INVITED COMMENTARY

Comparing MRS and PET

In this issue of *The Journal of Nuclear Medicine*, Tsuchida et al. (*1*) report 2 interesting relationships that they observed between proton magnetic resonance spectroscopy (MRS) measurements and measurements of hemodynamics and oxygen metabolism with PET in 11 patients with severe occlusive carotid artery disease. First, they report that the ipsilateral–contralateral ratios of *N*-acetyl-aspartate to the sum of creatine and phosphocreatine (NAA/Cr) measured in hemispheric white matter correlated significantly with ipsilateral–contralateral cortical blood flow and with cortical oxygen metabolism. Because NAA is generally assumed to be restricted to neurons, this finding can be interpreted as indicating neuronal loss in the white matter distal to carotid artery occlusive disease that parallels the reduction in cortical blood flow and metabolism in the same hemisphere. Such an interpretation is consistent with previous pathologic findings of selective neuronal necrosis in both human and animal brains subjected to focal ischemia (*2*). Findings of incomplete brain infarction have also been reported on the basis of reduced uptake of the central benzodiazepine radioligand [^{123}I]iomazenil (*3*) in noninfarcted areas of brain or failure of cerebral oxygen metabolism to improve in noninfarcted brain after extracranial–intracranial bypass surgery (*4*). Second, Tsuchida et al. report that the ipsilateral–contralateral ratio of choline to the sum of creatine and phosphocreatine (Cho/Cr) in white matter correlates strongly with regional oxygen extraction fraction (rOEF) but not with blood flow or oxygen metabolism. Increased rOEF indicates a reduction in blood flow compared with oxygen metabolism. Thus, the areas with a high rOEF also had increased choline. The biologic interpretation of this second observation is more difficult. Choline is a constituent of cell membranes and is increased in conditions in which cell membranes are undergoing damage, such as multiple sclerosis and acute ischemia. Why choline should be increased in areas of brain in which the increased rOEF serves to maintain both oxygen metabolism and neurologic function is not clear. Interpreting this finding as ongoing low-level cellular membrane damage caused by low-level chronic ischemia does not seem justified on the basis of the available evidence. The elevation in choline may reflect previous tissue damage caused by transient ischemic attacks or stroke or the activity of macrophages scavenging the membranes of previously damaged tissue.

The clinical relevance of these findings is problematic. Two independent studies provide good evidence that increased rOEF distal to a stenotic or occluded carotid artery is a strong independent predictor of subsequent stroke (*5,6*). However, in the absence of an empiric trial, one cannot assume that revascularization surgery, such as an extracranial–intracranial bypass, would benefit these patients. The morbidity and mortality from surgery and the long-term risk of stroke in patients who undergo surgery are not known. Substitution of MRS-measured Cho/Cr for direct measurement of rOEF to identify patients at high risk of subsequent stroke is not justified. Although the correlation coefficient between ipsilateral–contralateral rOEF and Cho/Cr was strong, the number of patients in this study was too few to assume that such a strong correlation will be a consistent finding. Previous attempts to substitute other methodology for PET measurements of rOEF in identifying patients at high risk of stroke have not been successful (*7*). An independent prospective study is necessary to show that these MRS measurements can identify a group of patients with carotid occlusive disease and a higher risk of subsequent stroke (*8*).

William J. Powers
Washington University School of Medicine
St. Louis, Missouri

REFERENCES

1. Tsuchida C, Kimura H, Sadato N, Tsuchida T, Tokuriki Y, Yonekura Y. Evaluation of brain metabolism in steno-occlusive carotid artery disease by proton MR spectroscopy: a correlative study with oxygen metabolism by PET. *J Nucl Med.* 2000;41:1357–1362.
2. Garcia JH, Lassen NA, Weiller C, Sperling B, Nakagawara J. Ischemic stroke and incomplete infarction. *Stroke.* 1996;27:761–765.
3. Nakagawara J, Sperling B, Lassen NA. Incomplete brain infarction of reperfused cortex may be quantitated with iomazenil. *Stroke.* 1997;28:124–132.
4. Powers WJ, Martin WRW, Herscovitch P, Raichle ME, Grubb RL. Extracranial-intracranial bypass: hemodynamic and metabolic effects. *Neurology.* 1984;34:1168–1174.
5. Yamauchi H, Fukuyama Y, Nagahama Y, et al. Evidence of misery perfusion and risk for recurrent stroke in major cerebral arterial occlusive diseases from PET. *J Neurol Neurosurg Psychiatry.* 1996;61:118–125.
6. Grubb RL Jr, Derdeyn CP, Fritsch SM, et al. The importance of hemodynamic factors in the prognosis of symptomatic carotid occlusion. *JAMA.* 1998;280:1055–1060.
7. Yokota C, Hasegawa Y, Minematsu K, Yamaguchi T. Effect of acetazolamide reactivity and long-term outcome in patients with major cerebral artery occlusive diseases. *Stroke.* 1998;29:640–644.
8. Derdeyn CP, Grubb RL Jr, Powers WJ. Cerebral hemodynamic impairment: methods of measurement and association with stroke risk. *Neurology.* 1999;53:251–259.

Received Sep. 2, 1999; revision accepted Sep. 17, 1999.

For correspondence or reprints contact: William J. Powers, MD, Washington University School of Medicine, Campus Box 8225, East Building Imaging Center, 4525 Scott Ave., St. Louis, MO 63110.