No differences in uptake were observed in other organs. **Conclusions:** This preliminary work further supports the capacity of this CatD targeted CA to help differentiate between AD mice and controls.

IC-P-025 WITHDRAWN

IC-P-026 AMYLOIDOSIS INDUCES REORGANIZATION OF THE HIPPOCAMPAL METABOLIC NETWORK

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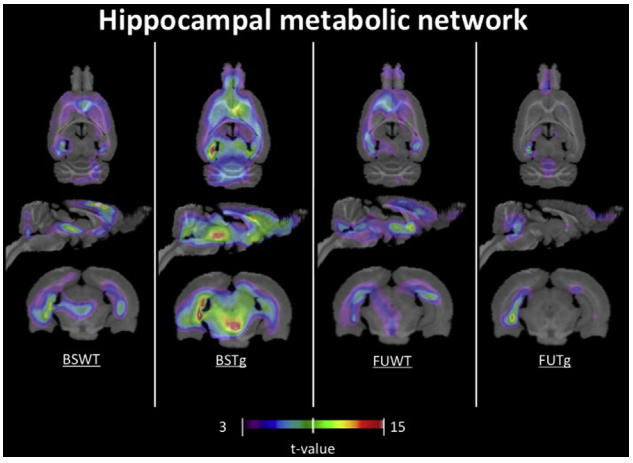
Background: Rat transgenic models of human brain amyloidosis constitute a unique opportunity to explore the impact of amyloid pathology on imaging biomarkers without the bias of tau pathology invariably present in the human brain. The cerebral metabolic rate of glucose measured by Positron Emission Tomography using [^{18}F] FDG is often used as a biomarker of neurodegeneration in Alzheimer's disease (AD). Metabolic network refers to population-based maps depicting large-scale organization of brain glucose utilization. There has been growing evidence, suggesting that brain amyloidosis modulates metabolic changes observe in the progression of AD pathophysiology. Here, we investigate the effect of amyloidosis on hippocampal metabolic network in wild type (wt) and transgenic (Tg) Mcgill-R-Thy1-APP rats, which express amyloidosis in the absence of tangles or cell depletion. We hypothesized adaptations of brain metabolism in early stages of amyloidosis followed by declines in the metabolism in aged animals. **Methods:** A total of 17 rats (10 WT, 7 Tg) were used for this study. The FDG-PET acquisition was done longitudinally with 11.5 mo (baseline) and 16.8 mo (follow-up). Individual FDG SUVRs were generated using pons as a reference region. Population based correlation analysis were generated using the dorsal and ventral hippocampi. Tg and wt hippocampal metabolic networks maps were compared at voxel- levels using Fisher's Z transformation. **Results:** WT hippocampal metabolic network [Baseline vs follow-up] contrast did not reveal significant differences. As compared to McGill-R-Thy1-APP rat showed increased strength of correlation and recruitment of additional cortical areas at baseline, while in the follow up it a drastic decline in the hippocampal metabolic network was noted. When performed Fisher's Z transformations, baseline Tg showed significant correlation in subcortical structures such as thalamus and small regions in medial temporal lobe compared to baseline and follow-up WT. Baseline Tg showed significant correlation in medial temporal lobe, bilateral hippocampi, amygdala, and cingulate cortex compared to follow-up Tg (figure 1). **Conclusions:** These results demonstrate that amyloidosis per se alter brain metabolism and large-scale brain metabolic networks. Similar to what has been reported in humans, while early brain amyloidosis evokes enhances and declines of glucose metabolism, late stages of amyloidosis leads to significant hypometabolism.



IC-P-027 DYNAMICS OF LONGITUDINAL BIOMARKER CHANGES IN THE MCGILL-R-THY1-APP RAT

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Background: Rat transgenic models of human brain amyloidosis constitute a unique opportunity to explore the impact of amyloid pathology on imaging biomarkers without the bias of tau pathology invariably present in the human brain. Due to its size, the McGill-R-Thy1-APP rat is ideal for multi-modal neuroimaging observations as compared to transgenic mouse. Here, we studied the associations between the rates of structural brain remodeling as a function of the rate of progression of hypometabolism in transgenic rats. We hypothesize regional specific interactions between biomarkers. **Methods:** McGill-R-Thy1-APP rat (n=9) and wild type (wt; n=12) had [^{18}F]FDG and structural MRIs scans at 11-month (baseline) and 16-month (follow-up). Structural images were acquired using a Bruker 70/30USR Biospect MRI (FISP; TE/TR: 2.5/5.0ms; FOV: 3.6cm^3; isotropic 250um voxels; 8 angles). Voxel-based morphometry was performed to obtain longitudinal deformation maps. [^{18}F]FDG PET images were acquired and analyzed as described previously (3). For both scans, longitudinal difference maps were generated. Global uptake values obtained from these maps were then correlated with structural deformation maps using a voxel-level linear model. **Results:** The olfactory bulb, anterior pituitary lobe, multiple cortical areas, lateral ventricle, and a portion

of the hippocampus showed association between [^{18}F]FDG declines and structural shrinkage. The left motor cortex and thalamic nuclei as well as the right primary somatosensory cortex showed dissociation between structural changes (expansion) and [^{18}F] FDG declines. **Conclusions:** McGill-R-Thy1-APP allows for longitudinal biomarker measures without confounding effects of neurofibrillary tangles or cell death. In fact, the present results suggest that brain abnormal amyloid aggregates present in the McGill-R-Thy1-APP rat leads to expansion or shrinkage of grey matter structures and progressive hypometabolism. However these processes occur in synchrony in specific brain regions. These suggest a complex interface between amyloid pathology and pathophysiological mechanisms involved in structural declines in transgenic animals.

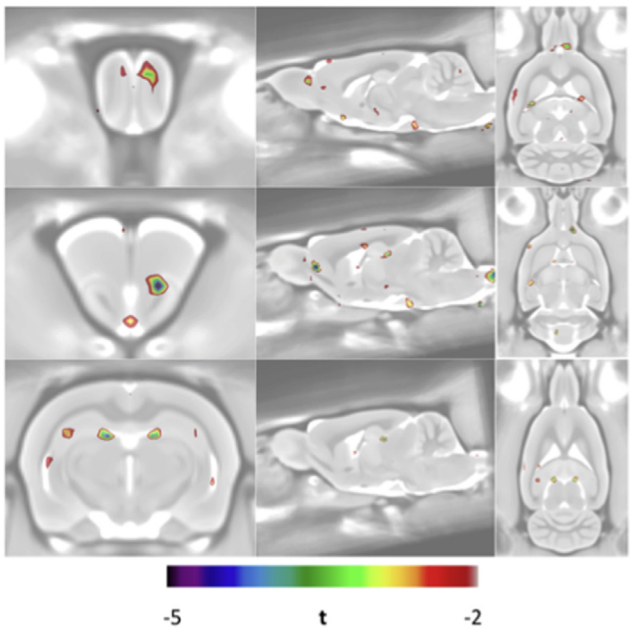

Figure 1. t-stat map of regions that shrink when the metabolism decreases throughout the brain.

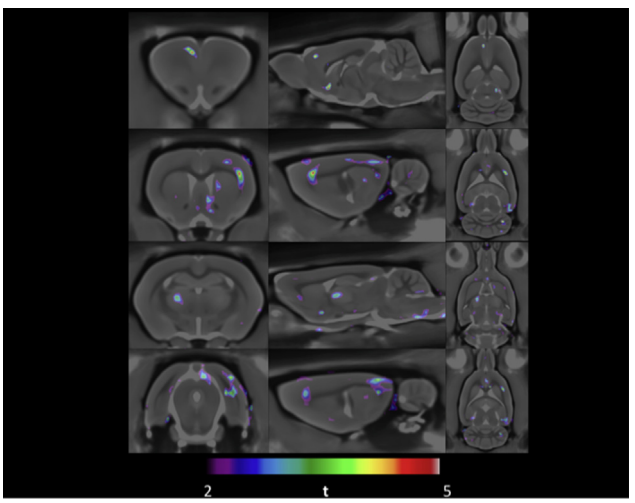

Figure 2. t-stat map of regions that expand when the metabolism decreases throughout the brain.

IC-P-028 **DIFFERENTIAL MRI RELAXATION IN ALZHEIMER'S PATIENTS WITH MUTANT HFE AND TRANSFERRIN GENOTYPES**

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Background: Iron accumulation in the brain and oxidative stress are observed in a number of neurodegenerative disorders such as Alzheimer's disease (AD). Common mutations that lead to high iron overload has been associated with two gene variants within the HFE gene, C282Y and H63D, and within the transferrin (Tf) gene, C2. Within Alzheimer's disease these mutations are found with increased frequency in patients (estimates are between 20-50%). The goal of this work was to understand how HFE and C2 mutations effect transverse relaxation in the AD brain with the hypothesis that these mutations will result in increased transverse relaxation rate within the brains of AD C282Y, H63D, or C2 carriers. **Methods:** Thirty-eight mild Alzheimer's disease patients (13M, 25F) were enrolled. Of these, 7 subjects (1M, 6F) were heterozygous and 1 subject homozygous (1F) for the H63D mutation, 3 subjects (2M, 1F) were heterozygous C282Y mutation, and 4 subjects were heterozygous (2M, 2F) for the TfC2 mutation. All patients were scanned on a 3.0 T system and group based parametric map analysis was performed on the stratified patient populations: those with high iron mutations (IRON +; H63D, C282Y, or C2) and those with all wild-type genes (IRON –). **Results:** The group based R_2 parametric analysis demonstrates that AD patients with high iron mutations (IRON+) have increased R_2 rates specifically within white matter regions of interest. **Conclusions:** The stratification of AD patients based on IRON + genetics and determination that there are relaxation differences specifically in white matter is a highly novel finding. The cause for the white matter relaxation metrics are believed to be multi-faceted and not only related to the high iron status of AD IRON + carriers. As the relaxation rate alterations are found exclusively in white matter, we hypothesize that there are white matter modifications in AD IRON +