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Pattern of cerebral hypoperfusion in Alzheimer's disease and mild cognitive impairment measured with arterial spin-labeling MR imaging: Initial experience☆

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Abstract. *Purpose:* To prospectively determine if pulsed arterial spin-labeling perfusion magnetic resonance (MR) imaging depicts regional cerebral hypoperfusion in subjects with Alzheimer's disease (AD) and mild cognitive impairment (MCI), compared with perfusion in cognitively normal (CN) subjects, that is consistent with results of fluorodeoxyglucose (FDG) positron emission tomography (PET) and hexamethylpropyleneamine oxime (HMPAO) single photon emission computed tomography (SPECT) studies of similar populations. *Materials and methods:* Institutional review board approval and informed consent were obtained. 20 subjects with AD (13 men, 7 women; mean age = 72.9 years), 18 with MCI (9 men, 9 women; mean age = 73.3 years), and 23 CN subjects (10 men, 13 women; mean age = 72.9 years) underwent arterial spin-labeling and volumetric T_1-weighted structural MR imaging. Perfusion images were coregistered to structural images, corrected for partial volume effects (PVEs) with information from the structural image to determine tissue content of perfusion voxels, and normalized to a study-specific template. Analyses of perfusion differences between groups, with and without corrections for PVEs, were performed on a voxel-by-voxel basis with a one-tailed fixed-effects analysis of covariance model adjusted for age. In addition, tests were performed with and without accounting for global perfusion. *Results:* The AD group showed significant regional hypoperfusion, compared with the CN group, in the right inferior

Abbreviations: AD, Alzheimer's disease; CN, cognitively normal; FDG, fluorodeoxyglucose; HMPAO, hexamethylpropyleneamine oxime; MCI, mild cognitive impairment; PVE, partial volume effect.

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parietal cortex extending into the bilateral posterior cingulate gyri ($P<0.001$), bilateral superior and middle frontal gyri ($P<0.001$), and left inferior parietal lobe ($P=0.007$). When PVEs from underlying cortical gray matter atrophy were accounted for, the AD group still showed hypoperfusion in the right inferior parietal lobe extending into the bilateral posterior cingulate gyri ($P<0.001$) and left ($P=0.003$) and right ($P=0.012$) middle frontal gyri. With a more liberal voxel-level threshold of $P<0.01$, the MCI group showed significant regional hypoperfusion relative to the CN group in the inferior right parietal lobe ($P=0.046$), similar to the region of greatest significance in the AD group. *Conclusion:* Arterial spin-labeling MR imaging showed regional hypoperfusion with AD, in brain regions similar to those seen in FDG PET and HMPAO SPECT studies of similar populations; this hypoperfusion persists after accounting for underlying cortical gray matter atrophy.

Results of neuropathologic studies suggest that evidence of Alzheimer's disease (AD) may be present in the brain years or even decades prior to the onset of clinical symptoms [1,2]. Currently, multiple potential therapies are being developed to attempt to halt or disrupt the disease process before neurons are irrevocably lost [3]. Evaluation of the effectiveness of these potential treatments will be enhanced by identification of patients at the earliest stages of the disease and by the possibility of objectively measuring disease progression. Because of this, there is currently great interest in the characterization of AD by means of objective measures such as brain imaging, particularly in early stages of the disease process.

Fluorodeoxyglucose (FDG) positron emission tomography (PET), which is used to measure glucose metabolism, and technetium 99m hexamethylpropyleneamine oxime (HMPAO) single photon emission computed tomography (SPECT), which is used to measure cerebral blood flow, consistently show reduction of cerebral metabolism or blood flow in studies of subjects with AD. The most characteristic reductions of metabolism or blood flow are seen in the temporo-parietal association cortices, in the posterior cingulate cortex, and, to a lesser extent, in frontal association cortices with relative sparing of the primary motor and sensory cortices [4–6]. More recently, PET and SPECT have been used to examine subjects with genetic predisposition to AD, family history of AD, very mild AD, or mild cognitive impairment (MCI) in an attempt to characterize functional patterns associated with preclinical or early disease. The results of these studies suggest a similarity between regions most affected in AD and those regions affected in subjects who have high risk of developing dementia, which suggests that detection of such functional changes may be useful for early detection of AD [7–17].

Arterial spin-labeling perfusion magnetic resonance (MR) imaging is another method used to assess brain perfusion and function in dementia [18]. To the extent that regional metabolism and perfusion are coupled, arterial spin-labeling MR imaging, at which arterial blood water is labeled as an endogenous diffusible tracer for perfusion, may depict functional deficiencies in a way similar to FDG PET and HMPAO SPECT [19]. Moreover, arterial spin-labeling MR imaging offers several advantages over these techniques: It is entirely noninvasive and free of exposure to ionizing radiation, intravenous contrast agents, and radioactive isotopes; it can be performed with most MR imagers in 10–15 min;