Investigating the role of bvFTD-affected networks in socioemotional behavior

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Title of project or programme

Investigating the role of bvFTD-affected networks in socioemotional behavior

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,046,259.63

Start date of award

15/04/2008

Total duration of award in years

8

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Basic Behavioral and Social Science... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Frontotemporal Dementia (FTD)... Mental Health... Neurodegenerative... Neurosciences... Rare Diseases

Research Abstract

DESCRIPTION (provided by applicant): The behavioral variant of frontotemporal dementia (bvFTD) is one of only a handful of neurologic syndromes for whom initial clinical diagnosis relies entirely on assessment of patients' social and emotional symptoms. Until recently, no measures of socioemotional behavior were psychometrically validated in neurodegenerative disease patients. In its first four years, this project has directly addressed this problem by successfully developing such measures, a subset of which have already been incorporated into an FTD testing module promoted by National Institute of Aging through the National Alzheimer's Disease Coordinating Centers. Now that these tests have been developed, we hope to use them to model the neural systems underlying human socioemotional behavior in both healthy and disease states. This proposal builds on the recent discovery that each major neurodegenerative disorders initially targets a distinctive intrinsically connected functional network (ICN) in the brain. Three of these ICNs have been identified as the initial site of dysfunction in different clinical subtypes of bvFTD: the ventral salience network (SN), the task control network (TCN), and the semantic- context network (SCN). Still, little is known about the specific socioemotional behaviors driven by these ICNs, either in normal cognition or in disease. By identifying how these tests reflect network connectivity, we can use them to more easily screen patients for early bvFTD, measure symptom progression, and better predict patients' underlying neuropathology. The Specific Aims of this project are to elucidate the contribution of these three neural networks to normal social behavior and to the socioemotional symptoms of bvFTD: AIM 1: To clarify how the three bvFTD networks correspond to socioemotional behavior and cognition in healthy normal adults. We will collect resting-state MRI (rsMRI) and social testing data from 40 younger controls (ages 20-45), which together with data collected from healthy older controls (ages 45-90) during the first phase of this project. We hypothesize that scores on measures of visceral emotional reactivity will correlate with SN connectivity; social self-control will correlate with TCN connectivity; and tasks requiring applied socioemotional knowledge will correlate with SCN connectivity. AIM 2: To determine how these three networks relate to severity of social dysfunction in bvFTD. We will collect rsMRI and social data from 50 bvFTD patients, which when added to data collected during the first phase of this project, will provide adequate power to investigate the correspondence between patients' socioemotional symptoms and network dysfunction. AIM 3: To examine socioemotional and network dysfunction occurring at the earliest stage of bvFTD. For this more exploratory aim, we will collect rsMRI and social data yearly from a cohort of 30 presymptomatic carriers (PC) and 30 non-carriers (NONC) from families with FTD-causing gene mutations, to examine patterns of progressive change in socioemotional function in PCs who later develop a behavioral phenotype, and identify socioemotional changes in PCs that correspond to altered connectivity in the three ICNs.

Lay Summary

PUBLIC HEALTH RELEVANCE: The goal of this project is to elucidate the contribution of three neural networks to normal social behavior and to the socioemotional symptoms of bvFTD. By

developing our understanding of the network underpinnings of normal social functioning throughout adulthood, we will have a foundation on which to model how these circuits malfunction to cause the behavior symptoms of bvFTD and other neurologic and psychiatric disorders. In addition, by identifying the specific relationships between behavior and network connectivity in bvFTD patients, we will maximize our ability to measure symptom progression in upcoming clinical trials for FTD.

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