Multimodal MRI Analysis of Cerebral Blood Flow and Free Water Fraction in ADNI3 Cohort

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Introduction:

Late onset Alzheimer's disease (LOAD) is a serious public health problem, social burden, and economic cost without any proven preventative treatment. It is ranked as the sixth cause of death and leading cause of dementia in the United States, afflicting nearly six million Americans (alz.org). Pathological hallmarks of LOAD including amyloid plaques, tau tangles, atrophy, and impaired metabolism are tied to impairments in blood flow or inflammation. Furthermore, LOAD patients present with several co-morbidities linked to inflammation and hypoperfusion including vascular disease, thyroid disorders, sleep apnea, osteoporosis, and glaucoma. Comorbid psychiatric symptoms of LOAD, such as mood swings, depression, and hallucinations are also associated with cerebral hypoperfusion or neuroinflammation. However, very few studies have been able to categorize the relationship of cerebral perfusion perturbation and inflammation in the normal aging and diseased LOAD brain, which might be important for preventive as well as symptomatic treatment trials. To better understand these relationships, we perform a multi-modal analysis between free water (FW) images as a surrogate marker of neuroinflammation and quantitative cerebral blood flow (qCBF) images from the ADNI3 study (adni.loni.usc.edu).

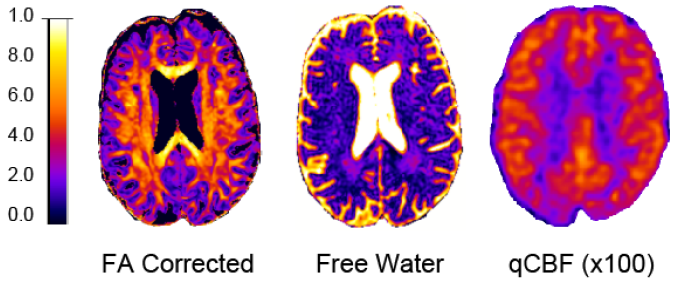

Fig. 1: Brain maps from a single subject

Methods:

All MRI sequences were collected with a GE 3.0T system and an eight-channel head-coil by Invivo. T1 anatomical images were collected using Accelerated Sagittal IRFSPGR (TE= min full, TR=2300ms, TI=400ms) with 1x1x1mm resolution. The qCBF images were estimated from the Axial 3D pCASL[1] (Eyes Open) sequence (TE=10.5ms, TR=4885ms, PL Delay=2000ms) with 1.9x1.9x4mm resolution and reported in ml/min/100g. FW images were calculated from single shell DTI sequence[2] (TE=Minimum, TR=7200) with 1x1x2mm resolution and reported by fraction range from zero to one. Brain images were registered and normalized to the T1 template using ANTs[3]. Normal and LOAD subjects (n=102) were grouped into cohorts by cognitive status and LOAD pathology status based on amyloid PET imaging. Voxel wise parallel ICA analysis was performed on these cohorts to assess association between qCBF and FW images. Statistics were performed with R and voxel clusters with significant values were collected.

Discussion:

We aim to understand how chronic and acute LOAD pathology from aging and disease cause neuroinflammation and how that inflammation affects cerebral blood flow. We hypothesize that (1) acute injury (asymptomatic LOAD pathology), similar to the body's response, is followed by increased blood flow and inflammation to facilitate healing of the pathology insulted area; (2) chronic brain inflammation may then lead to decreased blood flow, nutrition delivery, and waste clearance, worsening the disease state. Further research is required to better understand how capillary and venous cerebral flow is related to inflammation, as well as how basal perfusion changes alter functional hyperemia and neurovascular coupling.

References:

1. Alsop, D. C. *et al.* Recommended implementation of arterial spin-labeled Perfusion mri for clinical applications: A consensus of the ISMRM Perfusion Study group and the European consortium for ASL in dementia. *Magn. Reson. Med.* (2015). doi:10.1002/mrm.25197

2. Pasternak, O., Sochen, N., Gur, Y., Intrator, N. & Assaf, Y. Free water elimination and mapping from diffusion MRI. *Magn. Reson. Med.* 62, 717–730 (2009).

3. Avants, B. & Gee, J. C. Geodesic estimation for large deformation anatomical shape averaging and interpolation. in *NeuroImage* (2004). doi:10.1016/j.neuroimage.2004.07.010

Highlights:

Multi-modal MRI analysis of quantitative cerebral blood flow (qCBF) and free water (FW) diffusion offers a unique perspective to better understand the relationship of blood flow and inflammation in aging and brain diseases. Knowledge of inflammation and blood perfusion to the brain will inform better diagnostic and treatment outcomes.