Genetic characterization of atypical parkinsonism

https://neurodegenerationresearch.eu/survey/genetic-characterization-of-atypical-parkinsonism/

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Country

USA

Title of project or programme

Genetic characterization of atypical parkinsonism

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 707,416.51

Start date of award
Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Clinical Research... Clinical Research - Intramural... Dementia... Genetics... Human Genome... Lewy Body Dementia... Neurodegenerative... Neurosciences... Parkinson's Disease

Research Abstract

The Neurodegenerative Diseases Research Unit (NDRU) focuses on atypical parkinsonism

syndromes to unravel molecular genetic mechanisms involved in the pathophysiology and to discover targets for rational therapeutic development. Over the last year we have undertaken several ambitious projects. In collaboration with the Johns Hopkins Pathology department, we performed exome sequencing of a pathologically confirmed cohort of dementia with Lewy bodies (DLB) patients. Our study found that 25% of cases carried either a high risk variant or causative mutation in one of three genes (GBA, PSEN1, APP). Further we confirmed that the APOE e4 allele significantly increases risk for disease and decreases survival. Taken together, these results highlight that genetic factors are playing a prominent role in the pathobiology of DLB, and strongly support the notion that DLB occurs along a spectrum between Parkinson disease and Alzheimer dementia. As part of a multi-center, international collaboration we performed a genome-wide association study in multiple system atrophy (MSA). This study found several interesting genetic loci that could reveal important insights into the disease etiology. Follow up replication studies of larger cohorts will have to be performed to confirm their role in MSA. Ongoing projects in our laboratory include: (1) genotype-phenotype analyses of pathologically confirmed atypical parkinsonism cohorts using custom-designed genotyping chips; (2) a genome-wide association study in DLB; (3) candidate gene analyses in MSA and DLB; and (4) a natural history study of atypical parkinsonism syndromes. In summary, we have successfully applied modern genomic approaches. The projects highlighted above have already identified several genetic variants that are implicated in the pathobiology of DLB and MSA. Additional follow-up studies are required for replication, fine-mapping and a more refined dissection of genetic factors involved in atypical parkinsonism syndromes.

Lay Summary
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

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