

Regional and Global Cerebral Blood Flow is Reduced in Patients with Post-Stroke Dementia

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Introduction:

Stroke is one of the most important risk factors for dementia. In stroke survivors who do not have immediate, severe cognitive impairment, the risk of developing dementia is significantly increased [1]. Stroke may also exacerbate or trigger the development of neurodegenerative pathology, the severity of which may relate to the degree of medial temporal atrophy [2]. In pathological studies, a significant association was reported between cortical microinfarcts and Alzheimer's disease (AD) [3], with microinfarcts confined to watershed cortical areas, indicating that disturbed haemodynamic factors are involved in the genesis of vascular lesions which may precede Alzheimer's symptoms. Damage to subcortical grey-matter structures has also been suggested to be key to development of dementia after infarction [4]. In this work, we therefore aimed to determine if there are underlying differences in regional cerebral perfusion between post-stroke survivors with and without dementia, and whether these match perfusion abnormalities in AD.

Methods:

Patient Recruitment: Four groups of subjects were recruited from the local clinical old age psychiatry, geriatric medicine and neurology services; patients with post-stroke dementia (PSDEM, n=11, mean age 85± 4y), post-stroke patients with stable cognitive function (PSSTAB, n=28, 83± 3y), Alzheimer disease patients (AD, n=21, 83± 4y) and age and sex matched healthy controls (CON, n=30, 83± 3y). All subjects underwent comprehensive cognitive testing and MRI scanning. The study was approved by the local ethics committee and written informed consent was obtained from each subject prior to scanning.

MRI Experiments: MR measurements were conducted on a 3T whole body system (Achieva, Philips Medical System, Netherlands) using an 8 channel head coil. A T₁ weighted anatomical scan was acquired at 1.2 mm isotropic resolution for each patient using a standard 3D MPRAGE sequence (TE/TR 4.6/9.6 ms). A FAIR sequence [5] was implemented with GE EPI readout, and co-centred imaging/inversion slabs of 24/48 mm thickness (TE/TR=23/4000 ms, 4 slices of 6mm thickness, 64×64 matrix size, 4×4 mm² resolution, 10 ms bipolar gradient at 14 mT/m for bulk flow suppression). As 2 of the subject groups had suffered stroke and all subjects were elderly, dynamics of arterial blood delivery were measured using multiple FAIR inflow times, rather than making assumptions regarding spin delivery rate or collateral perfusion. A total of 9 inflow times (TI, 500, 650, 800, 950, 1100, 1400, 1700, 2000 and 2300 ms) with 20 pairs of images were acquired. Additionally a further 30 image pairs were collected at TI of 1700 ms to increase sensitivity at that TI.

Data Processing and Analysis: FAIR images were motion corrected (AIR), and separated into control and tagging types for each inflow time. The mean image for each type was computed, from which the difference images dM and magnitude images M were generated. The M images at multiple TI were used to calculate T₁ and fully relaxed images M₀ on a pixel by pixel basis. CBF values were calculated [5] using the dM images at TI=1700ms assuming the blood T₁ was 1490 ms and blood brain partition coefficient of 0.9 ml/g. The anatomical images were mapped into standard space and segmented into gray matter (GM), white matter (WM) and CSF using SPM5. The GM and WM regions of interest (ROI) were mapped back into individual patients by inverting the registration process. These ROIs were then applied to the dM, M₀, T₁ and CBF images to generate a mean value for each region. To investigate any differences in CBF between the vascular territories, the standard-space brain was partitioned into anterior cerebral artery (ACA), posterior cerebral artery (PCA), middle cerebral artery (MCA) and lenticulostriate artery (LSA) regions based on literature definitions of the anatomical boundaries of these vascular territories [6]. These territories were further segmented into GM and WM and again transformed into patient space to calculate mean parameters in each area. Time to peak dM signal (TTP) was also calculated for each ROI. Group comparisons were made using one way ANOVA and post-hoc t-test (SPSS 17, Chicago, IL).

Results:

CBF maps are illustrated in figure 1 for typical subjects in each group. Global GM:WM ratio (figure 2) was significantly reduced in AD and PSDEM vs CON. Regionally, the PCA and LSA vascular territories had significantly reduced GM:WM CBF in the AD and PSDEM vs CON (all p<<0.01), while CBF did not vary between groups in the ACA or MCA territories. There were no differences in TTP or WM CBF between any group.

Discussion:

Significant differences in CBF were observed between post-stroke patients who had suffered cognitive decline compared to those patients who had remained cognitively intact. CBF in cognitively intact patients appeared normal for age, while those with cognitive decline were very similar to AD patients (who had similar cognitive function). Regionally, CBF was most affected in deep gray matter structures supplied by the lenticulostriate artery (basal ganglia). Although lowest values were seen in post-stroke patients with dementia, there was no statistically significant difference compared to patients with AD. These data support the hypothesis that vascular effects are important development of cognitive dysfunction.

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References:

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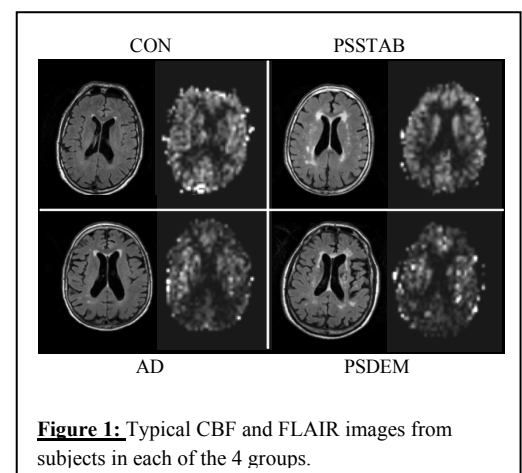


Figure 1: Typical CBF and FLAIR images from subjects in each of the 4 groups.

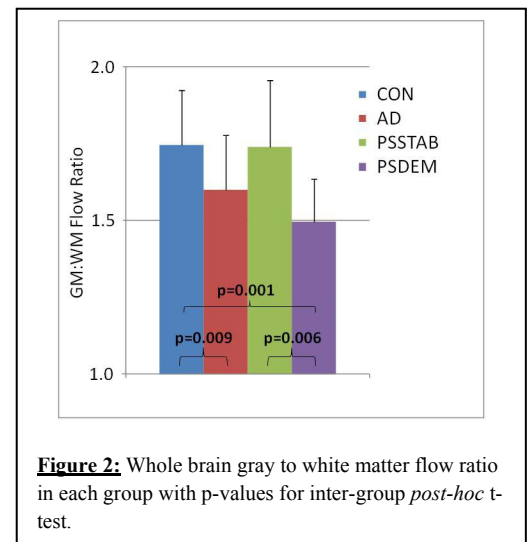


Figure 2: Whole brain gray to white matter flow ratio in each group with p-values for inter-group *post-hoc* t-test.