Greater Blood Flow Reduction in Mild Diffuse Lewy Body Disease than in Mild Alzheimer's Disease

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Introduction: MRI may play an important role in the evaluation of new therapies for dementia and, ultimately, their clinical use. Functional imaging with PET, SPECT, and Arterial Spin Labeling (ASL) MRI have demonstrated hypometabolism and hypoperfusion in parietal, temporal, and frontal association areas in Alzheimer's Disease, the most common age-related dementia. The utility of this pattern of decreased function as a quantitative marker for AD depends in part on its close connection to the pathology of the disease and its absence in other dementias. Diffuse Lewy body disease (DLB) is arguably the most common age-related dementia after AD. Previous studies in severe DLB have identified decreased metabolism or blood flow in the occipital cortex relative to AD (1-3). The aim of this current study is to use arterial spin labeled (ASL) perfusion MRI to measure regional cerebral blood flow (rCBF) in patients with DLB and to compare the magnitude and spatial distribution of the changes to normal controls and patients diagnosed with mild AD.

Methods: Images were obtained in 16 subjects diagnosed with mild probable AD, 7 subjects diagnosed with mild probable DLB, and 18 normal age-matched controls. Diagnosis of AD or DLB was made by experienced clinicians using established clinical criteria (4,5). In particular, DLB is distinguished from AD based on minimal memory impairment, marked fluctuations in cognition, attention, and alertness, emergence of parkinsonian signs, REM sleep disorder and often hallucinations or delusions. Subjects with a clinical history or imaging signs of cerebrovascular disease were excluded. All subjects underwent a battery of neuropsychological testing that included the Folstein Mini-Mental status examination (MMSE). MRI was performed on a 3 Tesla whole body scanner using the head coil. ASL (6) was performed using flow driven adiabatic inversion and an improved version of a previously published method for subtracting off-resonance saturation effects (7). A background suppressed 3D Fast Spin Echo sequence with cubic resolution of 3.8 mm was employed for ASL imaging. Voxelwise statistical comparison was performed using the SPM2 (Wellcome Department of Cognitive Neurology) compare groups function and global normalization. The tests were thresholded at a voxel significance of $p<0.05$ uncorrected for multiple comparisons across brain regions and only clusters with sufficient voxels for a corrected significance of $p<0.05$ were retained.

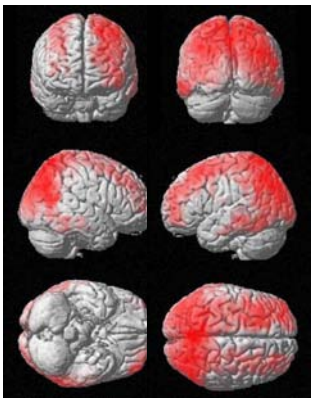

Figure 1. Areas with decreased rCBF in DLB relative to controls

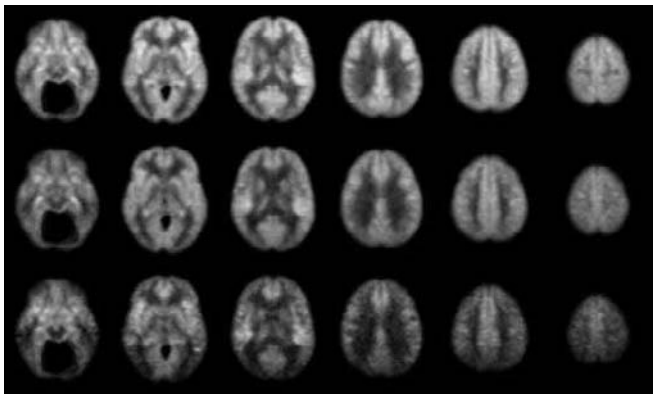

Figure 2. Average rCBF images in controls, top, AD, middle, and DLB, bottom.

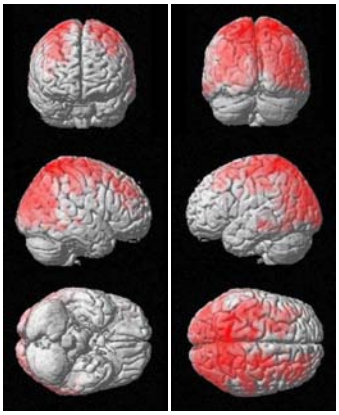

Figure 3. Areas with decreased rCBF in DLB relative to AD.

Results: Performance on the MMSE (score ±SD) was 28.1 ± 2.3 for aged-matched controls, 25.3± 2.7 for AD subjects, and 27.7 ± 1.6)for DLB subjects ($P<0.02$ for group differences). Significant decreases in blood flow were found in DLB (Figs 1 and 2), most notably in the parieto-occipital cortex and to a lesser degree in the frontal cortex. Decreases were more prominent in DLB than in the mild AD cohort(Fig 3).

Conclusion: In mild DLB, blood flow is markedly reduced in the same cortical association areas observed in AD. Despite a greater magnitude of rCBF reduction, the DLB subjects showed relatively less impairment on cognitive testing. This finding suggests hypoperfusion in association areas may be associated with decreased cholinergic function, which is more severe in DLB than AD, rather than other forms of AD pathologies. The regional pattern of decreased blood flow measured with ASL may have limited specificity for separating DLB and AD.

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