WWTF Project CS15-033

Imaging the functional and molecular impact of poly-unsaturated fatty acids on dopamine-dependent cognitive functions: a combined [11C]-(+)-PHNO PET/MRI study at different stages of cognitive impairment

Abstract

This study will investigate the impact of poly-unsaturated fatty acids (PUFAs) on the neural substrate of dopamine-mediated cognitive functions. Correlates of presynaptic dopamine (DA) function will be investigated using the 3T Siemens mMRBiograph, which enables simultaneous positron emission tomography and functional magnetic resonance imaging (PET/fMRI). We will use d-amphetamine-induced in vivo DA release and the agonist radioligand [11C]-(+)-PHNO for quantifying presynaptic DA release and its impact on fMRI blood-oxygen dependent (BOLD) response in dopaminergic networks. fMRI and PET will be performed during resting state and performance of working memory (WM) tasks. Deficits in WM are a cognitive hallmark of schizophrenia (SCZ), a disorder intrinsically linked to DA dysfunction. The paradigm will be applied to patients with SCZ, to subjects at risk mental state for SCZ (ARMS), and to healthy control subjects. Healthy and ARMS subjects will be randomized to PUFA supplementation or placebo (crossover, double-blind) and will undergo three scans (baseline, post-PUFA, post-placebo).In parallel, phospholipase A2 (PLPA2) and PUFA dependent modulation of dopamine transporter (DAT) functional properties [1] will be studied in vitro in HEK cells and dopaminergic neuronal cultures. Together with advanced molecular techniques for studying DAT function, this innovative approach will allow to clarify the role of the interaction of membrane lipids with DA function in cognition.

Scientific disciplines:
501011 - Cognitive psychology (34%) | 301406 - Neuropharmacology (33%) | 302054 - Nuclear medicine (33%)

Keywords:
working memory, poly-unsaturated fatty acids, dopamine, dopamine transporter, PET, fMRI, [11C]-(+)-PHNO, BOLD, resting state, amphetamine, schizophrenia, at-risk mental state

Principal Investigator:	Matthaeus Willeit
Institution:	Medical University of Vienna
Collaborators:	Wolfgang Wadsak (Medical University of Vienna) (Co-Principal Investigator)

Status: Completed (01.03.2016 - 28.02.2021) 60 months

Funding volume: EUR 593,900

Further links about the involved persons and regarding the project you can find at
https://archiv.wwtf.at/programmes/cognitive_sciences/CS15-033