in whole brain SUVs compared to BuChE-KO controls (p=0.037). This significant decrease had not been observed in our previous investigations of cerebral metabolism in a BuChE expressing 5XFAD model (vs. control counterparts) at 5 months. **Conclusions:** We have previously observed variation in cerebral glucose metabolism with Aβ pathology in 5XFAD mice. Our current investigations suggest that BuChE may also be a modulator of cerebral glucose metabolism in AD, whereby the presence/absence of BuChE could significantly impact not only pathology but also brain function over the course of AD. Comparison of these 5XFAD/BuChE-KO brain metabolism results with those in BuChE expressing 5XFAD counterparts is currently underway. Furthermore, regional assessment of brain metabolism and corroborating neuropathology in these animals may further implicate BuChE in the progression of AD and may highlight the potential role of targeted BuChE imaging approaches for AD diagnostics.

IC-P-023 PILOT STUDY OF ALTERED COPPER METABOLISM AS A BIOMARKER FOR EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE WITH $^{64}CUCL_2$-PET/CT

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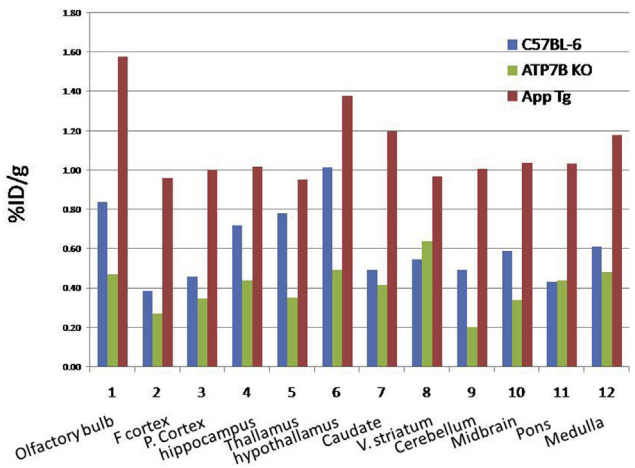
Background: Copper is a trace element required for development and normal function of human brains. Emerging body of evidence suggests the role of copper in pathogenesis of Alzheimer's disease. The aim of this study was to explore the potential of altered copper metabolism as a biomarker for early diagnosis of Alzheimer's disease with positron emission tomography/computed tomography (PET/CT) using copper-64 chloride ($^{64}CuCl_2$) as a radioactive tracer ($^{64}CuCl_2$-PET/CT). **Methods:** APPSWE transgenic mice (N=4, 14 weeks old,), a mouse model of Alzheimer's disease, were subjected to PET/CT after intravenous injection of copper-64 chloride ($^{64}CuCl_2$) as a tracer, using a small animal PET/CT scanner. A group of wild type C57BL/6 mice (N=4, 13 weeks old) and another group of *Atp7b* $^{-/-}$ knockout mice (N=4, 6 to 7 weeks old), a mouse model of Wilson's disease, were used as controls. PET quantitative analysis was performed to compare ^{64}Cu uptake in the brains of the APPSWE transgenic mice with the ^{64}Cu uptake in the brains of C57BL/6 and *Atp7b*$^{-/-}$KO mice, respectively. **Results:** Increased ^{64}Cu uptake was detected in the brains of the APPSWE transgenic mice, compared with the ^{64}Cu uptake in the brains of the C57BL/6 mice and the *Atp7b*$^{-/-}$ KO mice, respectively. In addition to increased ^{64}Cu uptake in the cortex, large increase of ^{64}Cu uptake was also detected in the regions of olfactory bulb and caudate of the APPSWE transgenic mice. Furthermore, cerebral ^{64}Cu uptake in the brains of the *Atp7b*$^{-/-}$ KO mice was found to be lower than the cerebral ^{64}Cu uptake in both the C57BL/6 mice and the APPSWE transgenic mice. Decrease of cerebral ^{64}Cu uptake in the *Atp7b*$^{-/-}$ KO mice was likely secondary to metabolic trapping of ^{64}Cu in the liver of *Atp7b*$^{-/-}$KO mice as visualized on the PET/CT images. **Conclusions:** Increased ^{64}Cu uptake was detected in the brains of APPSWE transgenic mice, compared with the ^{64}Cu uptake in the brains of C57BL/6 mice and *Atp7b*$^{-/-}$ KO mice, respectively. The findings support further investigation of altered copper metabolism as a biomarker for early diagnosis of Alzheimer's disease with PET/CT using $^{64}CuCl2$ as a radioactive tracer ($^{64}CuCl_2$-PET/CT).



IC-P-024 A NOVEL POSITRON EMISSION TOMOGRAPHY CONTRAST AGENT TARGETING CATHEPSIN D SHOWS PREFERENTIAL *IN VIVO* RETENTION IN AN ALZHEIMER'S DISEASE MOUSE MODEL

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Background: Early detection of Alzheimer's disease (AD) pathology remains a serious challenge for both diagnosis and development of treatment. Cathepsin D (CatD), a lysosomal aspartyl protease, is over-expressed in AD and therefore is a potential biomarker. Previously, we introduced a novel Contrast Agent (CA) that was preferentially taken up by CatD over-expressing cells (*in-vitro*) and able to transverse the BBB in mice (*ex-vivo*). We have also found that a Near-Infrared-labeled version of this CA demonstrates prolonged *in-vivo* retention in the brain of a transgenic (Tg) mouse model of AD at 12 months compared to age matched wild type controls. Here, we present the performance of a CA labeled with ^{68}Ga evaluated by micro Positron Emission Tomography (microPET). **Methods:** The CA consists of a Cell Penetrating Peptide (CPP; the Tat peptide from HIV-1), attached to a CatD cleavage sequence followed by a ^{68}Ga labeled DOTA chelator flanked by a fluorescent dye. The CPP allows the agent to cross the blood brain barrier bidirectionally. In the presence of elevated levels of CatD, cleavage of the CatD site removes the CPP resulting in prolonged retention of the imaging moeity. For this study, Tg AD mice (N=8, 5XFAD model) and non-Tg age matched littermates (N=8) at 2 and 4.5 months of age received an intravenous tail vein CA injection of ~12 MBq of CA under isofluorane anesthesia. Mice were scanned for 3 hours using the Inveon preclinical microPET system (Siemens Medical Solutions, Knoxville TN, USA). Regions of interest were identified in reconstructed images and were used to measure the uptake and washout of the CA in the brain, liver, kidneys and bladder. **Results:** The Tg mice demonstrated significantly greater uptake ($p<0.05$) of the CA in the brain in the first two hours following injection at 4.5 months but not 2 months of age compared to controls.

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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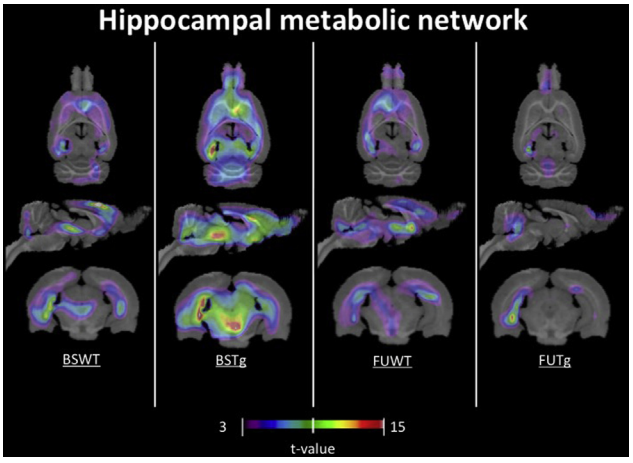
Background: Rat transgenic models of human brain amyloidosis constitute a unique opportunity to explore the impact of amyloid pathology on imaging biomarkers without the bias of tau pathology invariably present in the human brain. The cerebral metabolic rate of glucose measured by Positron Emission Tomography 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