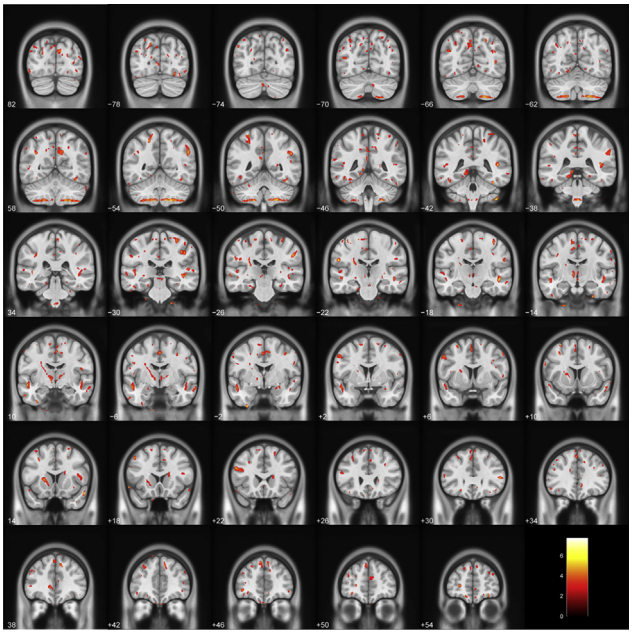
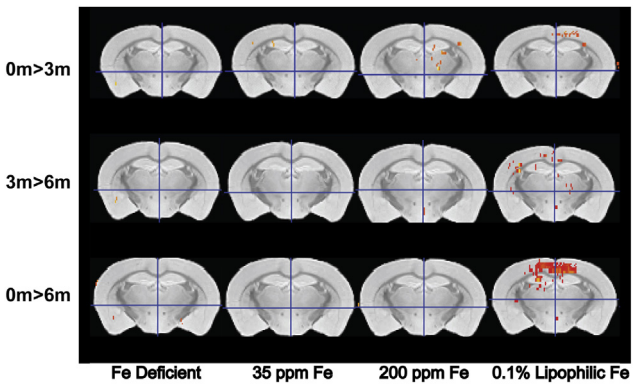


patients. Considering that R2 relaxation rate is a factor of iron content and tissue structure, this pattern could be indicative of white matter alterations in Alzheimer's disease. This hypothesis is congruent with data showing that AD has an integral white matter component.

IC-P-029 MAGNETIC RESONANCE IMAGING OF APP/PS1/TAU MICE ON GRADATED IRON DIETS

Mark D. Meadowcroft[1], Douglas G. Peters[1], Michael P. Haaf[2], Qing X. Yang[1], James R. Connor[1], *[1]The Pennsylvania State University - College of Medicine, Hershey, PA, USA; [2]Ithaca College, Ithaca, NY, USA. Contact e-mail: mmeadowcroft@hmc.psu.edu*

Background: There is converging evidence that iron overload is involved in both amyloid-beta (Aβ) plaque and neurofibrillary tangle (NFT) formation. Our previous results have demonstrated that hypo-intensities on T_2- and T_2*-weighted MRI datasets coincide with Aβ plaques in AD and transgenic neural tissue. There are crucial unanswered questions in the current literature on how iron and amyloid fibrils are involved in plaque and tangle genesis in the living brain and the neurotoxic impact of amyloidogenesis. We hypothesize that iron is a cofactor in the genesis of Aβ plaques and plays a synergistic function in relation to Aβ plaque neurotoxicity. The goal of this research is to 1) determine the *in vivo* relationship between iron and AD pathology, 2) observe the effects of different iron diets on spatial and learning memory using escape maze tasks, and 3) establish the cyto-architectural basis of AD pathology in relation to MR metrics. **Methods:** Four groups of six APP/PS1/Tau transgenic mice were randomized into four diet groups consisting of Fe deficient, 35 mg/kg Fe, 200 mg/kg Fe, and 0.1% lipophilic iron. Mice were scanned on a 7.0 T system at baseline and at three month increments for one year along with cognitive and blood biomarker measures. Group based parametric map analysis and region of interest (ROI) based transverse relaxation metrics were generated. **Results:** Group based transverse parameter maps and ROI analysis of mice fed the iron diets demonstrate that mice have shorter transverse relaxation in a gradated step-wise fashion with increasing iron diet in the same cortical regions. **Conclusions:** The parametric group analysis and segmentation changes confirm that high iron diets significantly alter the APP/PS1/Tau brain. Our previous data has shown that transverse relaxation is a measure of plaque formation and iron loading; as such, the cortical relaxation changes are hypothesized to reflect an accumulation of iron and Aβ plaques genesis in the cortex. This research will generate new information for understanding the role of homeostatic iron overload in Aβ plaque and NFT formation within the AD brain to determine how iron levels affect plaque morphology, pTau formation, iron management, inflammatory response, and cognition.



IC-P-030 COMPARISON OF REFERENCE REGIONS FOR IMPROVED DETECTION OF CHANGE IN FLORBETAPIR PET FROM PHASE 3 SOLANEZUMAB TRIALS

Adam S. Fleisher[1], Abhinay D. Joshi[2], Karen Sundell[3], Yun-Fei Chen[1], Michael D. Devous, Sr.,[2], John Seibyl[4], Kenneth Marek[5], Eric R. Siemers[6], Mark A. Mintun[2], *[1]Eli Lilly and Company, Indianapolis, IN, USA; [2]Avid Radiopharmaceuticals, Philadelphia, PA, USA; [3]Eli Lilly, Indianapolis, IN, USA; [4]Molecular NeuroImaging, New Haven, CT, USA; [5]Molecular Neuroimaging, New Haven, CT, USA; [6]Lilly Research Laboratories, Indianapolis, IN, USA. Contact e-mail: afleisher@lilly.com*

Background: Amyloid-PET is commonly utilized in Alzheimer's disease(AD) anti-amyloid therapy trials for eligibility requirements and longitudinal evidence of target engagement. Improving methodologies to detect longitudinal change in amyloid-PET is of particular importance. Although cerebellum is a widely utilized reference region for cross-sectional quantitative evaluations, it may not be optimal for longitudinal assessments. We compared use of atlas based cortical white matter and whole-cerebellum reference regions for accuracy and power for detecting longitudinal change in Phase 3 solanezumab trial data. **Methods:** Florbetapir-PET scans were analyzed from 140 participants (72 placebo, 68 solanezumab) with mild dementia due to AD from the 18-month, randomized, placebo-controlled EXPEDITION 1&2 solanezumab studies. Participants had florbetapir positive scans at baseline, determined by mean cortical-to-whole-cerebellar standard uptake