Neuroimaging of New and Novel Alzheimer’s Disease (AD) Mice from the MODEL AD Consortium

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Introduction

The Model Organization Development and Evaluation for Late-Onset Alzheimer’s Disease (MODEL-AD) Consortium is developing the next generation of AD models based on human genomic and imaging data. Preclinical studies have the advantage of being able to directly correlate findings to the observed neuropathology. The MODEL-AD imaging cores utilize existing state of the art translationally relevant medical imaging methodologies as well as ascertain feasibility of emerging imaging methods for increased diagnostic sensitivity.

Methods

Two primary imaging modalities will be utilized: high-field MRI (9.4T and 17.6T) and PET/CT. Deep MRI phenotyping is based on the accepted human-AD standards like ADNI (Structural T2W, FLAIR, diffusion, perfusion (PWI), susceptibility, and functional MRI and MR spectroscopy). Novel histological vessel painting combined with PWI will assess vascular alterations. PET imaging will evaluate brain metabolism (18F-FDG), regional perfusion (64Cu-PTSM), amyloid (18F-AV45), tau (18F-AV145), neuroinflammation (18F-CPPC and 18E-DG4145), and astrocytic (18F-FEBU) markers in new mouse models.

Vessel Analysis

Paxinos-Franklin Atlas

Figure 1: MODEL-AD imaging cores utilized standardized acquisition and data analysis processing workflows. These workflows are updated as new and improved methods are validated.

PET Tracers

Figure 2: MODEL-AD Consortium Platform Mice

Figure 3: MRI diffusion tensor (DT) imaging for axonal (AD), radial (RD) and mean (MD) diffusivity with fractional anisotropy (FA), and pseudo-colored (color) maps provide quantitative information about the underlying tissue microstructure. Multi-echo T2 images and data show anatomical structure and reports water content. Susceptibility-weighted imaging (SWI) is sensitive to tissue iron and potential location of tissue microbleeds. MODEL-AD uses these imaging metrics to phenotype new and emerging models. Images are from 10-month-old male mice.


Additional Information

MODEL-AD was established with funding from The National Institute on Aging (U54 AG054345-01, U54 AG054349-01). Aging studies are supported by the Nathan Shock Center of Excellence in the Basic Biology of Aging (NHP5 AG038070).

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Figure 4: MODEL-AD Consortium Platform Mice

Figure 5: Individual category ordered adjacency matrices of 18F-FDG PET for 12-month-old C57Bl/6J mice on control diet (left) compared to high fat diet (HFD, right) illustrating significant regional metabolic differences due to HFD.

Conclusions

The MODEL AD consortium continues to develop new and novel AD mouse models and the neuroimaging cores will deeply phenotype these models using existing and emerging neuroimaging methods and analytic approaches. All data will be made available via the Sage Knowledge Network (https://adknowledgeportal.synapse.org).

References

See full reference list in the supplemental materials.