Determinants of Neurodegenerative Decline in Primary Progressive Aphasia

https://www.neurodegenerationresearch.eu/survey/determinants-of-neurodegenerative-decline-in-primary-progressive-aphasia/

Principal Investigators

ROGALSKI, EMILY J

Institution

NORTHWESTERN UNIVERSITY AT CHICAGO

Contact information of lead PI
Country

USA

Title of project or programme

Determinants of Neurodegenerative Decline in Primary Progressive Aphasia

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,596,133.03

Start date of award

15/03/2012

Total duration of award in years

4

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Primary Progressive Aphasia, Atrophic, Nerve Degeneration, Amyloid, cerebral atrophy

Research Abstract
DESCRIPTION (provided by applicant): Primary progressive aphasia (PPA) is a clinical dementia syndrome caused by neurodegenerative brain disease, with language impairment as

the primary feature. Although functional decline invariably occurs, the factors influencing the time course of decline and severity of symptoms in PPA have not been fully elucidated. Furthermore, PPA is associated with two main classes of underlying pathology: Alzheimer pathology (PPA-AD) and frontotemporal lobar degeneration (PPA-FTLD) pathology, but there is currently no reliable in vivo method for identifying the nature of the pathology. Numerous autopsy series, including one from our Center, indicate that approximately 30% of cases with the PPA phenotype have PPA-AD pathology while the other 70% show PPA-FTLD pathology. However, the reliable identification of clinical and anatomical features of underlying pathology in living patients remains an ongoing challenge. The proposed studies are directed at establishing potential markers for disease etiology and progression. The Specific Aims include: 1) To follow 40 patients with the PPA syndrome using MR imaging at 6-month intervals over an 18-month time period to quantify and characterize how brain atrophy changes over time; 2) to determine the temporal relationship between cognitive change and the quantity and location of atrophy; and 3) to use the new [18F]-AV-45 PET imaging compound to identify amyloid burden in PPA patients as a marker of AD pathology and to identify its relationship to atrophy. Longitudinal rates of regional (i.e., medial temporal) atrophy have been useful in predicting cognitive decline in the amnestic dementia of the Alzheimer's type. Therefore, we predict that atrophy rates in language related brain areas will be useful in differential diagnosis and monitoring of disease progression in PPA, potentially pointing the way to an outcome measure for clinical trials. The clinical, cognitive and anatomical features associated with amyloid burden will be identified. Data from this project will determine whether the temporal progression of atrophy is related to cognitive decline, anatomical site of primary atrophy, or putative underlying pathology based on amyloid burden. This project represents the first multidimensional study of longitudinal course using the new antemortem amyloid biomarker [18F]-AV-45 in PPA. In addition to their theoretical interest, the results from this study are of crucial importance for defining objective biomarkers of disease type and progression, which will inform therapeutic treatment strategies for this relatively underserved dementia population. Results from this project will also fill gaps n our knowledge of the relationship between atrophy patterns and both clinical progression and underlying pathology in patients with PPA. The approach in Aim 1 is driven by atrophy patterns and free of clinical bias, while Aims 2 and 3 consider the relationship with cognitive performance and amyloid positivity, respectively. This is of considerable importance for increasing the accuracy with which we assign patients to therapeutic trials.

Lay Summary
This application proposes the first study of comprehensive 6-month comparisons of clinical and neuroimaging features of PPA, their longitudinal changes and their association with amyloid burden. This new information will elucidate our understanding of the neurobiology of PPA by bridging clinico-anatomical features and markers of underlying pathology, with an overarching goal of informing therapeutic strategies. The data will also provide quantitative measures of longitudinal course of PPA, yielding relevant benchmarks for clinical trials and providing disease-staging expectations for patients and families.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A