

## Research Project

Computer aided Methods for Diagnosis and Early Risk Assessment for Parkinson's Disease Dementia

## Third-party funded project

**Project title** Computer aided Methods for Diagnosis and Early Risk Assessment for Parkinson's Disease Dementia

Principal Investigator(s) Roth, Volker;

Co-Investigator(s) Calabrese, Pasquale; Fuhr, Peter; Gschwandtner, Ute;

Organisation / Research unit

Departement Mathematik und Informatik / Biomedical Data Analysis (Roth)

Departement Psychologie / Health & Intervention

Department

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Neurodegenerative disorders begin insidiously in midlife and are relentlessly progressive. Currently, there exists no established curative or protective treatment, and they constitute a major and increasing health problem and, in consequence, an economic burden in aging populations globally. Parkinson's disease (PD), following Alzheimer's disease (AD), is the second most common neurodegenerative disorder worldwide, estimated to occur in approximately 1% of population above 60 and at least in 3% in individuals above 80 years of age. In Switzerland, about 15'000 persons are diagnosed with PD. In addition to motor signs, which due to recent medical progress can be treated satisfactorily in most cases, non-motor symptoms and signs severely affect the well-being of patients. They include mood disorders, psychosis, cognitive decline, disorders of circadian rhythms, as well as vegetative and cardiovascular dysregulation. Neurodegeneration in PD progresses for years before clinical diagnosis is possible, at which time e.g. 80% of dopaminergic neurons in the Substantia nigra are lost already. Therefore, any clinical targeting disease modification, prognosis and personalized treatment including guiding the indication for deep brain stimulation (DBS) requires reliable and valid biomarkers. The main goal of this research project is the identification of a pertinent set of genetic and

neurophysiological markers for diagnosis and early risk assessment of PD-dementia. Our approach has a distinct interdisciplinary basis, in that it fosters close collaborations between physicians, neuroscientists, psychiatrists, psychologists, computer scientists and statisticians. Based on current research findings we postulate that a combination of (1) quantitative electroencephalographic measures (QEEG, e.g. frequency power and connectivity patterns and network analysis), (2) genetic biomarkers (e.g. MAPT, COMT, GBA, APOE) and (3) neuropsychological assessment improves early recognition and monitoring of cognitive decline in PD. To test this hypothesis, this project proposes an interdisciplinary long-term study of patients diagnosed with PD without signs of dementia, among them a subgroup of patients undergoing DBS.

The workup of the proposed study includes collection of clinical, neuropsychological, neurophysiological and genotyping data at the baseline, as well as at 3, 4 and 5 years follow-ups. Sophisticated statistical models that can deal with noisy measurements, missing values and heterogeneous data types will be used to extract the best combination of biomarkers and neuropsychological variables for diagnosis and prediction of prognosis of PD-dementia. Besides this clinical perspective, this project further aims at deciphering the unknown disease mechanisms in PD both on a genetic and neurophysiological lev-

el, with particular emphasis of the interplay of genetic markers and temporal changes in the functional connectivity of the brain over time.

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