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Advancing Genetic Analysis of Aging through Multivariate Brain Imaging Embeddings

The genetic underpinnings of brain structural changes with aging hold the key to understanding degenerative and neurological diseases. Traditional deep learning methods have typically approached aging by attempting to predict chronological age from brain MRI and using the resulting predictions as a phenotype, an approach that considers aging as a univariate phenomenon and thereby fails to capture its inherent complexity and heterogeneity. We introduce a novel multivariate method for the genetic analysis of age-related imaging traits, which integrates supervised contrastive learning for medical image embedding with multivariate genetic association testing. Our method harnesses the power of state-of-the-art supervised contrastive learning to generate medical image embeddings that are not only predictive of biological aging but also retain the heterogeneity of age-related changes. Applying multivariate association testing to these embeddings, using T1 brain MRI scans from 33,000 UK Biobank participants, our method outperforms standard supervised models in age prediction and enhances the discovery of significant genetic associations. We show that these discovered genetic loci have clear effects on brain structure, and their inclusion in genetic predictors of disease risk markedly improves their accuracy. In summary, our approach offers a robust framework that enhances the prediction and understanding of age-related changes in human biology, potentially paving the way for early interventions and refined disease risk assessments.

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