MAX PLANCK INSTITUTE
FOR HUMAN COGNITIVE AND BRAIN SCIENCES

Monday, September 12, 2022, 15:00 hrs
Zoom Meeting

Institute Colloquium

Malte Brammerloh

Department of Neurophysics

Iron-induced transverse MRIrelaxation in the substantia nigra: Biophysical modeling fosters anatomical interpretation

The loss of dopaminergic neurons in the substantia nigra leads to the primary motor symptoms of Parkinson's disease but starts more than ten years before diagnosis. Dopaminergic neurons contain iron in the pigment neuromelanin. Thus, iron-sensitive MRI promises to map these neurons and their loss. However, the exact mechanisms of MRI contrast in the substantia nigra are not well understood, hindering the development of robust biomarkers. We propose and validate a biophysical model of iron-induced transverse MRI relaxation in the substantia nigra, combining quantitative 3D iron histology with ultra-high-field and -resolution post mortem MRI. We quantify a missing but central parameter of this model, the susceptibility of neuromelanin-bound iron, using quantitative susceptibility mapping at cellular resolution. We demonstrate that iron in dopaminergic neurons, although being only a tiny fraction of all tissue iron, contributes predominantly to iron-induced effective transverse relaxation rate R2* and propose biomarkers of this iron pool. We leverage our understanding of iron-induced transverse relaxation to revisit the interpretation of a potent diagnostic marker of Parkinson's, the swallow tail sign. Our results provide directions for developing biomarkers for early detection of dopaminergic neuron depletion in Parkinson's disease.