Assessment of Cerebral Blood Flow in Amyotrophic Lateral Sclerosis Using Arterial Spin Labeling MR Imaging

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Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder affecting both upper and lower motor neurons. Currently, there are no objective and sensitive measures to identify and evaluate the pathologic changes in the brain of ALS. Previous studies using PET or SPECT demonstrated reduced regional cerebral metabolism or perfusion throughout the brain in patients with ALS.[1-3] In contrast, patients with progressive muscular atrophy appeared to have normal or near normal cerebral metabolism and perfusion.[4-5,] These studies suggest that measurement of brain perfusion maybe a useful tool for the early diagnosis and monitoring of disease progression. Arterial spin label (ASL) perfusion imaging is a non-invasive technique to assess the cerebral blood flow (CBF) without exposure to radioactive tracers. The purpose of this study is to evaluate the utility of ASL for the detection of CBF abnormalities in patients with ALS.

Materials and Methods

20 patients (12 M, 8 F, mean age 55.6) with ALS according to El Escorial criteria and 9 healthy subjects (5 M, 4 F, mean age 54.3) were included in this study. All patients underwent MR examination on a 3T Siemens Tim Trio scanner with a 12-channel phased-array head coil. A pseudo-continuous ASL sequence was used for the perfusion scan. Interleaved images with and without labeling were acquired using a spin-echo EPI sequence. Sequence parameters were as follows: TR/TE = 4000/28 ms, FOV = 220 x 220 mm^2, number of sections = 16, slice thickness 5 mm, matrix = 96 x 96, labeling delay = 1200 ms, labeling duration = 1500 ms. Total acquisition time was 5:32 minutes. In house software based on Matlab (The MathWorks, Natick, MA) and SPM5 (Wellcome Department of Cognitive Neurology, UK, London) were used for image analysis. The raw ASL data were first realigned, smoothed and then labeled and control scans were subtracted to obtain CBF data. The CBF images were registered to structural images and spatially normalized to a study-specific brain template. Two-sample t test were used in SPM5 to examine the absolute and relative CBF difference between patients with ALS and healthy subjects. Global CBF values were included in the model as covariate to get relative CBF. Imaging results were thresholded at an uncorrected level of $p < 0.005$ with cluster size of 20 voxels. A threshold of whole brain false discovery rate (FDR)[6] of $P < 0.05$ was also used.

Results and Discussion

Representative CBF maps were shown in Figure A. Relative CBF differences between patients with ALS and healthy subjects ($p < 0.005$, uncorrected) were shown in Figure B. Significantly reduced CBF in ALS patients compared with healthy subjects was found in bilateral sensorimotor cortex, superior temporal lobe, left anterior cingulate gyrus, calcarine and precuneus cortex. Absolute CBF differences showed the similar findings. At a FDR corrected level of $p < 0.05$, hypoperfusion in ALS was shown in the right sensorimotor cortex, superior temporal lobe and calcarine cortex. The pathologic hallmark of ALS is loss of giant pyramidal Betz cells in the motor cortex. Widespread motor cortex atrophy which extended to primary sensory area has been reported in neuropathologic studies.[7] The observed hypoperfusion of sensorimotor cortex in our study is consistent with the pathologic changes in ALS. Cingulate gyrus is also considered as motor area. Several investigators have reported hypoperfusion or hypometabolism findings in the cingulate gyrus in patients with ALS.[1-2] Other regions such as temporal, occipital and parietal lobes were also involved in our study, confirming that ALS is a multisystem disorder. Other extramotor systems can be involved to various degrees. Our study indicates that ASL perfusion may be used as a potential biomarker for the diagnosis and monitoring of disease progression in ALS.

References

1. Kew JJ, et al. Brain 1993;116 :655
2. Habert MO, et al. Amyotroph Lateral Scler 2007;8:9.
3. Rule RR, et al. Neurology; 2010; 74: 821
4. Dalakas MC, et al. Ann Neurol 1987;22:580
5. Kew JJ, et al. Neurology 1994;44:1101
6. Genovese CR, et al. Neuroimage 2002;15:870
7. Grosskreutz J, et al. BMC Neurol. 2006; 6: 17