Pleiotropy GWAS of Alzheimers Disease

https://neurodegenerationresearch.eu/survey/pleiotropy-gwas-of-alzheimers-disease/

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Country

USA

Title of project or programme

Pleiotropy GWAS of Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

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Start date of award

15/09/2016

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 including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Genetics... Human Genome... Neurodegenerative... Neurosciences

Research Abstract

PROJECT SUMMARY This proposal, entitled “Pleiotropy GWAS of Alzheimer’s Disease and Multiple Neurodegenerative Diseases,” describes plans to analyze existing neurodegenerative phenotype and genome-wide genotype data from existing genome-wide association studies

(GWAS) of multiple neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), and frontotemporal dementia (FTD), among others. While neurodegenerative diseases have distinct pathologies, there are also shared pathological features like protein aggregation in the brain (e.g., tau protein). This suggests that genetic studies combining neurodegenerative disease genetics studies may identify genetic risk factors contributing to one or more individual NDs ("pleiotropy") through these common features. The goal of these planned analyses is to identify genetic loci and variants with effects across multiple NDs. Our approach includes broad hypothesis-free analyses like GWAS meta-analysis, as well as targeted "drill-down" approaches like pathway analyses examining known biological pathways. These analyses will use publicly available data on genome-wide association study and whole genome/exome sequence datasets curated by individual groups, disease-specific consortia, and on the NIH Database of Genotypes and Phenotypes (dbGaP). This project will require extensive collection of genotypes from well-characterized cases and controls; systematic archiving of case-control and prospective cohort studies; a formally-structured data harmonization process; inclusion of multiethnic GWAS and WGS/WES studies; and longitudinal analyses in cohort studies of neurodegeneration in order to fulfill the mandate of the National Institute on Aging (NIA) RFA PAR-15-356. Our three aims include (1) harmonization and integration of genotype and phenotype data from multiple large-scale genetic studies of differeing neurodegenerative diseases; (2) estimating shared heritability between neurodegenerative diseases and performing GWAS and WGS/WES association study meta-analyses; and (3) performing analyses of intermediate and related phenotypes and incorporating functional annotation to identify truly functional pleiotropic variants and their causal effects on multiple neurodegenerative diseases. These analyses will examine both common and rare genomic variants and will use a similar strategy to existing genetic studies comparing neuropsychiatric disorders (e.g, schizophrenia, depression), with refinement and development of novel pleiotropy methods. We will leverage our considerable experience with large-scale genetic association and meta-analysis studies to identify new genetic risk factors for neurodegenerative diseases using data on tens of thousands of affected and unaffected individuals. Furthermore, we will create an online resource for data harmonization and sharing analysis results with investigators interested in shared genetic risk factors of neurodegeneration.

Lay Summary

Project Narrative Neurodegenerative diseases like Alzheimer's disease and Parkinson's disease are known to share some common pathological features like accumulation of tau protein in the brain. We hope to use this overlap to identify shared genetic contributors of risk to multiple neurodegenerative diseases by harmonizing and integrating genotype and phenotype data from multiple large-scale genetic studies of differeing neurodegenerative diseases. Using this data, we will estimate shared heritability between neurodegenerative diseases and perform GWAS and WGS/WES association study meta-analyses as well as extensions of these analyses to meaningful intermediate and related phenotypes and also by incorporating functional annotation to identify truly functional pleiotropic variants and their causal effects on multiple neurodegenerative diseases. The genetic studies proposed here will improve knowledge about the genes contributing to multiple neurodegenerative diseases and help to identify therapeutic targets for multiple diseases at the same time.

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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