Different Patterns of Hypoperfusion in Frontotemporal Dementia and Alzheimer's Disease by Arterial Spin Labeling MRI

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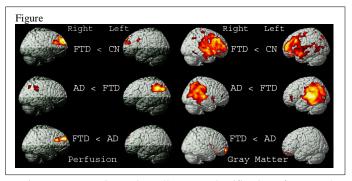
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Introduction: Frontotemporal dementia (FTD) and Alzheimer's disease (AD) are among the primary neurodegenerative diseases that affect cortical function. Clinically, FTD patients show profound alterations in personality and social conduct with relative preservation of memory function, while AD patients present usually multiple cognitive deficits including progressive worsening of memory function. Both illnesses, however, can present a broad spectrum of symptoms and clinical differentiation can be difficult in individual cases, especially at an early disease stage. Consistent with the clinical patterns, PET and SPECT studies have found a characteristic distribution of regional hypometabolism and hypoperfusion that involved primarily fronto-temporal regions in FTD and parietal-temporal regions in AD (1), suggesting that functional neuroimaging might aid a differential diagnosis between FTD and AD. However, PET and SPECT require injection of radioactive isotopes and are not widely available. Recently, we (2) and others (3) demonstrated that arterial spin labeling (ASL) MRI detects a pattern of regional hypoperfusion in AD similar to that measured with PET and SPECT. Moreover, we found that ASL-MRI already detects hypoperfusion in cases with mild cognitive impairments before dementia develops.[2] In this study, we tested: 1) whether ASL-MRI detects – similar to PET and SPECT - in FTD patients reduced perfusion in frontal lobe regions when compared to cognitively normal (CN) subjects and increased perfusion in parietal lobe regions when compared to AD patients; 2) if regions with gray matter (GM) loss coincide with regions of hypoperfusion; 3) the extent to which hypoperfusion and GM loss improve classification of FTD from CN and AD.

Methods: Twenty-one FTD patients (Age 62±7 yrs, MMSE 24±7), 24 AD patients (Age64 ±7 yrs, MMSE 19±7), and 25 CN (Age 62±7 yrs, MMSE 30±0) subjects were studied with ASL-MRI (4) and volumetric T1-weighted structural MRI at 1.5 Tesla. Five MRI slices (8mm thickness and 2 mm gap) were acquired using single-shot echo-planar imaging (EPI) acquisitions with a resolution of 2.3×2.3 mm^2. The other acquisition parameters for the labeled and reference scans were: TR=2.5s, TE=15ms, TI$_2$ (time from labeling pulse to the excitation pulse)=1500ms. Labeled and reference scans were then subtracted to obtain perfusion-weighted imaging (PWI) data. Then PWI images were registered to structural images, corrected for partial volume effects and spatially normalized to a study-specific brain template. Systematic group effects on perfusion and GM density were tested voxel-wise using Statistical Parametric Mapping (SPM2). Logistic regression was used to test the value of perfusion or GM density for group classification.

Results: The figure depicts systematic perfusion and GM density differences between FTD, AD and CN subjects, superimposed on a template brain. Light gray areas indicate regions covered by ASL-MRI or structural MRI. FTD patients showed hypoperfusion bilaterally in the superior and middle frontal gyri and left anterior cingulate gyrus (p < 0.001) in comparison to CN subjects and in right superior frontal gyrus (p < 0.001) in comparison to AD patients. AD patients, on the other hand, had hypoperfusion bilaterally in inferior parietal gyrus and in the left precuneus (p < 0.001) in comparison to FTD patients. In addition to hypoperfusion, FTD patients had less GM bilaterally in the superior, middle and inferior frontal gyri, and the superior temporal gyrus (p < 0.001) in comparison to CN subjects and bilaterally in the anterior cingulate, and right inferior frontal gyrus (p < 0.001) in comparison to AD patients. AD patients, on the other hand had less GM bilaterally in the superior, middle and inferior temporal gyri, left precuneus and posterior cingulate, and right superior and inferior parietal gyri (p < 0.001) in comparison to FTD patients.

Figure

Overall correct classification of FTD and CN reached 67% with perfusion and 60% with GM density, while classification of FTD and AD reached 78% with perfusion and 62% with GM density. When perfusion and GM density were combined together, only perfusion significantly contributed (all p < 0.05) to group classification between FTD and CN and between FTD and AD, suggesting that perfusion achieves better classifications than GM loss.

Conclusions: Detection of characteristic pattern of regional hypoperfusion by ASL-MRI in FTD and AD, which is similar to that by PET and SPECT, suggests that ASL-MRI may have similar value than PET and SPECT in separating FTD from normal aging and in differentiating between FTD and AD. Furthermore, better classifications with perfusion than with GM loss suggests that ASL-MRI is more sensitive than structural MRI in detecting FTD and AD pathology.

References

  1. Varrone A, et al. *Eur J Nucl Med Mol Imaging* 2002; 29(11):1447-1454. 2. Johnson N et al. *Radiology*, In press.
  3. Alsop DC, et al. *Ann Neurol* 2000; 47(1):93-100. 4. Jahng GH et al. *Magn Reson Med* 2003; 49(2):307-314.