Cerebrovascular reactivity defect in multiple sclerosis

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Purpose: One of the emerging techniques for mapping cerebrovascular reactivity (CVR), which represents potential vascular capacity of regulating cerebral blood flow (CBF) supply, is hypercapnia perfusion MRI with breathing 5% CO2 as a vascular dilatory stimulus. CVR is an important mechanism for maintaining constant CBF of brain, and the impaired CVR, if exists, may contribute to cellular respiration failure and neurodegenerative processes. Multiple sclerosis (MS) is an inflammatory demyelinating disease with devastating progressive neurodegeneration of poorly understood etiology. In this study, we used pseudo-continuous arterial spin labeling (pCASL) to detect whether there is CVR impairment, which might be responsible for neurodegenerative process, in patients with MS during hypercapnia challenge.

Materials and Methods: Nineteen patients with relapsing remitting (RR) MS (9 males and 10 females; mean age, 44.4 years; range, 23 to 65 years) and 19 healthy volunteers (12 males and 7 females; mean age, 40.1 years; range, 20 to 65 years) were studied. Patients with cardiac, pulmonary, and hematologic diseases were excluded and no caffeine was taken within 4 hours prior to MRI in all subjects. The mean disease duration for the patient group was 5.1 years (range 0.67-14 years) and the mean EDSS score was 2.5 (range 0-6). MR imaging was performed on a 3.0T whole body MR scanner with a 12-channel array head coil. CVR was measured with a robust multi-slice pCASL MRI with quantitative CBF (ml/min/100g) maps generated during both room air (baseline) and mild hypercapnia (mixed 5%CO2, 21%O2, and 74%N2) exposure. The following parameters of pCASL were used: TR/TE=3950/17ms, 52 repetitions (i.e. 26 pairs of tag and control images), FOV=22cm, in-plane matrix=64x64, slice thickness=5mm and total axial slices of 32, gradient echo EPI readout, slice-selective gradient=8mT/m, postlabeling delay = 1230ms, label offset = 89m. The pCASL acquisition time is 3min15sec. End-tidal CO2 (EtCO2) was recorded continuously during the scan using a capnograph device as an input function. After performing motion correction for the label and control image series separately, CBF calibration was conducted using the standard equation. The CVR (in %CBF/mmHg EtCO2) is calculated of percentage change of CBF per unit of EtCO2 change reflecting the difference between the average recordings of EtCO2 of mild hypercapnia and room air. CVR was computed and compared between patients and controls from global brain parenchyma, gray matter (GM), normal appearing white matter (NAWM), and lesions.

Results: Compared to healthy controls, RR-MS patients showed significantly decreased CVR (%CBF change/mmHg EtCO2) (Figure 1) of whole brain parenchyma (mean: 5.2±0.6% vs 2.8±0.5%, P=0.01), global GM (5.3±0.9% vs 3.1±0.4%, P=0.01), and global NAWM (5.3±0.7% vs 3.4±0.5%, P=0.02) without significant difference of baseline CBF between the two groups. In controls, the mean global GM CBF at baseline and mild hypercapnia were 67.7±9.1 and 98.6±17.9 ml/100g/min, respectively (Figure 2a and 2b). There was no significant difference of CBF change in lesions, indicating the normal CVR loss.

Conclusions: This is the first study to measure CVR abnormalities in MS. The preliminary data, which showed significant decrease of average global CVR in MS patients compared to controls using pCASL hypercapnia technique, indicate impaired vascular reactivity or CVR (%CBF change/mmHg EtCO2) results of cerebrovascular regulation to a vasodilatory stimulus (i.e. 5% CO2).


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