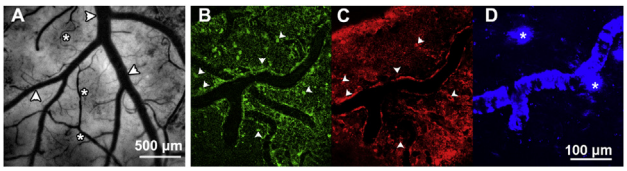

Figure 1. *In vivo* NADH fluorescence imaging of AD mice reveals chronic tissue hypoxia and cellular metabolic shift. A) Characteristic NADH pattern after reduction of oxygen supply. Arrowheads pointing to a vein; asterisks at arteries. B) Two-photon imaging under the same conditions shows numerous cells with increased signal (green). C) A subset of those cells stain positive for the astrocyte marker SR101 (red). Arrowheads at cells double positive for NADH and SR101. D) Cortex also shows heavy CAA (blue) and tissue plaques (blue, asterisks).

indicate that under those conditions a subset of cells may adapt by up-regulating glycolysis to overcome the deficient oxidative phosphorylation. The population of cells with increased NADH signal is likely a combination of neurons and glia. This work can lead to new strategies that target metabolic pathways to halt AD progression.

IC-P-031 APPLICATION OF DOUBLE MR IMAGING TO DETECT AMYLOID OLIGOMERS IN THE BRAIN OF APP/PS1 TRANSGENIC MODEL MICE

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Background: We have developed two types of potential imaging agents using ^{19}F-MRI: ^{19}F-containing styrylbenzoxazole derivative (Shiga-X22) and curcumin derivative (Shiga-Y5). Shiga-Y5 detects both Aβ oligomers and Aβ aggregates, while Shiga-X22 only detects Aβ aggregates. Thus, the Shiga-Y5 images subtracted by Shiga-X22 may reflect the images of Aβ oligomers. In this study, we applied double MR probe-imaging to detect amyloid oligomers in the brain of APPswe/PS1dE9 double transgenic model mice. **Methods:** All experimental procedures were approved by the Animal Care and Use Committee of our University. Six APPswe/PS1dE9 double transgenic mice at age of 20-month-old were used. We simultaneously injected Shiga-Y5 and Shiga-X22 at a dose of 200 mg/kg into the tail vein of three mice. At 3-h after the injection, ^{19}F chemical shift imaging was obtained using a 7-tesla MR scanner. Another three mice were killed by overdose of sodium pentobarbital and we removed the brain. Then, the concentrations of Aβ oligomers were measured by enzyme-linked immunosorbent assay (ELISA). **Results:** The ^{19}F MR signal of Shiga-Y5 appeared mainly in the olfactory bulb, the subcortical area, and the cerebellum. In contrast, the ^{19}F MR signal of Shiga-X22 displayed predominantly in the olfactory bulb, the cortex, and the cerebellum. Then, we produced a subtracted image by subtracting ^{19}F MR images of Shiga-X22 from that of Shiga-Y5. ^{19}F MR signal in the subtracted image was located in the subcortical area. ELISA measurement showed that Aβ oligomers uniformly distributed in the brain except for the brainstem, and there is no specific region showing the accumulation of Aβ oligomers. In contrast, the level of insoluble Aβ was significantly less in the subcortical area where the concentration of insoluble Aβ was relatively low. The imbalance between relative high level of Aβ oligomers and the less level of insoluble Aβ in the subcortical area may contribute to intense ^{19}F MR signal in the subtracted image. **Conclusions:** We employed double probe MR images using Shiga-Y5 and SHiga-X22 to detct Aβ oligomers in the brain of AD model mouse.

IC-P-032 *IN VIVO* TWO-PHOTON IMAGING OF THE EFFECTS OF TAUOPATHY AND AMYLOIDOPATHY ON SYNAPSE DYNAMICS IN THE RTG4510 AND J20 TRANSGENIC MODELS RESPECTIVELY

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Background: A progressive loss of synapses occurs at the early clinical stages of Alzheimer's Disease (AD) and has been correlated with cognitive deficits in AD patients. However, it is relatively unknown how synapse dynamics are affected by the two main pathological hallmarks of AD; the intracellular accumulation of tau and the extracellular accumulation of amyloid β protein, Here we used *in vivo* two-photon microscopy to assess the temporal dynamics of axonal boutons and dendritic spines in transgenic mouse models of human tauopathy (rTg4510) and amyloidopathy (J20). The Tg4510 model expresses the P301L tau mutation downstream of a tetracycline-operon-responsive element, whilst the J20 expresses both the *Indiana* (V717F) and *Swedish* (K670N, M671L) mutation on the amyloid precursor protein gene. **Methods:** Following a craniotomy, adeno-associated virus expressing green fluorescent protein (GFP) was injected into layer 2/3 of the somatosensory cortex to enable the visualisation of neurons and a cranial window was implanted for long-term imaging. GFP-labelled neurons were imaged in Tg4510s, J20s and wild-type littermate controls during a time period which spanned the onset of pathology. The gross morphology of axons and dendrites and the dynamics of their synaptic structures were assessed as the pathology progressed. In the rTg4510 experiments, a third group of animals received doxycycline to determine the effects of suppressing the pathogenic P301L transgene. In the J20 experiments, the density and size of amyloid plaques and the effects of plaque proximity on synapse density were also assessed. **Results:** In rTg4510s, gross morphological changes such as the presence of dystrophic neurites were visible as the tauopathy progressed and these were found to have a distinctive morphological phenotype prior to neurite degeneration. Alongside this, synapse instability and loss were also observed and could be prevented by suppressing the P301L transgene. In J20 animals, amyloid plaques increased in size and density over time and spine density was affected by the dendrite's proximity to plaques. **Conclusions:** Both tauopathy and amyloidopathy had effects on synapses as the respective pathology progressed. These results will inform subsequent drug discovery studies to identify novel therapies to stabilize synapse loss in AD.

IC-P-033 RESTING-STATE NETWORK DYSFUNCTION IN ALZHEIMER'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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