The Contribution of Genetic Risk for Alzheimer's & Cardiovascular Disease to Recovery from Traumatic Brain Injuries

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Polygenic risk scores (PRS) represent the genetic likelihood of developing a phenotype and represent an exciting opportunity for the development of personalized medicine. This study used PRS to determine if individuals at high-risk for Alzheimer's (AD) or cardiovascular disease (CVD) would recover differently after TBI compared to low-risk individuals.

GWAS with the Illumina Global Screening Array was performed on DNA available for a subset of the TBI-Model Systems cohort (N=189). PRS were chosen from the PGS Catalog (https://www.pgscatalog.org) and calculated using the Michigan Imputation Server. 1-year follow-up data (1Y) for the Functional Independence Measure (FIM) was used to evaluate TBI recovery. FIM represents the subject's self-care ability after TBI and includes a cognitive and motor component.

ANCOVA models were used to elucidate the relationship between PRS risk groups (score in top 20% vs. 80%) and 1Y FIM scores. Covariates included age, education, FIM scores at discharge, injury severity, and genetic ancestry. *Post-hoc* analysis was conducted using 1Y FIM scores of subjects stratified by AD risk and *APOE* e4 carrier status, a major risk factor for AD onset. Additional *post-hoc* analysis evaluated hypertension at 1Y by CVD PRS groups using a cox survival model.

Individuals with high AD PRS had lower 1Y FIM scores than those with low risk ($p= 0.041$). *Post-hoc* analysis showed a trend for *APOE* e4 carriers with high AD PRS performing worse on FIM motor testing ($p=0.145$). There was not significant association between the CVD high-risk group and FIM scores ($p=0.389$). The cox survival model of hypertension trended towards earlier age of onset in the high-risk subjects ($p=0.155$).

This pilot study shows the potential for PRS to identify individuals at risk for worse TBI recovery, allowing for future research on early interventions and their effects on TBI recovery.