MAX PLANCK INSTITUTE
FOR HUMAN COGNITIVE AND BRAIN SCIENCES

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Institute Colloquium

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Mapping iron accumulation in the human brain: towards biomarkers with cellular specificity

Iron plays a central role in brain development and brain aging. Transmission of neuronal signals, optimization and maintenance of brain structure demand substantial energy and require iron as co-factor for energy supply, myelination and neurotransmitter synthesis. However, iron turns toxic and harmful when present in certain chemical forms and at high concentrations. Increased iron accumulation in age leads to faster brain decline, diminished cognitive abilities and increased risk of neurodegenerative diseases. Understanding these mechanisms and following iron trajectories both on the cellular and the whole brain level is key to an in-depth understanding of brain development, plasticity and aging.

Magnetic Resonance Imaging (MRI) is the method of choice for in vivo studies of the iron distribution in the human brain. Relaxation rates and susceptibility measurements provide a wealth of information on both the quantity and distribution of iron. It can potentially access iron dispersion down to the cellular level and provide unique information on the iron chemistry. I propose an innovative approach that combines multimodal quantitative MRI at 3T and 7T with biophysical modeling informed by quantitative iron histology. Thereby, brain tissue composition and cellular iron distribution can be linked to quantitative MRI measures. Two applications are selected to demonstrate how knowledge on MR contrast mechanisms can be employed to create sensitive and specific biomarkers of cellular iron distribution. The first example is a study in superficial white matter, where iron is accumulated in oligodendrocytes and potentially in the short association fibres. It is shown that iron in superficial white matter is not homogeneously distributed across the brain, but accumulated in iron deposits in U-fibre-rich frontal, temporal and parietal association areas. This observation is assigned to higher fibre density or late myelination.

In the second study, dopaminergic neurons in substantia nigra are mapped. This information is a first step towards a specific in vivo biomarker for the density of dopaminergic neurons and may therefore provide a future diagnostic for Parkinson's disease.