



Providing Choice & Value
Generic CT and MRI Contrast Agents

**FRESENIUS
KABI**

CONTACT REP

AJNR

Brain Perfusion and Vasoreactivity in Multiple Sclerosis

T. Koudriavtseva, E. Sbardella and C. Mainero

AJNR Am J Neuroradiol published online 15 January 2015
<http://www.ajnr.org/content/early/2015/01/15/ajnr.A4249.citation>

This information is current as
of July 29, 2025.

Brain Perfusion and Vasoreactivity in Multiple Sclerosis

Multiple sclerosis (MS) is a chronic disorder of the central nervous system, pathologically characterized by inflammation, demyelination, and neurodegeneration. In past years, there has been increasing attention paid to its ischemic-vascular aspects because abnormalities in CBF and CBV have been consistently described in both WM and GM, in all MS stages.¹ The enhanced expression of an hypoxia-inducible factor in normal-appearing WM and altered glial cell homeostasis and dysregulation of genes involved in hypoxic preconditioning also have been observed in MS lesions.¹ Finally, histopathologic similarities between ischemic and MS pattern III WM lesions and epidemiologic evidence of increased risk for developing ischemic stroke in patients with MS further support the presence of vascular abnormalities in the disease.¹

A recent study found that cerebral vasoreactivity (CVR) is also affected, adding further evidence of impaired CBF regulation in MS.² Using pseudocontinuous arterial spin-labeling perfusion MR imaging to measure CBF at normocapnia and hypercapnia (carbon-dioxide test), Marshall et al² reported decreased global CVR in the GM of patients with MS compared with healthy controls. Decreased GM CVR correlated positively with patients' GM atrophy index and negatively with their lesion volume.

The authors hypothesized that abnormalities in CBF regulation may cause neurodegeneration in MS by determining insufficient blood supply, with consequent neuronal dysfunction and death.² This explanation contrasts with previous hypotheses that attributed widespread decrease in cerebral perfusion in MS to reduced metabolic demand due to axonal degeneration.¹ Subsequent MR imaging examinations assessing the relation between WM perfusion- and diffusion-weighted imaging did not confirm this view.¹ Rather, reduced axonal activity and astrocyte energy metabolism were supposed to contribute to cerebral perfusion changes.¹ A recent work, however, found no relationship between reduced CBF and impaired axonal mitochondrial metabolism or astrocytic

phosphocreatine metabolism.³ A reduced cortical oxygen extraction fraction, independent of cortical and WM structural tissue damage, was recently shown in patients with MS relative to controls, even in early disease, indicating reduced oxygen metabolism that may be due to reduced CBF.⁴

Marshall et al² speculated that CVR abnormalities could be induced by vascular habituation to high concentrations of nitric oxide, a strong vasodilator, produced during chronic inflammatory processes. CVR, however, is determined by several interrelated factors, including vasodilators and constrictors derived from the endothelium, neuronal innervations, and blood perfusion pressure. Their balanced action is influenced by arterial blood pressure of carbon dioxide and oxygen, main regulators of CBF. It is likely that oxidative stress and inflammatory pathway activation leading to endothelial dysfunction and increased microvascular perfusion pressure due to an augmented resistance in postcapillary venules with a slowness of blood flow could contribute to overloading physiologic vasoregulation processes in MS.

In conclusion, cerebral blood perfusion is increasingly being established as a sensitive indicator of widespread brain dysfunction in MS, in addition to conventional MR imaging techniques. Its validation as an outcome measure for therapeutic trials may even allow testing of neuroprotective treatments from the earliest MS stages.

Disclosures: Tatiana Koudriavtseva—UNRELATED: consulting fees from Bayer Schering, and institutional grants from Merck Serono, Biogen Idec, Novartis, Bayer Schering. Caterina Mainero—UNRELATED: consulting fees from Biogen.

REFERENCES

1. D'haeseleer M, Cambron M, Vanopdenbosch L, et al. **Vascular aspects of multiple sclerosis.** *Lancet Neurol* 2011;10:657–66
2. Marshall O, Lu H, Briset JC, et al. **Impaired cerebrovascular reactivity in multiple sclerosis.** *JAMA Neurol* 2014;71:1275–81
3. Steen C, D'haeseleer M, Hoogduin JM, et al. **Cerebral white matter blood flow and energy metabolism in multiple sclerosis.** *Mult Scler* 2013;19:1282–89
4. Fan AP, Govindarajan ST, Kinkel RP, et al. **Quantitative oxygen extraction fraction from 7-Tesla MRI phase: reproducibility and application in multiple sclerosis.** *J Cereb Blood Flow Metab* 2015; 35:131–39

T. Koudriavtseva

E. Sbardella

Neurology Unit, Multiple Sclerosis Center
Regina Elena National Cancer Institute
Istituti Fisioterapici Ospitalieri
Rome, Italy

C. Mainero

Athinoula A. Martinos Center for Biomedical Imaging
Massachusetts General Hospital
Boston, Massachusetts
Harvard Medical School
Boston, Massachusetts