ADNI Alzheimer's Disease Neuroimaging Initiative

Polygenic Hazard Score (PHS)

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Contents

Page 1 Polygenic Hazard Score

Summary

Based on a combination of APOE and 31 other genetic variants, a **'polygenic hazard score' (PHS)** has been developed and validated for quantifying AD dementia age of onset[1].

Method

Briefly, AD-associated SNPs (at $p < 10^{-5}$) were first delineated using genotype data from 17,008 AD cases and 37,154 controls from Stage 1 of the International Genomics of Alzheimer's Project. Next, using genotype data from 6,409 AD patients and 9,386 older controls from Phase 1 of the Alzheimer's Disease Genetics Consortium (ADGC Phase 1), and corrected for the baseline allele frequencies using European genotypes from 1000 Genomes Project, a total of 31 AD-associated SNPs were identified from a stepwise Cox proportional hazards model to derive a polygenic hazard score (PHS) for each participant. Finally, by combining US population based incidence rates and the genotype-derived PHS for each individual, estimates of instantaneous risk (i.e. **cumulative incidence rate**) for developing AD were derived based on genotype and age. PHS computed for every participant represents the vector product of an individual's genotype for the 31 SNPs and the corresponding parameter estimates from the ADGC Phase 1 Cox proportional hazard model in addition to the *APOE* effects. Beyond *APOE*, PHS has been shown to predict cognitive and clinical decline[2], postmortem and *in vivo* measures of amyloid and tau pathology[3], and MRI measures of medial temporal volume[4].

Dataset Information

This methods document applies to the following dataset(s) available from the ADNI repository:

Dataset Name	Date Submitted
Polygenic Hazard Score (PHS) [ADNI1,GO,2]	07/30/2018

References

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4. Kauppi K, Fan CC, McEvoy LK, et al. Combining polygenic hazard score with volumetric MRI and cognitive measures improves prediction of progression from mild cognitive impairment to Alzheimer's disease. *Front Neurosci* 2018;12:260.

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