# Hippocampal Surface Mapping of Genetic Risk Factors in AD via Sparse Learning Models

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## Abstract

Genetic mapping of hippocampal shape, an under-explored area, has strong potential as a neurodegeneration biomarker for AD and MCI. This study investigates the genetic effects of top candidate single nucleotide polymorphisms (SNPs) on hippocampal shape features as quantitative traits (QTs) in a large cohort. FS+LDDMM was used to segment hippocampal surfaces from MRI scans and shape features were extracted after surface registration. Elastic net (EN) and sparse canonical correlation analysis (SCCA) were proposed to examine SNP-QT associations, and compared with multiple regression (MR). Although similar in power, EN yielded substantially fewer predictors than MR. Detailed surface mapping of global and localized genetic effects were identified by MR and EN to reveal multi-SNP-single-QT relationships, and by SCCA to discover multi-SNP-multi-QT associations. Shape analysis identified stronger SNP-QT correlations than volume analysis. Sparse multivariate models have greater power to reveal complex SNP-QT relationships. Genetic analysis of quantitative shape features has considerable potential for enhancing mechanistic understanding of complex disorders like AD.