

Multimodal brain mapping: Integration of cytoarchitecture, functional imaging, receptor distribution, and ultra-high resolution fibre tract imaging

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Transmitter receptors are key molecules of neurotransmission and connectivity. Their *regionally specific distribution patterns* differ between sensory, motor and multimodal association areas as well as between various areas within each of these major functional groups. The receptor-based regional segregation of the cerebral cortex is further differentiated by the *layer specific distribution patterns* of receptor densities. Thus, mapping of transmitter receptor distributions provides data for understanding the molecular basis of cortical organization and connectivity.

Borders of cortical areas and layers can be precisely defined by localized changes of the density of single or multiple receptor types calculated in single cortical layers or averaged over all layers. In most cases, receptorarchitectonic borders are found at precisely the same positions, where borders are also detectable in cytoarchitectonic, axonal tracing or functional neuroimaging studies as well as analysis of fibrearchitecture. Motor and multimodal cortices have a completely different, but regionally typical laminar distribution pattern. Receptorarchitectonics can also reveal hitherto unknown cortical areas (e.g., in the Broca region). Furthermore, distribution patterns of multiple receptors in each single area show a specific balance between the various receptors, i.e. the “receptor fingerprint”. The cluster analysis of fingerprints of cortical areas reveals segregated systems belonging to different functional modalities and embedded in a hierarchical organization. In conclusion, regional and laminar multiple receptor distribution patterns provide a comprehensive overview of known and novel organizational principles.

I will also present images resulting from a novel ultra-high resolution technique with an in-plane resolution of 1 μm based on the birefringent properties of myelinated fibers and polarization microscopy. The polarized light imaging (PLI) of cryosections through human and animal brains enables the detection of fibres and their spatial orientation at an in-plane resolution of 1.3 μm . The crossing of nerve fibres is directly visible as well as the course of diffuse fibers and the complete myeloarchitecture in the cerebral cortex and subcortical nuclei. Moreover, fibres with the same or similar orientation can be selectively visualized greatly enhancing the interpretation of these images. In conclusion, PLI provides a novel and – compared to DI - completely independent approach for the comprehensive analysis of the spatial course of nerve fibres in the grey and white matter of the brain at ultra-high spatial resolution. Parallel DI and PLI studies can, thus, be used to evaluate the strengths and restrictions of both methods. Moreover, PLI is a bridge between fibre imaging and axonal tract tracing studies. The latter technique demonstrates synaptic connectivity, i.e. the link between structural and functional connectivity.