PROJECTS SUPPORTED BY JPND

Good Vibes



Augmenting glymphatic transport with monitored vibrations to prevent Alzheimer's disease – Good Vibes

Alzheimer's disease (AD) is a leading neurodegenerative disease with increasing healthcare costs across the world in aging populations in the absence of effective treatment. AD is characterized by slow accumulation of protein such as b-amyloid into periarterial brain tissue with a strong link to several vascular risk factors. Recent studies suggests that a failure of glymphatic transport linked to damaged vascular pulsations contribute to AD.

Our collaborative findings with advanced micro & macroscopic neuroimaging have directed our focus towards mechanisms that have the potential to prevent AD by augmenting the pulsatile perivascular CSF solute efflux from the brain. We have developed wearable monitoring of the brain pulsations driving the paravascular solute transport. Our consortium has pioneering focused ultrasound (FUS) experience in removing b-amyloid plaques from paravascular structures in order to restore memory function in laboratory mice. We have also evidence of futher increasing efflux of solutes from paravascular space with electroacoustic (EAC) vibrations.

The major aim of this proposal is to understand how these physical oscillations can be used to improve glymphatic hydrodynamics and solute efflux to prevent AD. We will monitor brain water hydrodynamic paramaters such as solute transvection, blood-brain barrier (BBB) permeability and tissue elasticity using Gmeter technology combining direct-current electroencephalography (dcEEG) with water targeted near-infrared spectroscopy (wNIRS). We will monitor the efficiency for augmenting solute efflux with EAC & FUS techniques against golden standard tools of measuring CSF solute transport; multiphoton microscopy analyses in mice, light sheet microscopy along SPECT/MRI in pigs and in humans ultrafast MREG & TCD brain scanning in multinational datasets from this consortium. The Gmeter hydrodynamic monitoring can provide both early diagnostic information on early AD pathology, as well as, objective feedback information for optimizing the given treatment efficiency.

All in all, our original preliminary data, established collaborations and synergies within the proposed consortium, accesses to unique birth/patient cohorts, the special mechanistic knowhow and clinical experience in brain clearance makes us a cutting-edge crew in developing targeted and monitored treatment based on identifying directly the pathophysiological disturbances leading to AD pathology.

Total Funding: 1.56 M€

Duration: 3 years

Coordinator : Prof. Vesa Kiviniemi ⊠ : <u>vesa.kiviniemi@oulu.fi</u>





Consortium Members		
	Vesa Kiviniemi	University of Oulu, Finland
+	Gitte Moos Knudsen	University Hospital of Copenhagen, Denmark
	Jurgen Claassen	Radboud University Medical Center, Netherlands
	Róbert Bódizs	Semmelweis University, Hungary
+-	Maiken Nedergaard	University of Copenhagen, Denmark