Multi-modal MRI analysis for assessing memory impairment in the early stages of AD

Swati Rane1, Tracey Porchak1, Brandon Ally2, Erin Hussey1, Tricia Thornton-Wells1,2, Shashwath Meda1, John C Gore1,2, and Manus Donahue1,4
1Radiology and Radiological Sciences, Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States, 2Neurology, Psychiatry, Vanderbilt University, Nashville, TN, United States, 3Center for Human Genetics Research, Vanderbilt University, Nashville, TN, United States, 4Molecular Physics and Biophysics, Vanderbilt University, Nashville, TN, United States, 5Biomedical Engineering, Vanderbilt University, Nashville, TN, United States, 6Psychiatry, Vanderbilt University, Nashville, TN, United States

INTRODUCTION: Alzheimer’s disease (AD) is a neurodegenerative condition characterized by a pre-clinical stage with hypothesized, yet unproven, vascular and metabolic changes in brain regions such as the posterior cingulate (PCC), default mode network (DMN) and hippocampus (HF). It has been shown that abnormal baseline BOLD synchrony in DMN and HF is consistent with poor performance during memory encoding. Furthermore, individuals with mild cognitive impairment (MCI) suffer from memory and cognitive dysfunction, similar to AD patients, and may eventually progress to AD, but identifying which patients progress remains difficult. Currently Aβ plaques, which are prevalent in AD, are not reliably detectable with MRI. However, Aβ plaque deposition has been associated with reduced neurovascular coupling, inflammation and decreased vascular response, which can be interrogated with multi-modal MRI approaches. More specifically, subjects with familial risk of AD and those with MCI show increased baseline synchrony or task dependent activity, hypothesized to represent compensatory hemodynamic mechanisms.

Here, we employ multiple MRI techniques to characterize baseline hemodynamic changes in older healthy controls, adults at familial risk of AD and adults with MCI to achieve a multi-facetted comparison of the preclinical pathology of AD. We performed baseline BOLD MRI and cerebral blood flow (CBF) images acquired with pseudo-continuous arterial spin labeling (pCASL), in conjunction with cognitive testing, to quantify differences in functionally eloquent regions implicated in AD in subjects with varying AD-risk and cognitive performance as evaluated by Consortium to Establish a Registry for Alzheimer's Disease (CERAD) scores for verbal fluency and recall.

MATERIAL AND METHODS: All volunteers provided, informed written consent in accordance with the local IRB. Experiment: 21 subjects (8 controls, 7 subjects at familial risk of AD and 6 MCI subjects) were studied using a single-shot, echo-planar imaging (EPI) sequence to quantify BOLD contrast at 3T (Philips). 35 slices were acquired at a spatial resolution of 3 x 3 x 4 mm3 and TR/TE = 3000/35 ms (140 dynamics). For evaluating CBF, a pCASL scan with 15 slices (3.5 x 3.5 x 7 mm3) at TR/TE/T = 4000/1625/13 ms was acquired. Whole-brain T-weighted (1 mm3 isotropic) structural images were also acquired for registration purposes.

Analysis: BOLD. Preprocessing steps included high frequency noise removal, baseline drift correction, smoothing (FWHM=3 mm), and motion correction in FSL. BOLD data were registered to a 2 mm resolution MNI template. Baseline BOLD synchrony in DMN and HF is consistent with poor performance during memory encoding. Furthermore, individuals with mild cognitive impairment (MCI) suffer from memory and cognitive dysfunction, similar to AD patients, and may eventually progress to AD, but identifying which patients progress remains difficult. Currently Aβ plaques, which are prevalent in AD, are not reliably detectable with MRI. However, Aβ plaque deposition has been associated with reduced neurovascular coupling, inflammation and decreased vascular response, which can be interrogated with multi-modal MRI approaches. More specifically, subjects with familial risk of AD and those with MCI show increased baseline synchrony or task dependent activity, hypothesized to represent compensatory hemodynamic mechanisms.

CONCLUSION: We have employed multi-modal MRI analyses approaches to detect differences in preclinical stages of AD that may contribute to memory and cognitive dysfunction. We assessed the correlation between CBF, baseline BOLD fluctuations in the DMN, and the HF synchrony with CBF. Results of this study suggest that multi-modal MRI strategies to characterize neurodegenerative disorders and their relation to neuropsychological evaluations may have relevance for AD diagnosis and risk assessment.