A molecular anatomic imaging analysis of tau in progressive supranuclear palsy

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Country

USA

Title of project or programme

A molecular anatomic imaging analysis of tau in progressive supranuclear palsy

Source of funding information

NIH (NIA)

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€ 1,521,239.45

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15/09/2015

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2

The project/programme is most relevant to:

Neurodegenerative disease in general

Keywords

Progressive Supranuclear Palsy, tau Proteins, Image Analysis, Anatomy, Positron-Emission Tomography

Research Abstract
? DESCRIPTION (provided by applicant): Progressive supranuclear palsy (PSP) is a

devastating neurodegenerative disorder characterized by postural instability with falls, axial rigidity and vertical supranuclear gaze palsy. It affects approximately 20,000 Americans and is untreatable. It typically results in patients being confined to a wheel-chair and with dysphagia that can result in death after 7-8 years. At autopsy, patients with PSP show deposition of the protein tau in the brain. Unfortunately, studies of tau in PSP during life have not been possible due to the absence of a tau biomarker. Understanding the role of tau to the disease is critical as it is a major target for future treatments of PSP. A positron emission tomography (PET) ligand, [F18] AV-1451 (formerly [F18]-T807), has recently been developed which specifically binds to tau and provides us with the opportunity, for the first time, to assess the regional distribution o tau in the brains of living patients with PSP. The goal of this grant is to characterize the cross-sectional and longitudinal patterns of tau deposition in patients with PSP using this PET imaging ligand, and to determine whether tau deposition correlates to neurological outcomes and imaging measures of atrophy and white matter tract degeneration. To accomplish these aims we will recruit a total of 84 subjects diagnosed with possible or probable PSP. Each subject will undergo two serial assessments one year apart. For each assessment, subjects will undergo a neurological and swallowing evaluation, a 3T magnetic resonance imaging (MRI) that includes structural MRI and diffusion tensor imaging (DTI), and tau-PET using the AV-1451 ligand. Eighty four matched healthy controls from the Mayo Clinic Study of Aging that have already undergone a neurological evaluation and serial MRI and tau-PET scanning will be utilized for analyses. The regional distribution of tau-PET uptake across the brain in PSP compared to controls will be assessed using voxel-level analyses. Global and regional tau-PET burden measures will be generated for the baseline and follow-up brain scans. Statistical analyses will be performed to identify regions of the brain in which tau-PET burden correlates with specific neurological features, including gait, ocular motor, and executive dysfunction, and dysphagia. We will also determine the relationship between global and regional tau-PET burden and anatomical changes on MRI, including grey matter atrophy and white matter tract degeneration. The analyses will focus specifically on regions typically involved in PSP, including midbrain, superior cerebellar peduncle, thalamus, basal ganglia, cerebellum and superior frontal cortex. Lastly, we will determine whether tau-PET can help predict future decline in neurological and MRI outcomes. This mechanistic approach will increase our understanding of disease progression and the relationship between pathological processes and the neurological and anatomical features of PSP; knowledge that will be critical for the future development of effective therapies for PSP and to determine whether tau-PET measures could be useful to aid prognosis in individual subjects.

Lay Summary

PUBLIC HEALTH RELEVANCE Progressive supranuclear palsy is a neurodegenerative disorder that affects patients balance, eye movements, and swallowing, and is thought to be due to the presence of an abnormal protein known as tau, in brain tissue. In this study we will use a novel imaging technique to assess the distribution of tau in the brains of patients with progressive supranuclear palsy during life, and whether the amount and distribution of tau relates to specific clinical abnormalities and is associated with focal brain shrinkage. This study will improve our understanding of disease progression in patients with progressive supranuclear palsy and will be critically important for the development and testing of future treatments that will likely target tau.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Neurodegenerative disease in general

Years:
2016

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N/A

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