CALIFORNIA STATE SCIENCE FAIR
2014 PROJECT SUMMARY

Name(s)

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Project Number

S0422

Project Title

Genetics or Gender? Effect of APOE-e4 and Gender on Age-Related Brain Atrophy and Cognitive Decline in Alzheimer's

Abstract

Objectives/Goals

2/3 of the 5 million Alzheimer's disease (AD) cases over age 65 in the U.S. are women. Using linear mixed effects regression (LMER), this project investigated the role of gender, age, and APOE-e4 allele (major genetic risk factor) in cognitive/structural decline over time. I hypothesized that gender and APOE-e4 had similar and significant effect sizes on AD progression with interactions between risk factors also being significant.

Methods/Materials

I obtained approval to access Alzheimer's Disease Neuroimaging Initiative (ADNI), a global effort tracking clinical/imaging AD biomarkers. Using "open-source R project" for statistical computing, I examined over 24000 observations of 818 patients over 5 year longitudinal study across 3 cohorts (Healthy Controls (HC), Mild Cognitive Impairment (MCI), AD) with 168 LMER model-runs to understand effects of the risk factors (Phase1) and their interactions (Phase2). 3 psychometric tests (ADAS-Cog, CDR-SB, MMSE) and 4 structural volumes from UCSD MRI data (whole brain, hippocampus, entorhinal cortex, middle temporal) were examined. This study employed weight of evidence and AIC (Akaike's Information Criterion), a maximum likelihood based multimodel inference to examine relative plausibility of statistical models.

Results

Phase1: For HC cohorts, gender had significant effect on rates of cognitive and structural decline in ADAS-Cog and all structural regions. While gender impacted rate of cognitive decline in MCI cohorts, APOE-e4 had the highest effect on rate of structural decline. For AD cohorts, gender had higher effect size than APOE-e4 for all analyses.

Phase2: For HC cohorts, APOE-e4*age interaction impacted all brain regions and cognitive scores. In MCI, gender*age in Entorhinal Cortex and whole brain volume was found to be significant. While gender*age was significant for AD cohorts in Hippocampus, Entorhinal Cortex, and Mid-Temporal volumes, age*gender*APOE-e4 was significant for cognitive ADAS and CDR scores.

Conclusions/Discussion

With 95% confidence, I conclude that gender considerably affects cognitive and structural rates of decline in AD, having an effect size equal to or greater than APOE-e4. Interactions between age, APOE-e4, and gender play a major role in AD progression. Since women have higher rates of cognitive/structural decline than men, this study underscores the importance of female inclusive/targeted clinical trials to fight against Alzheimer's.

Summary Statement

This study assesses the impact of gender and its interactions with age and genetics on AD trajectory and deduces that female gender is equally or more important than genetic risk factor and needs to be accounted for in early AD diagnostics.

Help Received

My grandma for motivation; my family and teacher Mr. Wong for encouragement; my mom, Shanthi Pichai, for mentoring; and ADNI for valuable data.