Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS)

https://www.neurodegenerationresearch.eu/survey/longitudinal-evaluation-of-familial-frontotemporal-dementia-subjects-lefftds-2/

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Country

USA

Title of project or programme

Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS)

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 15,269,919.27

Start date of award

30/09/2014

Total duration of award in years

3

The project/programme is most relevant to:

Motor neurone diseases

Keywords

Frontotemporal Lobar Degenerations, Frontotemporal Dementia, PGRN gene, mutation carrier, C9orf72

Research Abstract
DESCRIPTION (provided by applicant): Frontotemporal lobar degeneration (FTLD) is a

neurodegenerative disorder that typically presents as behavioral changes and dementia, sometimes also associated with parkinsonism and/or amyotrophic lateral sclerosis. FTLD is at least as common as Alzheimer’s disease in people under the age of 65, and is devastating for affected individuals and their relatives. These features reinforce the importance of current effort to develop treatments for this disorder, particularly in the presymptomatic phase. FTLD is caused by dysfunction of two major proteins-microtubule associated protein tau and TAR DNA binding protein molecular weight 43. FTLD often presents as a dominantly inherited familial disorder (f-FTLD), usually due to mutations in the microtubule associated protein tau (MAPT), progranulin (PGRN), or chromosome 9 open reading frame 72 (C9ORF72) genes, which together account for at least 50% of f-FTLD. Several agents which impact tau or progranulin/TDP-43 protein pathophysiology have been identified, but it is not clear how efficacy of drugs can be assessed, particularly in presymptomatic individuals. Importantly, f- FTLD is currently the only practical context in which people in presymptomatic or very early symptomatic stages can be studied, making it the best context for testing drugs aimed at delaying symptom onset. Based on data from other familial neurodegenerative syndromes, we expect that the rates of clinical and biomarker change in f-FTLD are complex, with slower rates of decline in the early presymptomatic phase, followed by acceleration several years prior to development of symptoms and continuing through the symptomatic phase. The proposed study will enroll 300 members of f-FTLD families with a known mutation in MAPT, PGRN, or C9ORF72 (100 symptomatic mutation carriers, 100 asymptomatic mutation carriers, and 100 non-carriers) across 8 centers [Mayo Clinic Rochester (n=70 subjects), University of California at San Francisco (n=70), University of Pennsylvania (n=70), Mayo Clinic Florida (n=18), Harvard University (n=18), Columbia University (n=18), Washington University (n=18) and University of British Columbia (n=18)] to obtain annual assessments including key magnetic resonance imaging (MRI) measures, cerebrospinal fluid analysis, blood, behavioral, neuropsychological and functional assessment, for a total of four assessments per participant. Several aims will be addressed which focus on biofluid and neuroimaging biomarkers, with the ultimate goal of identifying which measures are optimal for assessing efficacy of potential disease-modifying or preventative therapies.

Lay Summary
PUBLIC HEALTH RELEVANCE: Frontotemporal lobar degeneration (FTLD) is a neurodegenerative disorder that typically presents as behavioral changes and dementia, sometimes also associated with parkinsonism and/or amyotrophic lateral sclerosis. FTLD is at least as common as Alzheimer’s disease in people under the age of 65, and is devastating for affected individuals and their relatives. These features reinforce the importance of current effort to develop treatments for this disorder, particularly in the presymptomatic phase.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Motor neurone diseases

Years:

2016

Database Categories:
N/A

Database Tags:
N/A