CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY

Name(s)

Mythri Ambatipudi

Project Number

S1201

Project Title

Using Circadian Rhythm Gene SNPs, Sleep-Wake Phenotypes, and MRI Morphometrics to Diagnose Cognitive Impairment Diseases

Abstract

Objectives/Goals

Early detection of Cognitive Impairment Diseases (CID) is challenging. Overlapping symptoms cause misdiagnosis & catastrophic effects. For e.g., Robin Williams's DLB (Dementia with Lewy Bodies) was misdiagnosed as Parkinson's(PD). Mistreating DLB aggravates hallucinations & depression. CID subjects suffer from nocturnal wakefulness & sundowning, symptoms similar to Circadian Rhythm Disorder (CRD). The objective is 1)Investigate if CRD influences CID 2)Use CR gene SNPs, sleep-wake phenotypes(SWP) & MRI morphometrics to differentiate DLB, PD & Alzheimer's(AD) 3)Identify machine learning algorithms (MLA) to predict rare DLB cases.

Methods/Materials

The project was conducted in 5 stages using PPMI/ADNI public databases: 1)Significance thresholds for DLB differentiation were calculated & potential DLB subjects identified 2)Pearson's chi-square test established association ($p<0.05$) between SWP & CID pathology 3)GWAS was conducted in PLINK. Manhattan plots identified SNPs with SWP association. Quality control on SNP data accounted for deviation from Hardy-Weinberg Equilibrium ($p<1e-6$), failed missingness (GENO>0.05) & frequency (MAF<0.01) & low genotyping (MIND>0.1). MDS analysis in R corrected population stratification 4)1.5T T1 MRI images were analyzed in Freesurfer. Chi-square test established SWP association with morphometric changes 5)Features were created with above results & MLA accuracies compared in Matlab/Weka with 34% holdout & 10-fold cross validation.

Results

32 potential DLB cases were identified. SWP association was noted for DLB ($p=8.9e-10$) & PD ($p=1.6e-3$), but not for AD ($p=0.33$). SWP association was noted for SNPs of DLB genes PODN, DDR2, & ATG10; CID gene APOE4 & REM-sleep gene ATG4C. Interestingly, migraine genes, CACNA1 & VARS were associated. Cortical thickness of visuospatial domains & caudate-binding ratios decreased more in DLB than PD/AD. Decision tree MLA was most effective.

Conclusions/Discussion

CRD influences DLB & PD disease pathologies & differentiates CID. Association with migraine genes is noteworthy, as white-matter lesions are found in migraine & CID subjects. Association with changes in visuospatial regions, areas controlling hallucination/orientation, is vital to DLB diagnosis. Decision tree MLA were most effective, as they group by similarity & split to make a conclusion before classifying. This multi-level screening process can be extended to accurately screen other diseases.

Summary Statement

This project identified Circadian Rhythm Disorder as a potential biomarker for diagnosing and differentiating cognitive impairment diseases.

Help Received

My science teacher and research club mentor, Mrs. Segal provided valuable guidance. My parents provided encouragement.