Using ASL MRI to measure perfusion and arrival time in patients with Frontotemporal Lobar Degeneration

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Target Audience

This study will be of particular interest to clinicians with an interest in neurodegeneration and imaging scientists with an interest in arterial spin labeling

Purpose

Frontotemporal Lobar Degeneration(FTLD) is a progressive neurodegenerative disease that starts with damage to the frontal and/or temporal lobes[1]. PET and SPECT studies have shown that patterns of metabolic and perfusion changes can be used to differentiate between patients with FTLD, patients with Alzheimer's Disease and controls[2]. An earlier study[3] has used ASL to show changes in perfusion between FTLD patients and other groups; however it did not allow for potential differences in arrival time between the groups, and did not consider the ventral regions that are the earliest affected in this illness. This study used a multi-inversion-time whole-brain ASL sequence to study regional and voxel-wise differences in perfusion and bolus arrival time between FTLD patients and controls.

Methods

This study was approved by the South Manchester NHS Research Ethics Committee. 7 patients diagnosed with FTLD (5F, mean age 66.4±8.1y) and 13 controls (3F, mean age 67.0 ±5.2 y) were scanned on a Philips Achieva 3T MRI scanner. A high-resolution 3D T1-weighted scan, a T2-weighted scan, and an ASL sequence with STAR labeling and EPI readout were taken. Acquisition parameters for the ASL scan were : TE: 21ms, TR: 3000ms; FOV: 224 x 224 mm; Matrix size: 64 x 64, Voxel size: 3.5mm x 3.5mm 20 slices; slice thickness: 5mm; 1mm slice gap;; Label thickness: 150mm; 10mm label gap; 20 pairs of control-label scans collected at 4 inversion times of 800ms, 1200ms, 1600ms and 2000ms. Vascular crushing was enabled to remove large vessel signal. An additional calibration scan with TR=10s and no labeling was collected to allow quantification of perfusion.

 All analysis was done in Matlab 2009 and SPM8. A single-blood-compartment model[4] was used to fit the ASL subtraction signal voxel by voxel to generate perfusion and arrival time maps. All images were transformed to MNI space by normalising an individual ASL control image to the SPM EPI template, and applying the same transformation to the ASL maps. The individual scan chosen was the fifth individual control image of the TI 800 ASL scans (from the 20 pairs), which has good grey/white matter contrast. Regions of Interest (ROIs) covering the whole brain, frontal and temporal regions were modified from the AAL library[5].

 Voxel-based analysis was carried out using a 2-sample t-test to compare perfusion and arrival time maps between groups.12 mm smoothing was applied; values were thresholded to p<0.001 uncorrected, with a cluster size of 10 voxels. Analyses were done both with and without global normalisation.

Results

 Data from 1 patient (F, 75y) and 1 control (M, 65y) were discarded because of inaccurate normalisation. Mean perfusion and arrival time values within the ROIs were calculated, and the values are shown in the table. Bolus arrival time is lower in patients in the left anterior temporal lobe: no other differences in perfusion or arrival time are significant. There is a significantly greater variation in perfusion in patients: the mean standard error in regional perfusion for patients is 2.75±0.48; for controls it is 1.81±0.30, and the p-value for a paired t-test is 0.012.

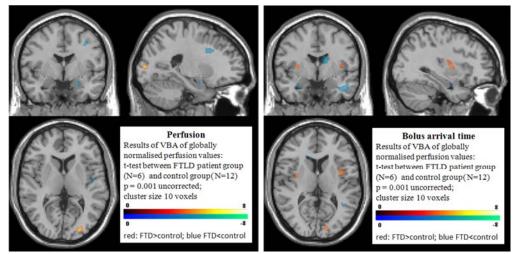|	Perfusion (ml/100ml/min)			Arrival time (ms)		
	Patients	Controls	t-test	Patients	Controls	t-test
Whole brain	38.1±16.6	39.0±9.4	0.89	740±75	691±77	0.24
L ant temp lobe	34.2±18.3	43.7±11.4	0.22	289±64	367±65	0.04 *
L post temp lobe	48.6±22.4	53.3±11.6	0.58	527±141	543±128	0.82
R ant temp lobe	27.1±14.8	36.9±10	0.15	306±88	354±55	0.20
R post temp lobe	38.5±14.1	42.8±10.9	0.51	459±99	551±126	0.16
Ant VM PFC	23.7 ±15.7	23.0±10.5	0.91	471±193	387±153	0.36
Post VM PFC	19.5±8.3	20.9±10.8	0.81	576±204	508±144	0.45

The images show the results of the VBA for perfusion and arrival time, including global normalisation. Perfusion was greater in right occipital regions and cerebellum in patients compared to controls and was lower in right frontal and temporal regions. Arrival time showed more bilateral differences, being longer in insular, occipital and medial temporal regions in patients compared to controls and shorter in the caudate, amygdala and temporal regions.

Analysis without global normalisation revealed similar arrival time results, but destroyed the perfusion differences.

Perfusion
Results of VBA of globally normalised perfusion values:
t-test between FTLD patient group (N=6) and control group(N=12)
p = 0.001 uncorrected;
cluster size 10 voxels
red: FTD>control; blue FTD<control

Bolus arrival time
Results of VBA of globally normalised perfusion values:
t-test between FTLD patient group (N=6) and control group(N=12)
p = 0.001 uncorrected;
cluster size 10 voxels
red: FTD>control; blue FTD<control

Discussion

The variation in perfusion values is much greater in the patient group; this could possibly be an effect of atrophy in a heterogeneous patient group. This variability contributed to a lack of widespread findings when considering absolute changes in perfusion. Differences in arrival time between the groups were also seen, suggesting that this could be a sensitive marker of micro-vascular differences that needs to be corrected for to obtain accurate perfusion estimates. These are preliminary results from a small patient group; recruitments is ongoing.

Conclusions

The VBA in this study shows differences in perfusion and bolus arrival time between patients with FTLD and healthy controls, which could in future possibly be used as an aid in diagnosis.

References

1. Neary et al; *Lancet Neurology* 2005;4(11):771-780   2. Foster et al; *Brain* 2007;130(10):2616-2635   3. Du et al; *Neurology* 2006;67(7):1215-1220
4. Parkes LM et al; MRM 2002;48(1):27-41.   5. Tzourio-Mazoyer et al; *NeuroImage* 2002;15(1):273-289.