Investigating haemodynamic changes in the default mode network in Alzheimer's Disease

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TARGET AUDIENCE: Researchers interested in perfusion and neural networks, in particular in Alzheimer's disease (AD).

PURPOSE: To investigate haemodynamic changes in AD and how this relates to resting state network (RSN) activity, in particular in the default mode network (DMN) comprising the posterior cingulate cortex/precuneus (PCC/PCu), medial prefrontal cortex (MPFC), and the inferior parietal lobule (IPL). Activity in the DMN is proposed to reflect the default brain function in the absence of external stimuli or tasks, and is thought to be disturbed in Alzheimer's Disease [1].
Aim: To use arterial spin labelling (ASL) measures of CBF to determine whether changes in DMN activity can be related to haemodynamic changes in AD.

METHODS: *MR acquisition:* 12 patients with Alzheimer's disease and 5 age-matched healthy controls (HC) and were scanned on a 7T Philips Achieva system with 32-channel receive coil. ASL data was collected using background suppressed FAIR scheme with GE-EPI readout (2.7x2.7x6mm, 7 contiguous slices, TR=3s, TE=24ms, FA=90º, 10 dynamics) at post-label delay times of 400, 700, 1000, 1300, 1700, 2000 ms. In addition, a base magnetisation (M_0) image and T_1 inversion recovery dataset was acquired to segment grey matter (GM), white matter (WM) and CSF (2.7x2.7x3mm, TR=10s, TE=24ms, 16 contiguous slices, FA=90º, 10 dynamics). A 5 minute GE-EPI resting state dataset was also acquired (1.9 x1.9 x2 mm, TR=2s, TE=25ms, 36 contiguous slices, FA=75º, 150 dynamics).
***Data analysis**: Perfusion data:* Analysis was performed using custom written MATLAB scripts. ASL label and control images were motion corrected within and between post-label delay sets, and perfusion weighted (PW) images (ΔM) inspected for motion prior to forming an average PW image at each post-label delay time. Any subjects with significant motion artefacts were removed from the group (4 AD patients). T_1 maps were segmented to generate partial volume maps of grey matter (FAST, FSL, fMRIB). The average PW images were then fitted to form tissue transit time (TTT) and perfusion (CBF) maps taking into account partial volume effects. CBF and TTT maps were interrogated in regions of interest (ROIs) assessed in *Asllani et al. 2008* [2] (cuneus, cingulate, inferior frontal, inferior parietal, insula, middle frontal gyrus, posterior cingulate, precentral and precuneus) ensuring ROIs were restricted within a GM mask. CBF and TT maps were transformed to MNI space to form group average maps. *Resting state data:* MELODIC (FSL, fMRIB) was used to verify that all subjects had clear DMN networks. Resting state data was transformed into MNI space for seed-based FC analysis; the PCC seed was defined as a square of 6 mm. For each subject, the mean BOLD signal time series was extracted from the PCC seed and the correlation coefficients between the PCC and other brain regions was assessed. Correlation values were extracted from the grey matter ROIs of the DMN; the medial prefrontal cortex (MPFC) and the left and right inferior parietal lobule (LIPL/RIPL), in addition CBF and TTT was assessed in these regions, as well as in the PCC.

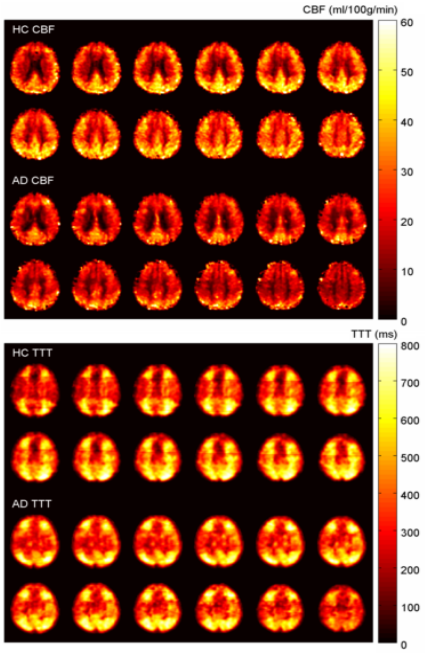

Figure 1: CBF and TTT group maps for AD patients and the HC group.

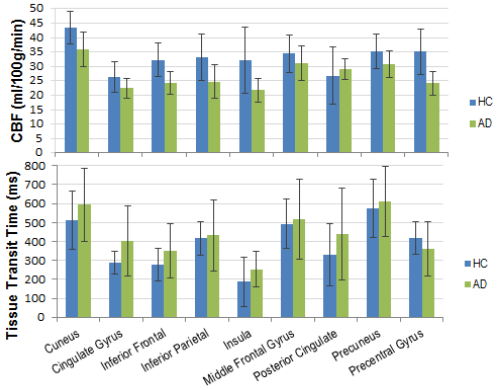

Figure 2: Mean CBF and TTT values in ROIs for AD patients and HC group.

RESULTS: Figure 1 shows the mean CBF and TTT maps in AD patients and HCs. Figure 2 shows a reduction of CBF in AD and an increase in TTT in predefined ROIs. No significant difference in atrophy was found between the AD and HC group, as assessed by the partial volume of GM. No significant difference in resting state correlation between the DMN nodes (MPFC/LIPL/RIPL) was found between the AD and HC groups. The LIPL showed a significant reduction in CBF in the AD group compared to the HC group (P = 0.03). No significant correlations were found between the resting state correlation between nodes of the DMN and underlying CBF and TTT.

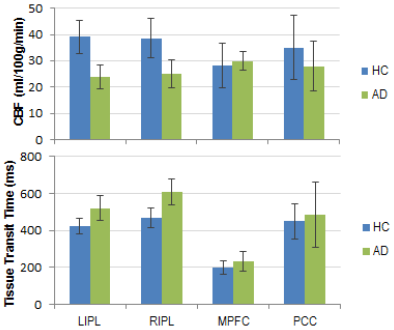

Figure 3: Mean CBF and TTT values in DMN nodes for AD patients and HC group.

DISCUSSION: We observed a reduced CBF and prolonged TTT in Alzheimer's Disease compared to age-matched healthy control subjects. Analysis of the DMN resting state network activity from seed-based correlation found no correlation with underlying CBF. Future work will assess these effects in a larger group size and across additional RSNs [3].

REFERENCES:

[1] Greicius *et al.* PNAS 101, 4637–4642, 2004. [2] Asllani *et al.* JCBFM 28: 725 – 736, 2008. [3] Agosta *et al.* Neurobiology of Aging, 33, 1564–1578, 2012.

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