

# Assessing Progression of Alzheimer's Disease: Predicting Cognitive Impairments and Amyloid Deposition Through PET and MRI

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Neurometabolic and vascular changes have been shown to pre-date amyloid deposition and cognitive impairment in Alzheimer's disease by several decades. However, these changes are not well characterized and lack clinical applications. The aim of this study was to elucidate metabolic and vascular changes that were indicative of Alzheimer's progression in transgenic Apoe4 mice and humans, and to use these changes for the development of machine learning approaches that could efficiently classify patients and predict cognitive impairment. MRI and PET images were obtained from the Alzheimer's Disease Neuroimaging Initiative and analyzed for glucose uptake, cerebral blood flow, and amyloid concentration. Region-wide and whole brain values were used to engineer features for ensemble learning and artificial neural networks. After training and cross-validation, the models achieved an average accuracy of 86.27% in distinguishing between three-month-old control and transgenic Apoe4 mice. In humans, the models achieved a comparable average accuracy of 82.89% in predicting the conversion from mild cognitive impairment to Alzheimer's disease within a three-year period. Furthermore, a normalized ranking of features prioritized glucose metabolism and cerebral blood flow over amyloid concentration when predicting changes in cognition. These results were validated by studying a novel therapeutic, Rapamycin, which ameliorated cognitive impairment in transgenic Apoe4 mice through vascular changes. This study presents the first translational machine learning approach for the early diagnosis of Alzheimer's disease, and can be used to assess pharmacological interventions and improve cohort selection in clinical trials.

## Awards Won:

Third Award of \$1,000