Multimodal Prediction of Alzheimer's Disease: An AI-Ensembled Approach Integrating MRI Imaging and Blood Based Biomarkers

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Alzheimer's disease (AD) impacts approximately 55 million people globally and is predicted to affect 139 million individuals by 2050. As most diagnoses occur after substantial neurodegeneration, opportunities for therapeutic intervention are limited. This research introduces a novel multi-modal diagnostic framework integrating MRI derived neuroimaging biomarkers with recent FDA-approved plasma biomarkers to enhance early and biologically valid prediction of AD progression. This study continues a previously built MRI-based Hybrid Artificial Intelligence (AI) model that classified T1-weighted MRI data of 1,000 ADNI participants into 5 groups: Normal Cognition (NC), Early Mild Cognitive Impairment (EMCI), Mild Cognitive Impairment (MCI), Late MCI (LMCI), and AD. MRI scans were segmented into 170 regions using the AAL-3 atlas, and then 13 volumetric biomarkers were identified. A random forest algorithm identified the most predictive markers and most impacted regions, which were used to train a 3-D ResNet-18 network validated through fivefold cross validation. To strengthen biological basis, plasma phosphorylated tau-217 (pTau217) and amyloid-ß 42/40 ratio (Aß42/40) were integrated as a multimodal validation layer. Elevated pTau217 and decreased Aß42/40 ratios demonstrated high concordance with the MRI-derived atrophic markers in the hippocampus and thalamus consistent with AI-predicted AD risk. The integrated framework resulted in high specificity (93.5%) and sensitivity (83%), providing robust biochemical evidence supporting the volumetric biomarkers, establishing a novel, AI-driven multi-modal platform that links neuroimaging to plasma biomarkers and demonstrating strong translational potential for early, clinically actionable Alzheimer's disease diagnosis.

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