

TAU IMAGING WITH [18F]T807 PET: THE NEW FRONTIER

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TAU IMAGING WITH [18F]T807 PET: THE NEW FRONTIER

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ZonMw

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4.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Research Abstract

Dementia is often diagnosed in a very late stage of the disease. Because of this, undiagnosed patients inexplicably slowly develop cognitive symptoms, leading to long periods of uncertainty and confusion for patients and caregivers alike. One of the key gains in dementia care would therefore be to improve and accelerate the diagnostic process. An improvement in diagnosis, and subsequent prognosis, could alleviate the psychological stress for all involved parties and

would allow for better and more efficient treatment of patients.

Alzheimer's disease (AD) is the most important cause of dementia. In AD research, there has been a clear focus on the role of amyloid-beta over the past two decades, which can be tested in-vivo with cerebrospinal fluid (CSF) measurements and positron emission tomography (PET) tracers. Especially the latter has caused a major paradigm shift in dementia research. This has led to incorporation of PET and CSF biomarkers into the diagnostic criteria for Alzheimer's disease. Amyloid-beta deposits, however, only moderately correlate with actual symptoms, disease severity and disease progression. Also, considering the relative ineffectiveness of amyloid treatments in AD at this point, the ultimate solution for dementia will unlikely result from solely investigating amyloid. Based on the close association of hyperphosphorylated tau with neuronal injury and cognitive status in post-mortem and animal literature, it can be hypothesized that tau pathology is the missing link for a better staging and assessment of prognosis in AD patients.

Another great interest in tau pathology comes from a large group of patients who suffer from dementia without amyloid pathology in the brain but mainly aggregations of tau. Neuropathological studies have consistently identified frontotemporal dementia (FTD) subtypes, progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) as "tauopathies". There is currently no reliable in- vivo diagnostic marker available for these tau-induced dementias, severely hampering accurate diagnosis especially in the early phases of the disease. The introduction of novel PET tracer [18F]T807 for hyperphosphorylated tau allows for the first time quantification of tau pathology in the living human brain. [18F]T807 is a promising compound due to its high affinity for tau in transgenic mice and post-mortem tissue, which has been confirmed by preliminary human PET studies. As such, [18F]T807 has great potential as a prognostic marker in preclinical and clinical stages of AD, and could be the first in vivo biomarker for the aforementioned "tauopathies". This would greatly enhance diagnosis, thus leading to improved patient quality of life, greater insight and understanding in caregivers and more (cost-)effective treatment of the disease. In addition, the possibility of quantifying tau is essential for developing and testing novel anti-tau therapies. Indeed, anti-tau therapies are empirically promising, but as of yet there is no way of verifying the results in vivo. [18F]T807 could therefore revolutionize treatment of tauopathies and could become the new gold standard tau PET biomarker to monitor treatment effects in tauopathies.

Although intriguing and very promising, tau imaging with PET is still in its infancy. The full potential of [18F]T807 can only be achieved when its uptake can be related reliably to the actual tau load in the brain. The overall aim of this proposal is to fully develop [18F]T807 as a tau marker that can be used for accurate and early diagnosis of several types of dementia, for prognostic purposes, and as a surrogate outcome measure in clinical trials that evaluate tau-modifying agents. In order to achieve this, we have assembled a consortium of specialists in 3 university medical centers, one technical university, one highly dedicated private radiopharmaceutical company, and representatives of patients and end-users, to provide the multidisciplinary collaborative network necessary to advance the state-of-the-art in PET imaging of tauopathies. Uniquely, patients and their caregivers will be intensively involved in the research and decision making processes over the course of this project. With their invaluable hands-on experience they provide insights often overlooked by clinicians and researchers. A well-validated tau PET tracer can be used to address fundamental questions about the mechanisms driving clinical symptoms in dementia and will have a significant impact on how patients are diagnosed and treated in the Netherlands and beyond. This study may thus facilitate yet another paradigm shift in dementia research as clinicians will be able to probe both

amyloid and tau load in their patients during life.

Lay Summary

Further information available at:

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Investments > €500k

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Netherlands

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Alzheimer's disease & other dementias

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