Ironsleep Abstract

The early stage of Parkinson's disease (PD) is characterized by dopaminergic dysfunction, synuclein and iron deposits and neuronal loss in small brain nuclei, which also regulate sleep and wakefulness. Alterations in Rapid Eye Movement (REM) sleep behaviour disorder (RBD) are among the earliest preclinical signs of progressing PD, while restless leg syndrome (RLS), often accompanied by Periodic Limb Movements (PLMS) during sleep, is associated with increased risk for PD. However, the pattern and the spread of PD pathology at preclinical stages and their link to the early preclinical symptoms progression remain largely unknown. This fragmentary knowledge is due, to a great extent, to complex and heterogeneous interactions between subcortical structures, their unexplored anatomy and the absence of non-invasive neuroimaging methods to detect and monitor disease progression within these small structures at early preclinical stages. In this interdisciplinary project, cutting-edge developments in ultrahigh resolution quantitative neuroimaging at 7T and recent advances in neuroanatomical techniques will be combined with state-of-the-art sleep research and genetics to unravel degeneration of subcortical nuclei in preclinical PD and associate them with REM sleep alterations. We will determine subtle anatomical changes in the substantia nigra and locus coeruleus, central to PD, and characterize sleep in healthy individuals with known polygenic risk for PD and in patients with RBD and RLS/PLMS and in PD patients. Using recently proposed neuroimaging biomarkers of cellular density of dopaminergic cells in substantia nigra we will establish a specific early-stage PD-risk assessment method. Importantly our approach will be based on prior exploration of existing neuroimaging datasets of healthy (N > 500) and clinical cohorts (N >500) and acquisitions of new qMRI data (N = 350) on well characterized cohorts and will constitute a novel invaluable open database. Critically, the project will facilitate translation of 7T findings to clinical practice by including data collected with clinically available 3T MRI. IronSleep will provide unprecedented development for high resolution neuroimaging biomarkers of early stage PD, unravelling patterns, mechanisms and dynamics of the spread of PD neuropathology and its relation to sleep disorders and arming clinicians with new PD detection tools.