Early detection of Huntingtons Disease: Longitudinal analysis of basal ganglia and cortical thickness

https://www.neurodegenerationresearch.eu/survey/early-detection-of-huntingtons-disease-longitudinal-analysis-of-basal-ganglia-and-cortical-thickness/

Principal Investigators

OGUZ, IPEK

Institution

UNIVERSITY OF PENNSYLVANIA

Contact information of lead PI
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USA

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Early detection of Huntingtons Disease: Longitudinal analysis of basal ganglia and cortical thickness

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4

The project/programme is most relevant to:

Huntington's disease

Keywords

longitudinal analysis, Basal Ganglia, Huntington Disease, Thick, Early Diagnosis

Research Abstract

PROJECT SUMMARY/ABSTRACT Huntington's disease (HD) is a neurodegenerative disease where brain abnormalities can be detected via MRI studies one to two decades prior to clinical diagnosis. Sensitive outcome measures are needed for enabling clinical trials during pre-manifest HD with the goal of intervention and treatment at the earliest stage possible. The PREDICT-HD study (NS040068) identified longitudinal alterations in the basal ganglia and cortical gray matter atrophy as the primary neuroimaging findings in pre-manifest HD patients. However, measurement noise is a serious concern as it can affect the ability to detect abnormalities early in the disease progression. The objective of this proposal is to develop innovative methods for quantifying the cerebral cortex and the basal ganglia in a temporally and spatially consistent manner and to leverage these techniques to improve the quantification of HD progression in patients from the existing PREDICT-HD database. We hypothesize that more accurate quantification will provide more sensitive measures of HD progression, leading to increased sensitivity to longitudinal changes prior to clinical diagnosis. The quantification is expected to be substantially more accurate than currently possible due to our novel temporal- and spatial- context-aware segmentation strategy, which leverages the inherent redundancy of longitudinal MRI data. Three specific aims will be fulfilled: Aim 1. Develop and validate a novel temporally and spatially consistent segmentation method for quantification of the basal ganglia in longitudinal studies of HD. The impact is expected to be especially large for structures with weak boundaries, such as the nucleus accumbens, which are hard to quantify with existing approaches. Validation will be accomplished via comparison with expert manual segmentations. Aim 2. Develop and validate a novel longitudinal cortical surface reconstruction method for temporally consistent cortical thickness quantification in longitudinal studies of HD. Our approach will utilize temporal image-to-image context while avoiding over-regularization. The validation will be based on reproducibility in test-retest scans and statistical discrimination power in population studies, using public datasets. Aim 3. Assess the increase in statistical sensitivity of imaging measures derived from our new segmentation approaches in a longitudinal pre-manifest HD cohort, and validate these imaging measures by documenting their association with known clinical outcome assessments (COA's) and genetic variables. We will use 1246 scans from Predict-HD to evaluate the sensitivity of developed methods and validate against clinical variables. We anticipate the proposed segmentation methods to substantially increase the sensitivity of existing imaging- based measures in HD. This will provide a means of developing and evaluating early therapeutic intervention strategies in order to prevent disease onset and slow disease progression. Equally significant, the innovative methods to be developed in this proposal are expected to be crucially important for increased sensitivity for other neurodegenerative disorders such as Alzheimer's disease or Parkinson's disease.

Lay Summary

PROJECT NARRATIVE Huntington Disease (HD) is an inherited neurodegenerative disease that is known to affect brain structure as early as 1-2 decades prior to clinical diagnosis. Sensitive quantitative MRI analysis approaches that can robustly detect these changes earlier than currently possible will provide a means of developing and evaluating early therapeutic intervention strategies, with the hope of preventing disease onset or slowing disease progression. The proposed research is to develop and thoroughly validate innovative image analysis approaches to provide such biomarkers, namely, basal ganglia volume and cortical thickness, in a highly accurate and robust manner.

Further information available at:

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Investments > €500k

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United States of America

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