MetAlz

Integration of Metabolomics and Complementary Approaches for Characterization of an Alzheimer’s Disease Model

Programm / Ausschreibung	FORPA, Forschungspartnerschaften NATS/Ö-Fonds, FORPA NFTE2015	**Status**	abgeschlossen
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Keywords			

Projektbeschreibung

Alzheimer's Disease (AD) currently affects more than 70.000 people in Austria and 27 million people worldwide with numbers expected to grow dramatically as the population ages. AD is a severe neurodegenerative disorder. Patients suffer from a range of symptoms, characterized by progressive memory loss and impairment in behavior, language, and visuospatial skills. Current diagnosis of AD relies largely on the documentation of mental decline, by which time the disease has already caused severe brain damage in individuals. Early diagnosis of AD is essential to treat the disease as there appears to be no treatment benefit in the fully symptomatic stage of the disease. Thus, there is a critical need for a simple and accurate method for detecting AD prior to the onset of these symptoms. In particular, there is a high demand for novel approaches to monitor global changes in metabolites in order to reveal biomarkers and associated molecular mechanisms that allow for early diagnosis in the preclinical and early clinical stages of AD, when treatment is likely to be most effective. Metabolic phenotyping allows monitoring the perturbations in a large pool of metabolites that reflects changes downstream of genomic, transcriptomic and proteomic fluctuations. Thus, metabolic phenotyping represents an accurate biochemical profile of an organism in health and disease aiding to further understanding of alterations in complex biological networks involved in AD. Furthermore, results from metabolic phenotyping can be translated across species since metabolic pathways are conserved through evolution, and are essentially similar in rodents and humans. This is of particular advantage with regards to drug development.

Here we aim to integrate NMR-based metabolic phenotyping (Madl group) with complementary approaches such as histology, behavioral studies, and biochemistry (QPS) to characterize commonly used AD progression models. We aim to:

1. Obtain a biomarker panel for AD (early) diagnosis in one rat and one mouse AD progression model using Metabolic Phenotyping
2. Integrate Metabolic Phenotyping and Complementary approaches for in-depth characterization of one of the AD progression models
3. Use our novel integrative approach in a proof-of-principle study to test the impact of a commonly used reference pharmaceutical compound on AD disease progression

Our approach will provide biomarker panels for early detection and for following progression of AD in the rodent models that can afterwards be translated to humans in a follow-up clinical study. Furthermore, the integration of metabolic phenotyping

with complementary techniques will not only allow an in-depth characterization of AD disease progression from the atom to the organism and vice versa, but also detailed insights into the modulation of complex disease mechanisms by pharmaceutical compounds.

Projektpartner

- Scantox Neuro GmbH