-grained layout of specialized sub-clusters for unimodal and multimodal (integrative) responses.

Additionally, using a correlated electrophysiological/morphological approach, we investigated the properties of excitatory neurons, GABAergic interneurons and their neuronal networks in different sensory cortical areas (primary visual, auditory and somatosensory cortex) in rodent brains. We provided electrophysiological data on synaptic physiology and 3D neuronal reconstructions (Feldmeyer *et al.* (2018), Emmenegger *et al.* (2018), Radnikow *et al.* (2018)).

2.4.1 (Achieved) Impact

The reported data sets and results are not only important for the general neuroscience and neuroimaging community, they are also instrumental for the creation of biologically detailed computational architectures of the visual, auditory and multi-sensory cortex. More specifically, the results are used to continuously improve the visuo-motor integration model (CDP4) to become the most comprehensive and biologically accurate model in the future.

The results on the organisation of the human multi-sensory cortex (bSTC) improve our understanding on how the brain integrates visual and auditory stimuli. Moreover, the study indicates that standard resolution fMRI may lead to wrong conclusions about the functional organisation of bimodal integrative cortex (bSTC), and that high spatial resolution fMRI at a millimetre scale is essential to accurately approach neuronal operations at the columnar level.

Parts of this Key Result were published in 20 scientific articles (April 2017 – March 2018).

2.4.2 Component Dependencies

Component ID	Component Name	HBP Internal	Comment
789	SP2 - Computational architecture of the functional organisation in visual and auditory processing streams in human and macaque monkey	Yes	1) Causal mechanisms driving visual cortical plasticity and perceptual learning in primates. Causal role of primate ventral tegmental area in cortical plasticity and perceptual learning. 2) Role of V1, V4 and frontal cortex in the awareness of weak visual stimuli.
861	SP2 - Selective attention in perception and learning in humans and monkeys	No	Shifts of attention activate homologous areas in human and monkey superior parietal lobe
862	SP2 - Ultra-high field fMRI of subunits in higher-level visual areas and face areas in human and monkey	partially	1) The first non-invasive (*in vivo*) visualisation of all 3 stripe compartments (thin, thick and interstripes) in area V2 of the nonhuman primate 2) Homology and specificity of natural sound-encoding in human and monkey auditory cortex

			3) Functional organisation of human multisensory STC using ultra-high field fMRI
793	SP2 - Properties of excitatory neurons and GABAergic interneurons and the neuronal networks in sensory cortical areas in rodent	No	Electrophysiological data on synaptic physiology and 3D neuronal reconstructions.

2.5 Integrative Maps and Models

This Key Result aggregated different streams of strategic data delivered by SP2, or matched such data with models.

2.5.1 (Achieved) Impact

The structural connectivity data of the Archi and HCP datasets have been transformed into group-based and individual parcellations of the cortical mantle (ID248) that can be compared and matched to post-mortem parcellations issued from microscopic imaging (ID325). They will be integrated in the HBP atlas to allow users to test their own hypotheses on the connectivity of architectonic areas. A massive set of outstanding high temporal resolution electrophysiology recordings obtained from epileptic patients has also been delivered for most of the cytoarchitectonic areas (ID341). They will provide a unique input to the modelling of SP6. A dedicated stand-alone software for efficient visualisation of these massive electrophysiological data has been delivered and will complement access through the HBP portal (ID863). Structural connectivity matrices designed for several standard parcellation schemes have also been delivered to allow graph-based analyses of brain dynamics (ID340). SP4 is already beta testing these matrices to improve the modelling of functional connectivity from fMRI.

The long-term objective of delivering a joint diffusion MRI (dMRI) and PLI acquisitions of the same post-mortem specimen to the community has reached a key milestone: a temporal lobe has been acquired with both modalities (300 microns versus 2 micron-resolution), and dedicated original cross-modality alignment software has been designed (ID790). The two aligned acquisitions, that will be provided to the community, have a unique validation dataset for the modelling of white or grey matter using diffusion MRI.

Parts of this Key Result were published in 5 scientific articles (April 2017 – March 2018).

2.5.2 Component Dependencies

Component ID	Component Name	HBP Internal	Comment
248	SP2 - New human brain parcellations based on microscopic post-mortem and *in vivo* data	partially	Connectivity, based on parcellation of the Freesurfer Desikan atlas available at group and individual level (80 subjects in the Archi database, 200 subjects in the HCP database)
790	SP2 - Crossing scales between dMRI and 3D-PLI	Yes	Parallel software code to re-scale vector-based imaging data
340	SP2 - Human connectivity matrix from atlas parcels	Yes	Diffusion MRI-based connectivity matrices computed for the 78 Archi subjects (group-based and individual) for 3 different parcellations (AAL,

			Freesurfer Desikan, BrainVISA constellation tuned to connectivity)
863	SP2 - Human Intracranial Electrophysiology Tools	Yes	HiBoP – 3D visualisation tool for MRI and EEG recordings
341	SP2 - Human iEEG recordings	Yes	iEEG obtained during cognitive tasks

2.6 Co-design/Methods and Big Data Analytics

The overall aim was to develop new algorithms and software tools, to improve SP2-generated data use, and to advance the transfer of human data-specific methods to the SP5 and SP7 Platforms. Regarding the co-design of the Neuroinformatics Platform, WP2.6 worked closely with WP5.4 to implement i) access of area-specific receptor measurements directly into their interactive atlas viewer, and ii) a python library for atlas-driven differential gene expression analysis, that has been tightly integrated as an interactive tool into the same atlas viewer. WP2.6 hereby significantly contributed to the realisation of CDP3 product 5 (more details and screenshots are available in the CDP3 deliverable).

There was significant progress in various forms of image processing, for example, tools were developed to stitch together large volumetric images (such as those produced by light-sheet fluorescence microscopy), and tools to automatically segment neurons in human brain tissue. A workflow was implemented to predict missing annotations in high-resolution images of histological series, using a deep neural network, to automate much of the cytoarchitectonic mapping. Integrating image data of different types from different individuals requires procedures for accurate image alignment. Several advances were made in this area, each addressing the challenges presented by different data types. A machine learning procedure was developed to identify vessel-like structures from cell-stained sections, so that they can serve as landmarks for a new robust image alignment procedure, which was also designed and developed by the WP. Improvements were made to the algorithm for automatically identifying homologous sulci in the brains of different individuals, to improve volumetric alignments of high quality whole-brain images. A diffeomorphic shape modelling framework was also developed for learning models of brain shape variability from populations of images, to achieve more accurate and robust alignments of whole-brain data, in situations where sulci are less easily identified. In addition, new models for simulating tissue and fibre arrangements were developed as precursor to achieve future integration between dMRI and PLI data.

Throughout SGA1, WP2.6 has fostered a close cooperation with WP7.2/SP7. In particular, the methods for neuron segmentation and microstructure detection have been analysed with respect to various HPAC hardware requirements, and the Deep Learning workflow for brain mapping has been set up and benchmarked on different HPAC systems to understand and optimise distributed training across many accelerator devices. This includes test setups on the general purpose cluster JURECA, as well as on the PCP systems JURON and JULIA. Several technical aspects of this cooperation have been reported within WP7.2. Finally, WP2.6 has pushed the setup of federated storage systems and workflows to enable SP2 researchers to upload large datasets to the HBP Platforms.

2.6.1 (Achieved) Impact

The report on workflow design has led to an agreement on data types, image services (BBIC, DVID, or similar technology) and permission management, and the resulting report means that developers now have a clear plan on the implementation of particular scenarios, where large data sets from an HBP partner need to be registered and visualised in the NIP, including data transfer, conversion and curation. Receptor measurements can now directly be viewed within the

interactive atlas viewer (TRL6). New algorithms have been developed (at TRL3 or 4), which allow the automation of tasks that would take a great deal of time if done manually. Some software has been used successfully by other HBP Tasks (e.g. T2.2.2, T1.3.1 and T1.3.3). In addition to their use within SP2, a number of the new developments is also close to becoming available through software packages that already have widespread use outside the HBP, such as the BrainVisa suite, and SPM. Several papers describing algorithmic developments are either published, submitted or still in preparation. Published papers include Mangin *et al.* (2016), Bludau *et al.* (2016), Ali *et al*. (2017) and Ginsburger *et al*. (2018). Papers and abstracts have been submitted to the MICCAI and OHBM conferences.

Parts of this Key Result were published in 7 scientific articles (April 2017 – March 2018).

2.6.2 Component Dependencies

Component ID	Component Name	HBP Internal	Comment
342	SP2 - Shape and appearance models for human brain variability	*No*	Shape-Toolbox to optimally align MR image data
797	SP2 - Robust matching procedure for incomplete sets of microstructures detected at different scales	No	A library to match microstructural landmarks extracted from histological sections based on appearance and spatial constraints, which exploits a coarse pre-alignment as well as the co-planarity of the features, to overcome the inherent difficulty of matching tissue microstructures with poor distinctiveness.
796	SP2 - Classifier for microstructural landmarks that can be used for cross-scale alignment of PLI data	*Yes*	A machine-learning based classifier that robustly detects vessel-like structures as typical microstructural landmarks in cell body-stained histological sections that can be found at different scales and across a range of consecutive sections. Although we intended to focus on data from a polarisation microscope / large area polarimeter in the original work plan, we shifted focus to the case of cell stained sections.
795	SP2 - Improved version of sulcus-based cross modality alignment toolbox	No	Toolbox DISCO embedded in the brainvisa suite (http://brainvisa.info)
875	SP2 - Simulated tissue/fibre models	Yes	Dictionary of synthetic datasets providing a broad spectrum of modelled, realistic fibre arrangements using PLI and dMRI
250	SP2 - Cell counts, cell and vascular segmentation for selected areas in human	*partially*	ZetaStitcher: a tool designed to stitch large volumetric images such as those produced by Light-Sheet Fluorescence Microscopes. BCFind2: a tool for point-neuron localisation using semantic deconvolution and mean shift HNeuronSegmentation: a tool for neuron segmentation in human brain tissue

302	SP2 - 3D-PLI data for selected human anatomical structures	Yes	3D-PLI modalities: blockface images, transmittance maps
801	SP2 - Workflow for automatic prediction of annotations in high-resolution histological sections across consecutive slices	*Yes*	Implementation of a novel workflow for predicting missing annotations in high-resolution images of histological series. The workflow will be based on a deep neural network architecture which is suitable for image segmentation tasks, and use a sparse set of manual annotations in some slices of the same stack as its training data to predict the same annotations in other sections. The network will therefore specialise for the case of one specific texture class in one image stack from the same subject. In this way, we expect to improve automation in cytoarchitectonic mapping, and to provide dense mappings for regions in whole-brain histological datasets.
800	SP2 - Integration of papaya prototype with JuBrain atlas and receptor measurements into NIP back end	*Yes*	Due to good progress with the interactive atlas viewer developed in Task 5.4.3 - which provides an open plugin architecture - and to support our ambitions to unify the viewer / front end architecture, we decided not to proceed with the integration of papaya, but instead implement the interactive access of receptor measurements directly into the interactive atlas viewer (component 2909). In this way, we performed a close co-development and co-design with SP5.
799	SP2 - Co-design of workflow for exposing high-resolution data from HPC centres to the HBP portal with metadata integration	No	Co-design of a workflow for exposing high-resolution data from remote sites (e.g. Jülich) to the HBP portal (SP5), including an agreement about data types, image service (BBIC, DVID, or similar technology), and permission management. Based on the report, a developer has a clear plan how to implement a particular scenario where large datasets from an HBP partner need to be registered and visualised in the NIP, including data transfer, conversion, curation.

3. Component Details

The following is a list of the newly released internal Components for this deliverable.

3.1 SGA1/SGA2-T2.4.3 Genetic factors contributing to inter-individual variation on morphology and architecture

Field Name	Field Content	Additional Information
ID	859	
Component Type	Data and software (JuGEx)	
Contact	CICHON, Sven	
Component Description	Individual genetic risk scores for 20 Alzheimer's Disease susceptibility variants in the 1000Brains sample. Genome-wide association data (phenotype: volume of a common neurobiological substrate (incl. dACC and insulae)) in the 1000Brains sample. JuGEx toolbox for combining gene expression data and cytoarchitectonic mapping data	
Latest Release	March 2018	
TRL	JuGEx: TRL7	
Location	data hosted by Subproject providing dataset	
Format	Txt, PLINK JuGEx: matlab script	
Curation Status	NIP curation storage	
Validation - QC	Pass	MÜHLEISEN, Thomas – already used in several analyses JuGEx tool already used for publication (Bludau *et al.* 2018)
Validation – Users	yes	Data and JuGEx already used in publication 359 downloads in the first 6 days after publication of the JuGEx Tool
Validation – Publications	Yes	Caspers, Röckner, *et al*. Pathway-specific genetic risk for Alzheimer's disease distinguishes regional patterns of cortical atrophy in older adults. Manuscript under review in Brain Structure and Function Andlauer, Mühleisen, *et al*. Genetic factors influencing the common

		neurobiological substrate for mental disorders. Manuscript *in preparation* JuGEx: Integration of transcriptomic and cytoarchitectonic data implicates a role for MAOA and TAC1 in the limbic-cortical network, Bludau, S., Mühleisen, T.W., Eickhoff, S.B. *et al.* Brain Struct Funct (2018).
Privacy Constraints	Human research	
Sharing	Not yet published -> confidential JuGex: published -> public authenticated	
License	Data: Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0) JuGEx: GNU public licence	
Component Access URL	see URLs to unpublished components JuGEx: https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/JuGEx/JuGEx.zip	
Technical documentation URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/JuGEx/JuGEx.zip	
Usage documentation URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/JuGEx/JuGEx.zip	
Component Dissemination Material URL	https://doi.org/10.1007/s00429-018-1620-6	Bludau, S., Mühleisen, T.W., Eickhoff, S.B. *et al.* (2018) Integration of transcriptomic and cytoarchitectonic data implicates a role for MAOA and TAC1 in the limbic-cortical network (2018) Brain Structure and Function

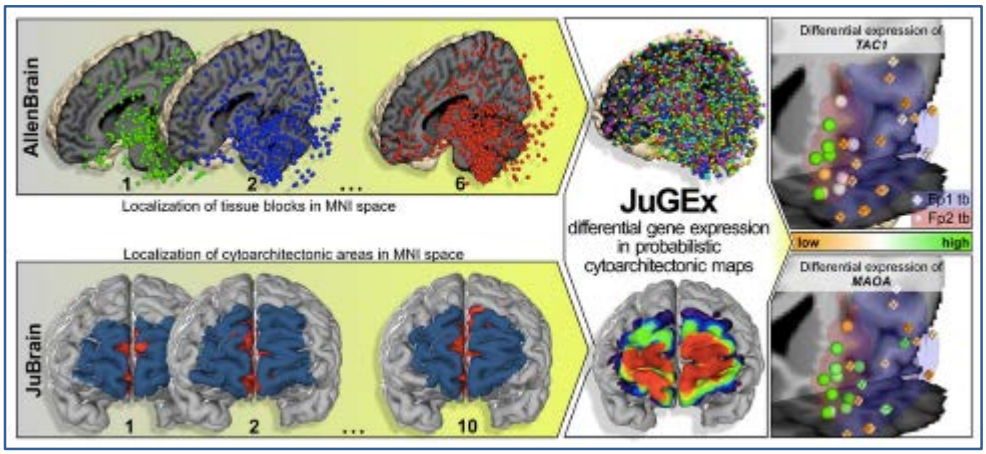

Figure 1: JuGEx

JuGEx is an integrated framework of the AllenBrain and JuBrain atlases for statistical analysis of differential gene expression in the adult human brain. The data of both atlases are based on post-mortem brains that have been scanned by MRI and transformed to a common reference brain (MNI152). The upper row displays the positions of TSs (coloured spheres) in three of six donor brains from AllenBrain. The transcriptional expression has been quantified in these TSs using oligoprobes of Agilent microarrays. The lower row shows an example of microstructural information quantified in the frontal pole areas Fp1 (blue) and Fp2 (red) in three of ten donor brains from the Jülich-Düsseldorf brain collection. To combine the data from the two modalities (transcriptome and cytoarchitecture), probabilistic JuBrain maps are used as masks to filter the TS-specific expression information as starting point for subsequent statistical analysis of differential expression of genes (JuGEx column). In the example above (far right column), we investigated the expression patterns of 25 candidate genes for Major Depressive Disorder (MDD) in the lateral Fp1 (blue) and the medial Fp2 (red). The cut outs are located at the frontal pole and display the left hemispheric part of area Fp1 and area Fp2. Analyses were performed using a permuted n-way ANOVA. Results show that TAC1 (upper panel, p = 0.0216) and MAOA (lower panel, p = 0.0292) are significantly stronger expressed in tissue samples of Fp2 (spheres) than in those of Fp1 (crosses). The mRNA expression level is indicated by a gradient running from orange (lower expression) to green (higher expression).

Figure taken from Bludau, S., Mühleisen, T.W., Eickhoff, S.B. et al. (2018) Integration of transcriptomic and cytoarchitectonic data implicates a role for MAOA and TAC1 in the limbic-cortical network (2018) Brain Structure and Function, https://doi.org/10.1007/s00429-018-1620-6

3.2 SP2 - Genetic variants and individual genomic profiles

Field Name	Field Content	Additional Information
ID	860	
Component Type	Data	
Contact	BOURGERON, Thomas	
Component Description	Genotype-phenotype relationship of patients with Phelan-McDermid syndrome (PMS), a step towards the identification of compensatory mechanisms for a better prognosis and possible treatments of patients with neurodevelopmental disorders. In a first study, we investigated 85 patients with different 22q13 rearrangements (78 deletions and 7 duplications that include the gene coding for the synaptic scaffolding protein SHANK3) and provided evidence for frequent corpus callosum abnormalities in these patients (for 10 out of 35 patients that were examined by MRI).	
Latest Release	March 2018	
TRL	NA	

Location	data hosted by Subproject providing dataset	
Format	csv, txt	
Curation Status	NIP curation storage	
Validation - QC	Pass	Published
Validation – Users	yes	
Validation – Publications	Yes	
Privacy Constraints	Human research	
Sharing	published -> public authenticated	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/MutationsGenesToASD/MutationsGenesToASD.zip	
Technical documentation URL	http://doi.org/10.1038/s41525-017-0035-2	
Usage documentation URL	http://doi.org/10.1038/s41525-017-0035-2	
Component Dissemination Material URL	http://doi.org/10.1038/s41525-017-0035-2	Tabet, A.-C., Rolland, T., Ducloy, M., Lévy, J., Buratti, J., Mathieu, A., … Bourgeron, T. (2017). A framework to identify contributing genes in patients with Phelan-McDermid syndrome. NPJ Genomic Medicine, 2, 32

3.3 SP2 – Cytoarchitectonic probability maps

Field Name	Field Content	Additional Information
ID	325	
Component Type	Data	
Contact	AMUNTS, Katrin	
Component Description	Probabilistic maps of cytoarchitectonically mapped areas – JuBrain Atlas	
Latest Release	Publicly available maps: 04.02.2016	

	Internal version: February 2018	
TRL	NA	
Location	data hosted by Subproject providing dataset	
Format	nii	
Curation Status	Tier 2 completed	
Validation - QC	Pass	publication
Validation – Users	Yes	Download of JuBrain Atlas, Citations of publications to brain areas
Validation – Publications	Yes	Areal maps are published in several publications
Privacy Constraints	Human research	
Sharing	Published, already publicly available -> public authenticated	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/JuBrain/Anatomy-v22c_update.zip https://jubrain.humanbrainproject.org Internal version including unpublished maps: see URLs to unpublished components	
Technical documentation URL	Details on the technique can be found in the related publications.	
Usage documentation URL	For SPM Anatomy Toolbox see http://www.fz-juelich.de/SharedDocs/Downloads/INM/INM-1/DE/Toolbox/Manual.pdf?__blob=publicationFile	
Component Dissemination Material URL	https://doi.org/10.1016/j.neuron.2015.12.001 https://doi.org/10.1093/cercor/bhv225	Amunts K, Zilles K. (2015) Architectonic Mapping of the Human Brain beyond Brodmann. Neuron 88:1086-107 Lorenz S *et al.* (2017) Two New Cytoarchitectonic Areas on the Human

		Mid-Fusiform Gyrus. Cerebral Cortex 27:373-385

3.4 SP2 - Preliminary investigation and characterisation of axon imaging by two-photon microscopy

Field Name	Field Content	Additional Information
ID	1582	
Component Type	Report	
Contact	COSTANTINI, Irene	
Component Description	Protocol for axon imaging by two-photon microscopy based on myelin autofluorescence in *ex vivo* mouse and rat samples	
Latest Release	M15 SGA1 (June 2017)	
TRL	NA	
Location	data hosted by Task providing dataset	
Format	tif	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	Data presented at a conference; protocol successfully applied on mouse and rat, axons imaging by two-photon microscopy was obtained
Validation – Users	Yes	The protocol will be applied in SGA2 in T2.3.4
Validation – Publications	No	
Privacy Constraints	Animal research	
Sharing	Not published - confidential	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0), when published	
Component Access URL	see URLs to unpublished components	
Technical documentation URL	Details to the technique can be found in the conference proceeding	

Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.1117/12.2284328	Irene Costantini, Miriam Menzel, Ludovico Silvestri, Nicole Schubert, Markus Axer, Katrin Amunts, Francesco S. Pavone (2017) Correlative polarized light imaging and two-photon fluorescence microscopy for 3D myelinated fibres reconstruction. Proc. SPIE 10413, Novel Biophotonics Techniques and Applications IV, 1041306

3.5 SP2 - Maps of different human neuronal circuits

Field Name	Field Content	Additional Information
ID	326	
Component Type	Data	
Contact	COSTANTINI, Irene	
Component Description	3D tiff maps of neurons labelled with different antibody: SMI32	
Latest Release	M18 SGA1 (September 2017)	
TRL	NA	
Location	data hosted by Task providing dataset	
Format	tif	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	Protocol successfully applied on mouse to obtain axons imaging by two-photon microscopy
Validation – Users	Yes	The protocol is successfully implemented and will be used in T2.3.1 in SGA2
Validation – Publications	No	In progress
Privacy Constraints	Human research	
Sharing	Not published - confidential	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0), when published	

Component Access URL	see URLs to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	NA	

3.6 SP2 - Multilevel maps of quantitative cell distributions and morphologies

Field Name	Field Content	Additional Information
ID	770	
Component Type	Data	
Contact	COSTANTINI, Irene	
Component Description	3D tiff Maps of neurons labelled with different antibodies: NeuN, PV	
Latest Release	M18 SGA1 (September 2017)	
TRL	NA	
Location	data hosted by Task providing dataset	
Format	tif	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	
Validation – Users	Yes	The protocol is successfully implemented and will be used in T2.3.1 in SGA2
Validation – Publications	No	In progress
Privacy Constraints	Human research	
Sharing	Not published - confidential	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0), when published	

Component Access URL	see URLs to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	NA	

3.7 SP2 - Multilevel maps of quantitative cell distributions and morphologies

Field Name	Field Content	Additional Information
ID	772	
Component Type	Data	
Contact	COSTANTINI, Irene	
Component Description	Mapping cellular structures onto molecular architecture using serial two photons microscopy in combination with clearing and immunostaining techniques. 3D tiff images of spatial distribution of different types of receptors together with different kind of cells, ultra-resolution imaging of receptors and subcellular structures.	
Latest Release	M24 SGA1 (March 2017)	
TRL	NA	
Location	data hosted by Task providing dataset	
Format	tif	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	
Validation – Users	Yes	The protocol is successfully implemented and will be used in T2.3.1 in SGA2
Validation – Publications	No	In progress
Privacy Constraints	Human research	
Sharing	Not published - confidential	
License	Attribution-NonCommercial-ShareAlike 4.0 International	

	(CC BY-NC-SA 4.0), when published	
Component Access URL	see URLs to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	NA	

3.8 SP2 - Quantification of multiple receptor distributions for selected areas

Field Name	Field Content	Additional Information
ID	249	
Component Type	Data	
Contact	ZILLES, Karl	
Component Description	Receptor densities (fmol/mg protein) of up to 19 different receptor binding sites for glutamate, GABA, acetylcholine, serotonin, noradrenaline, dopamine, and adenosine in primary sensory and motor cortical areas, in hippocampus, cingulate and entorhinal cortex, as well as in the basal ganglia, selected thalamic and brainstem nuclei using receptor autoradiography. Tables of the data (mean densities based on six to nine different human hemispheres), colour-coded autoradiographs, and laminar profile curves for each of the above listed brain structures.	
Latest Release	M24 SGA1 (31.03.2018)	
TRL	NA	
Location	data hosted by Subproject providing dataset	
Format	xlsx, txt, tif	
Curation Status	Tier 2	
Validation - QC	Pass	Published; regional differences in receptor densities in accordance with existing reports in the literature; multivariate analyses carried out with the data reveal a congruent relationship between regional differences in mean receptor

		expression patterns and belonging to functional neuronal systems
Validation – Users	Yes	Citations of publication
Validation – Publications	Yes	Zilles, K.; Bacha-Trams, M.; Palomero-Gallagher, N.; Amunts, K.; Friederici, A.D. (2015) Common molecular basis of the sentence comprehension network revealed by neurotransmitter receptor fingerprints. Cortex, vol 63, pp. 79-89. (Open Access)
Privacy Constraints	Human research	
Sharing	Published -> public authenticated	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/Receptors/receptors_updated.zip	
Technical documentation URL	Details to the technique (receptor autoradiography) can be found in the publication	
Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.1016/j.cortex.2014.07.007	

3.9 SGA1/SGA2_T2.1.3 Map of human fibre bundles and their microstructure

Field Name	Field Content	Additional Information
ID	339	
Component Type	Data	
Contact	POUPON, Cyril	
Component Description	Maps of bundles localisation and microstructure in MNI space	
Latest Release	2.0, January 2017	
TRL	TRL4	

Location	data hosted by Subproject	
Format	nii	
Curation Status	Tier 2	
Validation - QC	Pass	GUEVARA, Miguel Reproducibility of two subsets of the Archi database (39/39 subjects) and application on a psychiatry dataset
Validation – Users	Yes	U-bundle and long-bundle atlas used by Psychiatrists in Neurospin to study Bipolar Disorder, Autism and schizophrenia
Validation – Publications	Yes	Only conference abstracts for U-bundles
Privacy Constraints	Human research	
Sharing	Only partially published – confidential	Bundle atlas published, microstructure to be published
License	Attribution-NonCommercial-ShareAlike	
Component Access URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/hbp-data-000339/hbp-data-000339.zip	
Technical documentation URL	https://doi.org/10.1016/j.neuroimage.2016.11.066	
Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.1016/j.neuroimage.2016.11.066	Guevara M *et al.* (2017) Reproducibility of superficial white matter tracts using diffusion-weighted imaging tractography. Neuroimage 147:703-725

3.10 SP2 - 3D-PLI data for selected human anatomical structures

Field Name	Field Content	Additional Information
ID	302	
Component Type	Data	
Contact	AXER, Markus	
Component Description	3D-PLI modalities: blockface images, transmittance maps	

Latest Release	February 2018	
TRL	NA	
Location	data hosted by Task	
Format	nii, tif, pdf	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	Human research	
Sharing	Not yet published -> confidential	
License	Attribution-NonCommercial-ShareAlike	
Component Access URL	see URLs to unpublished components	
Technical documentation URL	See publications	
Usage documentation URL	See publications	
Component Dissemination Material URL	https://doi.org/10.1093/cercor/bhw010 http://ieeexplore.ieee.org/document/7950550/ http://ieeexplore.ieee.org/document/7950720/	Zeineh, M.M., Palomero-Gallagher, N., Axer, M., Gräßel, D., Goubran, M., Wree, A., Woods, R., Amunts, K., and Zilles, K. (2017). Direct Visualization and Mapping of the Spatial Course of Fiber Tracts at Microscopic Resolution in the Human Hippocampus. Cerebral Cortex 27, 1779-1794. Ali S, Rohr K, Axer M, Gräßel D, Schlömer P, Amunts K, Eils R, and Wörz S. (2017) Elastic Registration of High-Resolution 3D PLI Data of the Human Brain. Proc. IEEE Internat. Symposium on Biomedical Imaging: From Nano to Macro (ISBI 2017), Melbourne, Australia, April 18-21, IEEE Piscataway, NJ, pp 1151-1155. Ali S, Rohr K, Axer M, Amunts K, Eils R, and Wörz S. (2017) Registration of Ultra-High Resolution 3D PLI Data of Human Brain Sections to Their Corresponding High-Resolution Counterpart. Proc. IEEE Internat.

		Symposium on Biomedical Imaging: From Nano to Macro (ISBI 2017), Melbourne, Australia, April 18-21, IEEE Piscataway, NJ, pp 415-419.

3.11 SP2 - Morphological data of human neocortical pyramidal neurons

Field Name	Field Content	Additional Information
ID	327	
Component Type	Data	
Contact	MANSVELDER, Huib	
Component Description	Matching morphologies and physiologies of human pyramidal neurons	
Latest Release	December 2017	
TRL	NA	
Location	data hosted by Task providing data set	
Format	ASC, DAT	
Curation Status	Tier 2	
Validation - QC	Pass	
Validation – Users	Yes	
Validation – Publications	Yes	Deitcher *et al.* (2017) Comprehensive Morpho-Electrotonic Analysis Shows 2 Distinct Classes of L2 and L3 Pyramidal Neurons in Human Temporal Cortex. Cerebral Cortex 27:5398-5414
Privacy Constraints	Human research	
Sharing	Published – ready to be shared	
License	Attribution-NonCommercial-ShareAlike	
Component Access URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/NeuronMorphologies/EPhys_Morpho_Human_PYR.zip	
Technical documentation URL	See publication	

Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.1093/cercor/bhx226	Deitcher *et al.* (2017) Comprehensive Morpho-Electrotonic Analysis Shows 2 Distinct Classes of L2 and L3 Pyramidal Neurons in Human Temporal Cortex. Cerebral Cortex 27:5398-5414

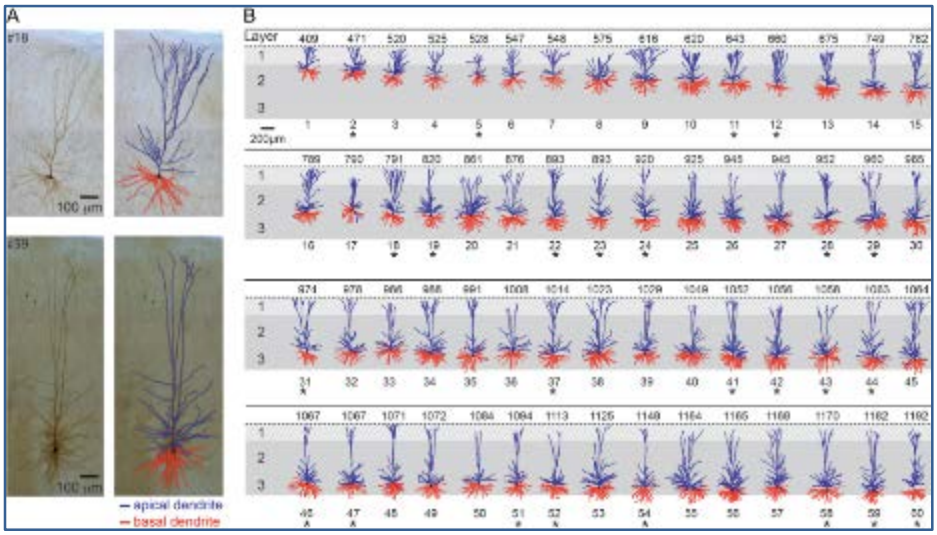

Figure 2. Pyramidal neuron reconstruction

Sixty 3D reconstructed layers 2 and 3 pyramidal cells from the human temporal cortex, arranged according to somatic depth with respect to pia surface. (A) Two exemplar cells (top, cell #18, bottom, cell #59; left: biocytin filled; right: 3D reconstruction). Apical dendrites are indicated in blue and basal dendrites in red. (B) Database used for the morphological analysis conducted in this study. The numbers on top of each cell indicate the depth from the pia in µm. The 25 neurons that were also characterised physiologically are marked by an asterisk.

Figure taken from Deitcher *et al.* (2017) Comprehensive Morpho-Electrotonic Analysis Shows 2 Distinct Classes of L2 and L3 Pyramidal Neurons in Human Temporal Cortex. Cerebral Cortex 27:5398-5414, https://doi.org/10.1093/cercor/bhx226

3.12 SP2 – 3D models of fibre tracts

Field Name	Field Content	Additional Information
ID	808	
Component Type	Data	
Contact	LÜBKE, Joachim	
Component Description	3D reconstruction and models of fibre tracts in the human brain	
Latest Release	March 2018	
TRL	NA	
Location	hosted by Task providing data set	

Format	tiff	
Curation Status	NIP curation storage	
Validation - QC	Pass	
Validation – Users	Yes	
Validation – Publications	Yes	Still in the process of data acquisition and analysis
Privacy Constraints	Human research	
Sharing	Not yet published -> confidential	
License	Attribution-NonCommercial-ShareAlike	
Component Access URL	See URL to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	NA	

3.13 SP2 - Morphological cortical connectivity profiles of neocortical pyramidal neurons

Field Name	Field Content	Additional Information
ID	328	
Component Type	Data	
Contact	MANSVELDER, Huib	
Component Description	Connections of L2/L3 pyramidal neurons and interneurons	
Latest Release	Expected mid-2018	
TRL	NA	
Location	data hosted by Task providing data set	
Format	ASC, DAT	
Curation Status	Tier 2	

Validation - QC	Pass	
Validation – Users	Yes	
Validation – Publications	Yes	Deitcher *et al.* (2017) Comprehensive Morpho-Electrotonic Analysis Shows 2 Distinct Classes of L2 and L3 Pyramidal Neurons in Human Temporal Cortex. Cerebral Cortex 27:5398-5414
Privacy Constraints	Human research	
Sharing	Published – ready to be shared	
License	Attribution-NonCommercial-ShareAlike	
Component Access URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/NeuronMorphologies/EPhys_Morpho_Human_PYR.zip	
Technical documentation URL	See publication	
Usage documentation URL	NA	
Component Dissemination Material URL	10.1093/cercor/bhx226	Deitcher *et al.* (2017) Comprehensive Morpho-Electrotonic Analysis Shows 2 Distinct Classes of L2 and L3 Pyramidal Neurons in Human Temporal Cortex. Cerebral Cortex 27:5398-5414

3.14 SGA1/SGA2 _T2.1.1 Full human brain activity maps (volumes)

Field Name	Field Content	Additional Information
ID	365	
Component Type	Data	
Contact	THIRION, Bertrand	
Component Description	Fifty maps of brain activity spanning various cognitive contrasts at 1.5mm resolution, recoded in 12 subjects (Individual brain charting project). The images are sampled in the volume.	
Latest Release	M21 (20.12.2017)	
TRL	NA	
Location	data hosted by Task providing data set	neurovault (see component access URL)

Format	nifti	
Curation Status	Tier 2 in process	
Validation - QC	Pass	
Validation – Users	Yes	The data are currently used as validation in system-level studies of brain cognition (Parietal team) or to study the existence of certain brain structures (Sarah Genon, JUELICH)
Validation – Publications	No	Paper under revision for scientific data, available under request
Privacy Constraints	Human research	
Sharing	Already publicly available - public authenticated	
License	Public Domain (CC0)	
Component Access URL	http://neurovault.org/collections/2138 See also raw data available on https://openfmri.org/dataset/ds000244/	
Technical documentation URL	http://project.inria.fr/IBC	
Usage documentation URL	http://project.inria.fr/IBC	
Component Dissemination Material URL	https://openreview.net/forum?id=BJaU__eCZ	

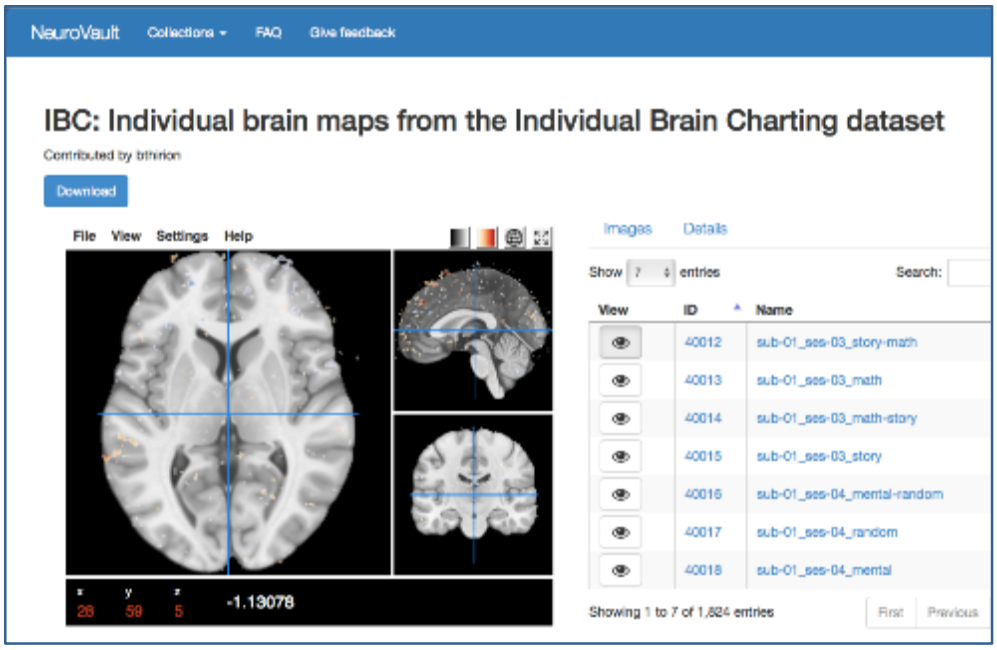

Figure 3. IBC dataset on neurovault.

See http://neurovault.org/collections/2138

3.15 SP2 - Selected multimodal regional maps with cognitive features

Field Name	Field Content	Additional Information
ID	773	
Component Type	Data	
Contact	GENON, Sarah	
Component Description	Functional parcellation and characterisation of 3 regions of interest (ROIs): 1) right dorsal premotor cortex, 2) left dorsal premotor cortex, and 3) hippocampus, evidenced by multimodal connectivity-based parcellation and functional characterisation. The subregions were identified by multimodal connectivity-based parcellation and their large-scale functional connectivity was characterised by a multi-modal approach as well.	
Latest Release	M24 SGA1 (31.03.2018)	
TRL	NA	
Location	data hosted by Task providing dataset	
Format	nifti	

Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	Publication of the first and second ROIs
Validation – Users	Yes	Citations of publication
Validation – Publications	Yes – for 1. and 2. ROI No – for 3. ROI	Genon, S., Li, H., Fan, L., Muller, V. I., Cieslik, E. C., Hoffstaedter, F., . . . Eickhoff, S. B. (2017). The Right Dorsal Premotor Mosaic: Organization, Functions, and Connectivity. Cereb Cortex, 27(3), 2095-2110. doi:10.1093/cercor/bhw065 Genon, S., Reid, A., Li, H., Fan, L., Muller, V. I., Cieslik, E. C., . . . Eickhoff, S. B. (2017). The heterogeneity of the left dorsal premotor cortex evidenced by multimodal connectivity-based parcellation and functional characterization. Neuroimage. doi:10.1016/j.neuroimage.2017.02.034
Privacy Constraints	Human research	
Sharing	Published -> public authenticated – for 1. and 2. ROI Not yet published -> confidential – for 3. ROI	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	1) ROI: http://anima.fz-juelich.de/studies/Genon_CBPrightPMd_2016 2) ROI: http://anima.fz-juelich.de/studies/Genon_LeftPMd_MultimodalCBP_2017 3) ROI: see URLs to unpublished components	
Technical documentation URL	Details to the technique/ method can be found in the publications	
Usage documentation URL	NA	
Component Dissemination Material URL	1) ROI: 10.1093/cercor/bhw065	

	2) ROI: 10.1016/j.neuroimage.2017.02.034	

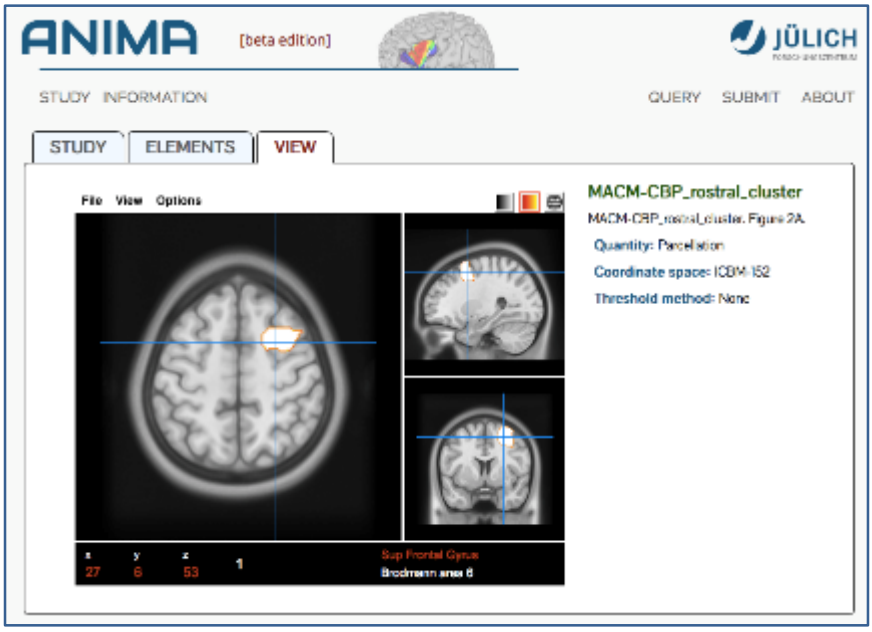

Figure 4. Anima

Rostral cluster of the functional parcellation of the right dorsal premotor cortex. See http://anima.fz-juelich.de/studies/Genon_CBPrightPMd_2016

3.16 SP2 - Computational architecture of the functional organisation in visual and auditory processing streams in human and macaque monkey

Field Name	Field Content	Additional Information
ID	789	
Component Type	Data	
Contact	VANDUFFEL, Wim ROELFSEMA, Pieter	
Component Description	1) Causal mechanisms driving visual cortical plasticity and perceptual learning in primates. Causal role of primate ventral tegmental area in cortical plasticity and perceptual learning. 2) Role of V1, V4 and frontal cortex in the awareness of weak visual stimuli.	
Latest Release	March 2018	
TRL	NA	
Location	data hosted by SP providing dataset	

Format	tiff, xlsx mat	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	Publication (Review process)
Validation – Users	No	
Validation – Publications	No	1) Publication submitted 2) Publication accepted in Science: van Vugt B, Dagnino B, Vartak D, Safaai H, Panzeri S, Dehaene S, Roelfsema PR The Threshold for Conscious Report: Signal Loss and Response Bias in Visual and Frontal Cortex.
Privacy Constraints	Animal research	
Sharing	Not yet published -> confidential	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	See URL to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	NA	

3.17 SP2 - Selective attention in perception and learning in humans and monkeys

Field Name	Field Content	Additional Information
ID	861	
Component Type	Data	
Contact	VANDUFFEL, Wim	
Component Description	Shifts of attention activate homologous areas in human and monkey superior parietal lobe	

Latest Release	January 2018	
TRL	NA	
Location	data hosted by SP providing dataset	
Format	Tiff, xlsx	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	Publication
Validation – Users	No	
Validation – Publications	Yes	
Privacy Constraints	Animal research	
Sharing	Published -> public authenticated	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	See URLs to unpublished components	
Technical documentation URL	See publication	
Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.1523/JNEUROSCI.1111-17.2017	John T. Arsenault, Natalie Caspari, Rik Vandenberghe, Wim Vanduffel (2018) Attention Shifts Recruit the Monkey Default Mode Network. Journal of Neuroscience 38:1202-1217

3.18 SP2 - Properties of excitatory neurons and GABAergic interneurons and the neuronal networks in sensory cortical areas in rodents

Field Name	Field Content	Additional Information
ID	793	
Component Type	Data	
Contact	FELDMEYER, Dirk	
Component Description	Using a correlated electrophysiological/morphological approach, we investigated the properties of excitatory neurons and GABAergic interneurons and their neuronal networks in different sensory cortical	

	areas (primary visual, auditory and somatosensory cortex) in rodent brains. This component provides electrophysiological data on synaptic physiology and 3D neuronal reconstructions.	
Latest Release	M24 SGA1 (31.03.2018)	
TRL	NA	
Location	data hosted by SP providing dataset	
Format	jpg, xls, dat	
Curation Status	NIP curation storage	
Validation - QC	Pass	Publication
Validation – Users	Yes	Citations of publication
Validation – Publications	Yes	Feldmeyer, D., Qi, G., Emmenegger, V., and Staiger, J.F. (2018). Inhibitory Interneurons and their Circuit Motifs in the Many Layers of the Barrel Cortex. *Neuroscience* 368**,** 132-151 Emmenegger, V., Qi, G., Wang, H., and Feldmeyer, D. (2018). Morphological and Functional Characterization of Non-fast-Spiking GABAergic Interneurons in Layer 4 Microcircuitry of Rat Barrel Cortex. *Cerebral Cortex*. Radnikow, G., and Feldmeyer, D. (2018). Layer- and Cell Type-Specific Modulation of Excitatory Neuronal Activity in the Neocortex. *Frontiers in Neuroanatomy* 12**,** 1.
Privacy Constraints	Animal research	
Sharing	Published -> public authenticated	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/hbp-data-000793/hbp-data-000793.zip	
Technical documentation URL	See publication	
Usage documentation URL	NA	

Component Dissemination Material URL	http://www.sciencedirect.com/science/article/pii/S0306452217303524 http://dx.doi.org/10.1093/cercor/bhx352 https://www.frontiersin.org/article/10.3389/fnana.2018.00001	

3.19 SP2 - Ultra-high field fMRI of sub-units in higher-level visual areas and face areas in human and monkey

Field Name	Field Content	Additional Information
ID	862	
Component Type	Data	
Contact	1) VANDUFFEL, Wim 2) VANDUFFEL, Wim and GOEBEL, Rainer 3) GOEBEL, Rainer	
Component Description	1) The first non-invasive (*in-vivo*) visualisation of all 3 stripe compartments (thin, thick and interstripes) in area V2 of the nonhuman primate 2) Homology and specificity of natural sound-encoding in human and monkey auditory cortex 3) Functional organisation of human multisensory STC using ultra-high field fMRI	
Latest Release	1) December 2017 2) March 2018 3) September 2017	
TRL	NA	
Location	data hosted by SP providing dataset	
Format	Tiff, xlsx, nifti	
Curation Status	Uploaded to an approved HBP data repository location/ NIP curation storage	
Validation - QC	Pass	Publication (review process)
Validation – Users	No	
Validation – Publications	1) Yes	

	2) publication submitted 3) Yes	
Privacy Constraints	Animal research Human Research	
Sharing	1) Published -> public authenticated 2) not yet published -> confidential 3) Published -> public authenticated	
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	1,2) see URL to unpublished components 3) https://object.cscs.ch/v1/AUTH_227176556f3c4bb38df9feea4b91200c/hbp-data-000862/hbp-data-000862.zip	
Technical documentation URL	See publication	
Usage documentation URL	NA	
Error! Reference source not found.	1) https://doi.org/10.1093/cercor/bhx337 3) https://doi.org/10.1523/JNEUROSCI.0146-17.2017	1) Xiaolian Li, Qi Zhu, Thomas Janssens, John T Arsenault, Wim Vanduffel (2017) In Vivo Identification of Thick, Thin, and Pale Stripes of Macaque Area V2 Using Submillimeter Resolution (f)MRI at 3 T. Cerebral Cortex 3) Gentile F, van Atteveldt N, De Martino F, Goebel R (2017) Approaching the Ground Truth: Revealing the Functional Organization of Human Multisensory STC Using Ultra-High Field fMRI. Journal of Neuroscience 37:10104-10113

3.20 SP2 - New human brain parcellations based on microscopic post-mortem and *in vivo* data

Field Name	Field Content	Additional Information
ID	248	
Component Type	Data	

Contact	MANGIN, Jean-Francois	
Component Description	Connectivity-based over-parcellation of Freesurfer Desikan atlas available at the group and individual level (80 subjects in the Archi database, 200 subjects in the HCP database)	
Latest Release	2.0, September 2017	Individual Archi parcellation, HCP group parcellation
TRL	TRL4	
Location	data hosted by SP providing dataset	
Format	gii, minf, csv, txt	
Curation Status	Tier 1	
Validation - QC	Pass	LEFRANC, Sandrine - Robustness to method's parameters, reproducibility on two subsets of the Archi database (39/39 subjects)
Validation – Users	Yes	Application to Bipolar Disorder in Cingulate area, to asymmetry studies in temporal areas. Used also to generate connectivity matrices tuned to individual subject architecture.
Validation – Publications	no	In progress
Privacy Constraints	Human research	
Sharing	Partially published -> confidential	Archi group parcellation published
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	see URLs to unpublished components	
Technical documentation URL	See publication	
Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.1016/j.media.2016.01.003	Lefranc S *et al.* (2016) Groupwise connectivity-based parcellation of the whole human cortical surface using watershed-driven dimension reduction. Medical Image Analysis 30:11-29

3.21 SP2 - Human connectivity matrix from atlas parcels

Field Name	Field Content	Additional Information
ID	340	
Component Type	Data	
Contact	MANGIN, Jean-Francois	
Component Description	Diffusion MRI-based connectivity matrices computed for the 78 Archi subjects (group-based and individual) for 3 different parcellations (AAL, Freesurfer Desikan, BrainVISA constellation tuned to connectivity)	
Latest Release	1.0, June 2017	delivered to the SP4 Barcelona group (G. Deco)
TRL	TRL4	
Location	data hosted by SP providing dataset	
Format	gii, csv, npy	
Curation Status	Tier 1	
Validation - QC	Pass	RIVIERE, Denis / ZAMORA-LOPEZ, Gorka - Data exchange and QC for compatibility with SP4 objectives
Validation – Users	Yes	SP4 Barcelona group
Validation – Publications	No	
Privacy Constraints	Human research	
Sharing	Partially published -> confidential	Group-based matrix public
License	Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0)	
Component Access URL	see URLs to unpublished components	
Technical documentation URL	See publication	
Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.1016/j.media.2016.01.003	Lefranc S *et al.* (2016) Groupwise connectivity-based parcellation of the whole human cortical surface using

		watershed-driven dimension reduction. Medical Image Analysis 30:11-29

3.22 SP2 - Crossing scales between dMRI and 3D-PLI

Field Name	Field Content	Additional Information
ID	790	
Component Type	Software	
Contact	AXER, Markus	
Component Description	Parallel software code to re-scale vector-based imaging data	
Latest Release	Feb. 2018 CORA V1.0	Runs on JURECA supercomputer at JSC, Forschungszentrum Jülich, Germany
TRL	TRL4	
Location	data hosted by SP providing dataset	
Format	pdf, nxx, h	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	Human research	
Sharing	Partially published -> confidential	
License	GNU General Public License Version	Software Freedom Law Center, “Copyleft and the GNU General Public License: A Comprehensive Tutorial and Guide” (Accessed March 3, 2017) https://copyleft.org/guide/comprehensive-gpl-guide.pdf
Component Access URL	see URLs to unpublished components	
Technical documentation URL	See publication	
Usage documentation URL	NA	

Component Dissemination Material URL	https://doi.org/10.3389/fnana.2016.00040	Axer, M., Strohmer, S., Gräßel, D., Bücker, O., Dohmen, M., Reckfort, J., Zilles, K., and Amunts, K. (2016). Estimating fiber orientation distribution functions in 3D-Polarized Light Imaging. Frontiers in Neuroanatomy 10

3.23 SP2 - Human iEEG recordings

Field Name	Field Content	Additional Information
ID	341	
Component Type	Data	
Contact	LACHAUX, Jean-Philippe	
Component Description	iEEG obtained during cognitive tasks	
Latest Release	Feb. 8 2018	
TRL	NA	
Location	data hosted by SP providing dataset	
Format	eeg, nii, csv	
Curation Status	Tier 2	Anatomical coordinates in MNI system
Validation - QC	Pass	LACHAUX Jean-Philippe
Validation – Users	Yes	Intracranial EEG researchers
Validation – Publications	No	
Privacy Constraints	Human research	
Sharing	Partially submitted for publication -> confidential	
License	Attribution-NonCommercial-ShareAlike 4.0 International	
Component Access URL	see URLs to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	

Component Dissemination Material URL	NA	

3.24 SP2 - Human Intracranial Electrophysiology Tools

Field Name	Field Content	Additional Information
ID	863	
Component Type	Software	
Contact	LACHAUX, Jean-Philippe	
Component Description	HiBoP – 3D visualisation tool for MRI and EEG recordings	
Latest Release	HiBoP 2.0.12b (Feb. 8 2018)	
TRL	TRL 4	MultiPatients/Multimodal Visualisation
Location	data hosted by SP providing dataset	
Format	exe	
Curation Status	Tier 2	Anatomical coordinates in MNI system
Validation - QC	Pass	LACHAUX Jean-Philippe
Validation – Users	Yes	Intracranial EEG researchers
Validation – Publications	No	
Privacy Constraints	No privacy constrains	
Sharing	Not yet published -> confidential	
License	Attribution-NonCommercial-ShareAlike 4.0 International	
Component Access URL	see URLs to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	https://www.youtube.com/watch?v=ShvEzf8eXUk	

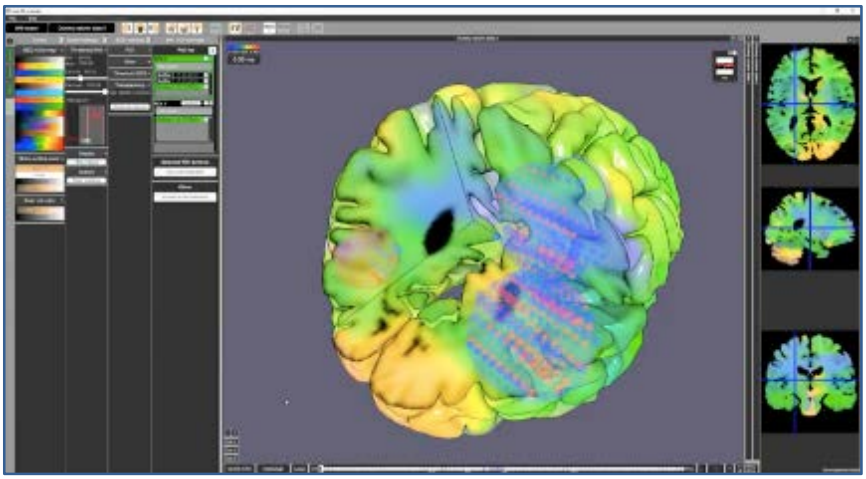

Figure 5. HiBoP

HiBoP - 3D visualisation tool for MRI and EEG recordings

3.25 SP2 - Shape and appearance models for human brain variability

Field Name	Field Content	Additional Information
ID	342	
Component Type	Software	
Contact	ASHBURNER, John BALBASTRE, Yael	
Component Description	Shape-Toolbox to optimally align MR image data. Combines rigid-body with diffeomorphic deformations. Deformations are constructed from principal modes of variation of velocity field plus an additional subject-specific velocity field (residual velocity).	
Latest Release	M23 SGA1 (February 2017)	• Shape variability model (no appearance). • No shape domain reduction (residual field). • Integrated rigid alignment. • Input images can have different dimensions.
TRL	TRL3/4	
Location	GitHub	
Format	Matlab package	
Curation Status	NA	
Validation - QC	Pass	Tested by developer
Validation – Users	Yes	

Validation – Publications	No	Paper submitted to MICCAI conference
Privacy Constraints	No privacy constrains	
Sharing	Already publicly available	
License	GNU General Public License 3.0	
Component Access URL	https://github.com/WTCN-computational-anatomy-group/shape-toolbox	
Technical documentation URL	with code	
Usage documentation URL	with code	
Component Dissemination Material URL	NA	

3.26 SP2 - Improved version of sulcus-based cross modality alignment toolbox

Field Name	Field Content	Additional Information
ID	795	
Component Type	Software	
Contact	MANGIN, Jean-Francois	
Component Description	Toolbox DISCO embedded in the brainvisa suite (http://brainvisa.info)	
Latest Release	3.0	Deliver vector fields to align any pair of brains involved in the process independently of SPM and BrainVISA.
TRL	TRL4	
Location	data hosted by SP providing dataset	
Format	Matlab script	
Curation Status	Tier 1	
Validation - QC	Pass	LEBENBERG, Jessica -

		Generate vector field aligning 7 post-mortem brains from different sources: Juelich, BigBrain, Archi database, ICBM atlas, Colin brain, Infant brains and foetus brains.
Validation – Users	Yes	Timo Dickscheid (SP2 JUELICH): alignment of the Jubrain to the Bigbrain for Bayesian prior of deep learning-based histological mapping. Brain development team of Neurospin (J Dubois, SP2 ramp-up)
Validation – Publications	Yes	Conference abstracts
Privacy Constraints	No privacy constrains	
Sharing	Not yet published -> confidential	Paper under review, and waiting for a dedicated release of Brainvisa suite
License	Attribution-NonCommercial-ShareAlike	
Component Access URL	See URLs to unpublished components	
Technical documentation URL	http://brainvisa.info	
Usage documentation URL	http://brainvisa.info	
Component Dissemination Material URL	https://doi.org/10.1016/j.media.2016.06.008	Overview only

3.27 SP2 - Robust matching procedure for incomplete sets of microstructures detected at different scales

Field Name	Field Content	Additional Information
ID	797	
Component Type	Software	
Contact	DICKSCHEID, Timo	
Component Description	A library to match microstructural landmarks extracted from histological sections based on appearance and spatial constraints, which exploits a coarse pre-alignment as well as the coplanarity of the	

	features, to overcome the inherent difficulty of matching tissue microstructures with poor distinctiveness.	
Latest Release	Not yet released	
TRL	TRL4	
Location	GitHub	
Format	Python	
Curation Status	NA	
Validation - QC	Pass	HAAS, Sarah - manual testing passed
Validation – Users	No	
Validation – Publications	Yes - The software has been used to compute a 3D reconstruction of the human subthalamic nucleus from ~400 cell-stained sections. This work has been presented at OHBM 2016.	Bludau, S., Dickscheid, T., Iannilli, F., and Amunts, K. (2016). Bludau S, Dickscheid T, Iannilli F, Amunts K (2016). 3D-reconstruction of cell distributions in the human subthalamic nucleus at 1 micron resolution. Publication *in preparation*.
Privacy Constraints	No privacy constrains	
Sharing	Publicly available	
License	Apache 2.0	
Component Access URL	https://github.com/FZJ-INM1-BDA/colamatch	
Technical documentation URL	https://github.com/FZJ-INM1-BDA/colamatch	
Usage documentation URL	https://github.com/FZJ-INM1-BDA/colamatch	
Component Dissemination Material URL	NA	Publication *in preparation*

3.28 SP2 - Classifier for microstructural landmarks that can be used for cross-scale alignment of PLI data

Field Name	Field Content	Additional Information
ID	796	
Component Type	Software	
Contact	DICKSCHEID, Timo AXER, Markus	
Component Description	A machine-learning based classifier that robustly detects vessel-like structures as typical microstructural landmarks in cell stained histological sections that can be found at different scales and across a range of consecutive sections. Although we intended to focus on data from a polarisation microscope / large area polarimeter in the original work plan, we shifted focus to the case of cell stained sections. We addressed the PLI alignment in a cooperation with Karl Rohr, Heidelberg, see Ali, S., Rohr, K., Axer, M., Amunts, K., Eils, R., and Wörz, S. (2017). Registration of ultra-high resolution 3D PLI data of human brain sections to their corresponding high-resolution counterpart. In 2017 IEEE 14th International Symposium on Biomedical Imaging (ISBI 2017), pp. 415–419.	
Latest Release	Not yet released	
TRL	TRL4	Technology validated in the lab
Location	GitHub	
Format	Python	
Curation Status	NA	
Validation - QC	Pass	Manual testing passed - HAAS, Sarah
Validation – Users	No	
Validation – Publications	The software has been used to compute a 3D reconstruction of the human subthalamic nucleus from ~400 cell-stained sections. This work has been presented at OHBM 2016.	Bludau, S., Dickscheid, T., Iannilli, F., and Amunts, K. (2016). Bludau S, Dickscheid T, Iannilli F, Amunts K (2016). 3D-reconstruction of cell distributions in the human subthalamic nucleus at 1 micron resolution.
Privacy Constraints	No privacy constrains	
Sharing	Publicly available	

License	Apache 2.0	
Component Access URL	https://github.com/FZJ-INM1-BDA/demics	
Technical documentation URL	https://github.com/FZJ-INM1-BDA/demics	
Usage documentation URL	https://github.com/FZJ-INM1-BDA/demics	
Component Dissemination Material URL	NA	Publication *in preparation*

3.29 SP2 - Simulated tissue/fibre models

Field Name	Field Content	Additional Information
ID	875	
Component Type	Data	
Contact	AXER, Markus POUPON, Cyril	
Component Description	Dictionary of synthetic datasets providing a broad spectrum of modelled, realistic fibre arrangements using PLI and dMRI	
Latest Release	February 2018	
TRL	NA	
Location	data hosted by Task providing dataset	
Format	txt, png	
Curation Status	Uploaded to an approved HBP data repository location	
Validation - QC	Pass	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	Human Research	

Sharing	Not yet (completely) published -> confidential	
License	Attribution-NonCommercial-ShareAlike	
Component Access URL	See URL to unpublished components	
Technical documentation URL	see publication	
Usage documentation URL	NA	
Component Dissemination Material URL	https://doi.org/10.3389/fphy.2018.00012	Kévin Ginsburger, Fabrice Poupon, Justine Beaujoin, Delphine Estournet, Felix Matuschke, Jean-François Mangin, Markus Axer and Cyril Poupon (2018) Improving the Realism of White Matter Numerical Phantoms: A Step toward a Better Understanding of the Influence of Structural Disorders in Diffusion MRI, Frontiers in Physics

3.30 SP2 - Cell counts, cell and vascular segmentation for selected areas in human

Field Name	Field Content	Additional Information
ID	250	
Component Type	Software	
Contact	SILVESTRI, Ludovico MAZZAMUTO, Giacomo	
Component Description	ZetaStitcher: a tool designed to stitch large volumetric images such as those produced by Light-Sheet Fluorescence Microscopes. BCFind2: a tool for point-neuron localisation using semantic deconvolution and mean shift HNeuronSegmentation: a tool for neuron segmentation in human brain tissue	
Latest Release	M21 SGA1 (December 2017)	
TRL	TRL4	
Location	ZetaStitcher: GitHub	

	BCFind2 & HNeuronSegmentation: HBP Collab and lab storage space	
Format	Python script	
Curation Status	NA	
Validation - QC	Pass	The software tools have been used successfully in T2.2.2, T1.3.1, T1.3.3
Validation – Users	Yes	The protocol is successfully implemented and will be used in T2.3.1 in SGA2
Validation – Publications	ZetaStitcher: Published BCFind2: Not yet published HNeuronSegmentation: Not yet published	
Privacy Constraints	No privacy constrains	
Sharing	ZetaStitcher: Published – public authenticated BCFind2: Not yet published - confidential HNeuronSegmentation: Not yet published - confidential	
License	ZetaStitcher: GPLv3 (GNU General Public License version 3) BCFind2: to be determined HNeuronSegmentation: to be determined	
Component Access URL	ZetaStitcher: https://github.com/lens-biophotonics/ZetaStitcher BCFind2 and HNeuronSegmentation: URLs to unpublished components	
Technical documentation URL	https://lens-biophotonics.github.io/ZetaStitcher/	
Error! Reference source not found.	https://lens-biophotonics.github.io/ZetaStitcher/	
Error! Reference source not found.	NA	The work was presented at the HBP Summit 2017

3.31 SP2 - Workflow for automatic prediction of annotations in high-resolution histological sections across consecutive slices

Field Name	Field Content	Additional Information
ID	801	
Component Type	Software	
Contact	DICKSCHEID, Timo	
Component Description	Implementation of a novel workflow to predict missing annotations in high-resolution images of histological series. The workflow is based on a deep neural network architecture which is suitable for image segmentation tasks, and uses a sparse set of manual annotations in some slices of the same stack as the training data to predict the same annotations in other sections. The network is therefore specialised for cases of one specific texture class in one image stack from the same subject. In this way, we improved automation in cytoarchitectonic mapping, and we can provide dense mappings for regions in whole-brain histological datasets.	
Latest Release	Not yet released	
TRL	TRL3	Experimental proof of concept
Location	data hosted by Task providing dataset (sciebo.de)	
Format	Python	
Curation Status	NA	
Validation - QC	Pass	Manual testing passed - SCHIFFER, Christian (JUELICH)
Validation – Users	Validation of results in the lab for human area V1, V2	KIEWITZ, Kai (UDUS)
Validation – Publications	No	
Privacy Constraints	No privacy constrains	
Sharing	Not yet published – do not share	
License	Apache 2.0	
Component Access URL	See URLs to unpublished components	

Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	NA	

3.32 SP2 - Integration of papaya prototype with JuBrain atlas and receptor measurements into NIP back end

Field Name	Field Content	Additional Information
ID	800	
Component Type	Software	
Contact	DICKSCHEID, Timo	
Component Description	Due to significant progress in the development of the interactive atlas viewer (developed in Task 5.4.3) - which provides an open plugin architecture - and to support our ambitions to unify the viewer / front end architecture, we decided not to proceed with the integration of papaya, but instead to implement the interactive access of receptor measurements directly into the interactive atlas viewer (component 2909). In this way, we performed a close co-development and co-design with SP5.	
Latest Release	Not yet released	
TRL	TRL6	
Location	data hosted by Task providing dataset (sciebo.de)	
Format	Java script	
Curation Status	NA	
Validation - QC	Pass	Manual testing passed – GUI, Xiaoyun (JUELICH)
Validation – Users	A pre-release of the software was demonstrated in a hands-on session during the HBP summit in Glasgow. Currently, the software is tested more intensively with neuroscientists in JUELICH.	
Validation – Publications	No	Abstract submitted to OHBM 2018, requesting a software demo booth to

		run a hands-on demonstration of the tool.
Privacy Constraints	No privacy constrains	
Sharing	Not yet published – do not share	
License	Apache 2.0	
Component Access URL	See URLs to unpublished components	
Technical documentation URL	NA	
Usage documentation URL	NA	
Component Dissemination Material URL	NA	

3.33 SP2 - Co-design of workflow for exposing high-resolution data from HPC centres to the HBP portal with metadata integration

Field Name	Field Content	Additional Information
ID	799	
Component Type	Report	
Contact	DICKSCHEID, Timo	
Component Description	Co-design of a workflow for exposing high-resolution data from remote sites (e.g. Jülich) to the HBP portal (SP5), including an agreement about data types, image service (BBIC, DVID, or similar technology), and permission management. Based on the report, a developer has a clear plan how to implement a particular scenario where large datasets from an HBP partner need to be registered and visualised in the NIP, including data transfer, conversion, curation. This component has been accidentally classified as 'software', and changed to 'report'. The work has been carried out in a co-design manner at different levels: 1) By contributing analysis and infrastructure testing to SP7 requirements, documented in MS7.2.2 ("User requirements analysis for hierarchical data store software") and MS7.2.5 ("Prototypical implementation of registration pipeline running on HPAC Platform")	

	2) By contributing analysis and infrastructure testing to SP5 requirements, documented in MS5.4.6 (“Preliminary NIP image format standardisation document”)

4. Conclusion and Outlook

During SGA1, SP2 has made significant progress on the six Key Results - human neurogenomics, morphology and architecture of the human brain, function and variability, comparative computational architecture of multi-modal processing streams, integrative maps and models, and co-design/methods and Big Data analytics (for details see section 3 and 4). Results were presented on 58 international conferences/symposia/workshops and published in 68 publications within the second year of SGA1.

SP2 researchers used a broad range of techniques and methodologies to investigate and generate data of the different levels and scales of the brain. These multi-modality and multi-scalability are necessary to understand the complex organisation of the human brain. The SGA1 phase was a key to strengthen the understanding and collaboration between these groups to bridge the levels and understand their connections and dependencies. Furthermore, collaboration with the other SPs led to outstanding results, e.g. simulation of Pyramidal Neurons (SP2/SP4/SP6, see Deitcher *et al.* 2017), development of the HBP Atlas through CDP3 (SP2/SP5), development of a visuo-motor integration model by CDP4 (SP2/SP4/SP10) and high-performance computing to analyse the brain's microstructure: nerve fibres and tracts (SP2/SP7).

Collaboration with the Neuroinformatics Platform (NIP), mainly driven by CDP3, improved developments to make data available and usable for the scientific community via the HBP Human Brain Atlas, part of the NIP (https://www.humanbrainproject.eu/en/explore-the-brain/atlases/). In SGA1, first datasets (e.g. JuBrain, receptors and iEEG recordings) are now curated in the NIP. The development of the atlas was and is highly dynamic, involving enormous efforts from experts from the different disciplines: it was built from scratch, and now includes reference data from SP2 and other SPs. Nevertheless, the functionality and service of the NIP needs to be further developed to allow a quick and easy integration of neuroscientific data. Remarkable progress has been made in the development of innovative viewers and spatial alignment of different imaging data and spaces to make the data available and usable through a user-friendly interface, which is a great example of a successful co-design process (CDP3). The first version of the multi-modal HBP Human Brain Atlas will be delivered in close collaboration with SP5 by the end of SGA2. To this goal SP2 and SP5 have to put great efforts in SGA2 from the conceptional and neuroinformatics side. Thus, the HBP Human Brain Atlas will be a unique, powerful and unified framework for multi-modal and multi-scale analyses addressing the brain's complexity, available for users within the HBP and the general scientific community. It is highly competitive compared to other efforts, e.g. in the US, and is a key element of a larger effort towards a Cellular Level 3D Coordinate Frameworks for the Human Brain (workshop in Washington, 31 March 2018). The next phase will build on these tools, enrich the atlas with new data sets, increase the functionalities, while taking into account user feedback, and integrate new partners, which are coming in through the Open Calls. Finally, we will transfer our data and link it to data from patients with brain diseases (Medical Informatics Platform).

A further highlight of the next phase will be the development of a multimodal model of the hippocampus by our joint efforts. Its complexity, its multi-level and multi-scale organisation, the relevance for a large number of brain diseases, and inter-species comparison, make it an extremely interesting and challenging project. SP2 will apply and centralise its entire spectrum of methods and techniques on this region to provide a unique, new, rich dataset of the hippocampus for the HBP Human Brain Atlas. It will include cytoarchitectonics, the molecular architecture obtained through receptor autoradiography, 3D Polarised Light Imaging, Two-Photon-Fluorescence Microscopy, electrophysiology, functional and diffusion MRI. Some of the methods will be applied in one and the same brain.

A unique project has been designed for the next phase to reconstruct the brain's nerve fibre architecture from the system's level (i.e. long-distance pathways) down to the cellular level (i.e. individual axons) in one and the same brain samples. A spatial range between centimetres to sub-micrometres will be bridged by means of a true multi-modal multi-scale approach using i) high-field and strong gradient diffusion MRI (dMRI), ii) 3D-Polarised Light Imaging (3D-PLI), and iii) Two-

Photon-Fluorescence Microscopy (TPFM). dMRI enables whole-human brain scanning at the macro-scale (>200 microns) without sectioning, while 3D-PLI can cover a whole human brain from the meso- to the micro-scale (>1 micron and <100 micron), based on sectioning. Ultimately, TPFM can reveal the fibre architecture within individual brain sections at the sub-micrometre scale (<1 micron).

SP2 will strengthen its expertise on the field of cross-species single cell genomics by a joined call with SP1 – Mouse Brain Organisation. Furthermore, SP2 will contribute to two further co-design projects in the fields of goal-directed navigation and the virtual brain (thevirtualbrain.org) selected by a Call for Expression of Interest. CDP4 will be continued in SGA2 to extend the already successful collaboration between SP2, SP4, SP6 and SP10 in the field of visuo-motor integration (see CDP4 Deliverable).

From an organisational point of view, most of the PIs will continue their work during the next phase to enrich and expand the already generated datasets, many of them are generated over a large time span, and are strongly supported by the respective institutions. Three partners, who were less active, or whose research does not fit within the next phase, will not contribute to SGA2. SP2 will benefit from the Open Calls, and become host SP for new partners, which will strengthen our efforts in the field of mapping, visuo-spatial navigation, genetics, and molecular neuroscience.