

MOUSE BRAIN ORGANISATION

SP1

What we do

Human and animal brains share many characteristics, but it is more difficult for scientists to work on the former; there are experiments that cannot be done on humans for ethical reasons and so they are done on mice instead.

The human brain shares with other non-human mammals many common features, which can be considered as basic building blocks of brain organisation. Therefore, choosing appropriate experiments to obtain strategic data that can be extrapolated to the human brain is a major goal in SP1. For this purpose, many neuroscientists suggest that the ideal experimental animals at present are rodents, because they can be manipulated to study many aspects from genes to behaviour. Furthermore, we can use relatively large numbers of animals at a relatively low cost.

The next challenge is what can be done with the data and how can it be interpreted. It seems that the most appropriate approach to better understand the brain is to link detailed structural data of the whole brain with genetic, molecular, cellular and physiological data. This integration allows the generation of models that present the data in a form that can be used to rationalise, make predictions and suggest new hypotheses to discover new aspects of the structural and functional organisation of the brain.

How we are organised

WP1.1 SUBCELLULAR AND MOLECULAR. Many different levels of molecular data are required to understand the function of single cells, circuits and brain function. This WP will therefore generate, obtain and integrate data at various subcellular and molecular levels. Since the initial phase of the Project, rapid technological advances have enabled this type of data to be analysed at in much greater detail, and some of these methods have meant that diversity across many cells, brain regions and the whole brain can be mapped.

WP1.2 CELL AND MICROCIRCUITRY. This WP aims to carry out novel analyses in order to generate the data needed for validated high-fidelity brain models. The work concentrates on four major brain regions: the neocortex, hippocampus, basal ganglia, and cerebellum. The data generated include the number and spatial distribution of neurons, glia, and specific types of synapses, as well as correlation between morphology and physiology.

WP1.3 WHOLE BRAIN. We propose to go beyond the state of the art by investigating meso-scale (millimetres to centimetres) multilevel maps of the mouse brain through an integrated view of anatomy and

functionality. In terms of anatomy, the intention is to determine the spatial distribution of different cell types, based on the expression of certain proteins, across the entire brain, and to refine the maps produced according to different neuronal types. This will be complemented by imaging of cortical functionality, investigating the functional connectivity involved when specific tasks are performed.

WP1.4 INTEGRATION OF MICRO-ANATOMICAL DATA. The various datasets produced by SP1 will be integrated in this WP; integration of external datasets that complement the core data produced by SP1 will also take place. Statistical modelling will reveal relationships between the various datasets that will be crucial for modelling and simulation activities in other HBP Subprojects such as SP4 and SP6. We will also use statistical and machine learning techniques to deduce principles of neuron morphology and neuroanatomical organisation.

WP1.5 MANAGEMENT AND SCIENTIFIC COORDINATION. This WP aims to ensure that work within SP1 is carried out according to the planned objectives and to coordinate HBP research on strategic mouse brain data, ensuring that the work is efficiently organised and documented and that the research contributes to the overall HBP goals.

SP LEADER Javier DeFELIPE

DEPUTY SP LEADER Egidio D'ANGELO

WORK PACKAGE LEADERS

- WP1.1 Subcellular and Molecular: **Antonino CATTANEO**
- WP1.2 Cell and Microcircuitry: **Javier DeFELIPE**
- WP1.3 Whole Brain: **Francesco PAVONE**
- WP1.4 Integration of Micro-Anatomical Data: **Douglas ARMSTRONG**
- WP1.5 Management and Scientific Coordination: **Javier DeFELIPE**

SP MANAGER Pilar FLORES ROMERO

Publication highlights

Miki T, Kaufmann WA, Malagon G, Gomez L, Tabuchi K, Watanabe M, *et al.* *Correspondence between presynaptic Ca²⁺ channel clusters and functionally defined vesicular docking sites in single central synapses.* Proc Nat Acad Sci USA 2017;114:E5246-E5255. DOI: 10.1073/pnas.1704470114.

Schmid F, Barrett MJP, Jenny P, Weber B. *Vascular density and distribution in neocortex.* NeuroImage 2017; pii: S1053-8119(17)30516-5. DOI: 10.1016/j.neuroimage.2017.06.046.

Eyal G, Verhoog MB, Testa-Silva G, Deitcher Y, Lodder JC, Benavides-Piccione R, *et al.* *Unique membrane properties and enhanced signal processing in human neocortical neurons.* eLife 2016;5:e16553. DOI: 10.7554/eLife.16553.

Kohus Z, Káli S, Rovira-Esteban L, Schlingloff D, Papp O, Freund TF, *et al.* *Properties and dynamics of inhibitory synaptic communication within the CA3 microcircuits of pyramidal cells and interneurons expressing parvalbumin or cholecystokinin.* J Physiol 2016;594:3745–3774. DOI: 10.1113/JP272231.

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<https://www.humanbrainproject.eu/en/about/project-structure/subprojects/>

