Memory loss in Alzheimer’s disease: underlying mechanisms and therapeutic targets (MEMOSAD)

https://www.neurodegenerationresearch.eu/survey/memory-loss-in-alzheimers-disease-underlying-mechanisms-and-therapeutic-targets-memosad/

Title of project or programme

Memory loss in Alzheimer’s disease: underlying mechanisms and therapeutic targets (MEMOSAD)

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
Professor	Franz	Adlkofer	VERUM- STIFTUNG FUER VERHALTEN UND UMWELT	Germany

Address of institution of lead PI

Institution	VERUM- STIFTUNG FUER VERHALTEN UND UMWELT
Street Address	
City	
Postcode	

Country

Germany

Source of funding information

European Commission

Total sum awarded (Euro)

2998696

Start date of award

01-01-2008

Total duration of award in months

42

The project/programme is most relevant to

- Alzheimer’s disease and other dementias

Keywords

Research abstract in English

MEMOSAD aims at defining the molecular mechanisms of Abeta- and Tau-induced synaptotoxicity and at developing disease-modifying therapeutics for the prevention of memory loss in Alzheimer disease (AD). Insoluble aggregates of the two proteins provide the pathological hallmarks of this incurable brain disorder. Early stage AD is characterized by a remarkably pure impairment of declarative memory and several lines of evidence suggest that this memory impairment is independent of the insoluble aggregates, does not require neuronal death and is caused by subtle and transient synaptic changes. The toxic Abeta and Tau species that cause synaptic dysfunction, their mechanism of toxicity and the link between both pathologies remain largely unknown, but recent data suggest that Abeta accumulation triggers Tau pathology. Consequently, primary neuronal cultures and animal models (C.elegans,zebrafish,mouse) will be employed to define the pathologic pathways leading from Abeta through Tau to synaptotoxicity. Initial experiments will investigate the effect of well-defined Abeta species on long term potentiation, synaptic morphology, gene expression, Tau phosphorylation/aggregation, axonal transport and behaviour. Similarly, we will investigate the functional consequences of Tau misfunction, aggregation, hyperphosphorylation and missorting in various cell culture systems (retinal ganglion cells, primary hippocampal neurons, organotypical slices) and animal models, especially with regard to intraneuronal trafficking and synaptic function. Once the toxic Abeta and Tau species are known and their mechanism of toxicity are defined, we will investigate how these pathways interact. Unravelling the pathologic pathways that lead from Abeta through Tau to synaptotoxicity and memory loss should reveal novel points for therapeutic intervention. Our aim is to deliver 3 or 4 validated therapeutic targets and at least 2 compounds with demonstrated therapeutic efficacy in mouse models of AD.

Lay summary