Diffusion-weighted imaging of stroke: a brief follow-up.

R N Bryan

AJNR Am J Neuroradiol 1998, 19 (6) 1003-1004
http://www.ajnr.org/content/19/6/1003.citation

In relapsing-remitting MS, a widely held belief is that neuronal function recovers from a conduction defect caused by myelin loss, loss resulting from upregulated sodium channels in the neuron. This belief implies that myelin is damaged but neurons survive. Alternatively, a number of investigators have published MR spectroscopic evidence of neuronal death in MS lesions, pointing to decreased N-acetyl aspartate (NAA) in those lesions. Falini et al recently documented lower lesion NAA levels in cases of progressive MS than in benign MS (2). NAA reduction is present even in normal-appearing white matter in progressive MS, which has been interpreted as wallerian degeneration, axonal spread of damage, or both. In this issue of the *American Journal of Neuroradiology*, Heide et al (page 1047) report NAA decreases that were localized to visual pathways in patients with abnormal visual evoked potentials. These decreases were even found in areas where T2 imaging was normal, confirming and extending earlier work by correlating the NAA drop with abnormal neuronal function.

What causes these reduced NAA levels and neuronal death? Insight into this question was provided by a recent elegant study using 3-D confocal microscopy to examine active and chronic MS lesions (3). This study documented substantial damage to axons as well as myelin. Indeed, axonal transection was present in all lesions, with more damage in more active lesions. Such data indicate that neurons too are affected by MS –perhaps by inflammation, or perhaps by a "final common pathway" similar to ischemic damage. This latter possibility hints that neuroprotective agents may be effective in treating the lesions of MS patients, and slowing the neuronal damage that results from the demyelinating process. Many of the processes that escalate axonal injury and cell death may be delayed with the use of neuroprotective agents.

Radiology and neuroradiology in particular can take some of the credit for these advances in our understanding of MS as the authors of the confocal microscopy study attest (3). Such investigations suggest the role neuroradiology can play in furthering our understanding of disease and identifying new therapeutic targets. Heide et al's study is particularly exciting from a neuroradiologic perspective because of its application of spectroscopy.

Spectroscopic imaging (SI), or the generation of maps of metabolites such as NAA, lactate, and other markers such as pH, has the potential to revolutionize neuroradiologic diagnosis. Spectroscopy has, with the use of single voxel techniques, demonstrated the ability to identify individual brain cell types, including specific malignancies and markers of early cerebral ischemia. The advent of routine SI, however, will likely shape a new paradigm for its use. Consider how the advent of imaging has aided T1-weighted, T2-weighted, and proton-density-based neurologic MR. Few neuroradiologists would try to make a diagnosis based on a single large T1-weighted or T2-weighted voxel over the brain. When the brain is imaged with 128 × 128 or even 64 × 64 voxels, however, diagnoses become more straightforward. When SI reaches the capability of providing 128 × 128 voxel images of the brain, the spatial distribution patterns of NAA and other metabolites will be much more clear. Such enhanced capability will make diagnoses of a host of new diseases as straightforward as establishing the distinction between MS plaques and metastases by T1 and T2 images. The article by Heide et al gives us a good first example of how analysis of the spatial distribution of metabolic markers can identify neurologic pathophysiology, even at a low resolution.

Spectroscopic imaging needs extensive additional refinement before it will be ready for routine clinical use. Studies demonstrating the utility of SI can only help encourage equipment vendors and researchers to push forward on various fronts to make this a standard clinical modality. Heide et al used echo-planar readout techniques and customized headcoils to boost signal-to-noise ratios, key methods needed for SI. Spectroscopic imaging would, of course, benefit from a higher field strength, a more expensive option than either of the two methods used by Heide et al. But if SI is to demonstrate its full potential, increases in signal-to-noise ratios resulting in acquisition time decreases and increased coverage are crucial. Clinical neuroradiologists –and their patients –eagerly await the technical advances needed to bring this tool into routine clinical practice.

A. GREGORY SORENSEN, MD
Massachusetts General Hospital
Boston, Massachusetts

References

1. Waxman S. **Demyelinating diseases –new pathological insights, new therapeutic targets (Editorial).** *N Engl J Med* 1998;338:323–325
2. Falini A, Calabrese G, Filippi N, et al. **Benign versus secondary-progressive multiple sclerosis: the potential role of proton MR spectroscopy in defining the nature of disability.** *AJNR Am J Neuroradiol* 1998;19:223–229
3. Trapp B, Peterson J, Ransohoff R, Rudick R, Mork S, Bo L. **Axonal transection in the lesions of multiple sclerosis.** *N Engl J Med* 1998;338:278–285

Diffusion-Weighted Imaging of Stroke: A Brief Follow-up

In this issue of the *American Journal of Neuroradiology*, Lövblad et al (page 1061) nicely address issues I raised in a previous editorial on the subject of diffusion-weighted imaging (DWI) of acute cerebral ischemia (1). The main question I previously posed related to the pathophysiology of increased DWI signals, reflecting decreased diffusion coefficients, as seen in the clinical setting of acute stroke. Does the signal reflect infarcted (dead) tissue or reversibly ischemic (live) tissue? Clearly treatment could depend on the underlying pathophysiology of the lesions identified.

The current article by Lövblad et al strongly supports

the concept that, in the clinical setting, DWI signal usually reflects acutely infarcted tissue, not tissue at risk of infarction. This conclusion is suggested by the normal DWI findings in a transient ischemic attack, presumably reflecting reversibly ischemic tissue, and the lack of "disappearing" DWI lesions during ischemic tissue recovery. In addition, the authors describe a patient with a slowly evolving posterior cerebral artery infarct who must have had an area-at-risk of infarction missed on initial DWI. Although these results are at odds with prior animal studies showing reversible DWI ischemic changes, they are compatible with most prior clinical studies. Clinical results show DWI to be a very sensitive technique for detecting early infarction, but an insensitive approach for detecting areas-at-risk of infarction.

Questions concerning DWI of cerebral infarction that still need more attention are: 1) What is the most practical DWI sequence? 2) Can simple, single axis DWI imaging suffice or are more complex diffusion parameters necessary? 3) What is the reproducibility of the observations, particularly in relation to the subtle changes of CT? and 4) How sensitive is DWI and combined techniques in revealing hemorrhage? Answers to these more detailed questions will help guide the routine implementation of this most important MR technique for the evaluation of acute stroke. We, however, still need a method for defining the elusive ischemic penumbra, at the area-at-risk of infarction. Perhaps a complementary MR technique such as perfusion imaging will meet this persistent challenge.

R. NICK BRYAN, MD, PHD
Senior Editor

References

1. Bryan RN. **MR Spectroscopy of Temporal Lobe Epilepsy: Good News and Bad News (Editorial).** *AJNR Am J Neuroradiol* 1998;19: 189

Therapy in Parkinson's Disease: Surgery, Pharmacy, and Surgery Again. But Now with a Spark?

In this issue of the *American Journal of Neuroradiology* Cohn et al describe the preoperative and postoperative MR evaluation of stereotactic pallidotomy (see page 1075). The authors prefer a turbo spin echo inversion recovery sequence for guidance, but perform no formal evaluation to prove that this is better than any other high resolution sequence that provides good gray/white matter delineation. For follow-up purposes, straightforward T1- and T2-weighted acquisitions are all that are necessary in most cases. This information, however, is not what is fun about this work. A brief history will show that the therapy of Parkinson's disease has come nearly full circle.

Before Hans Spatz established the existence of an "extrapyramidal" motor system in 1927, neurosurgical therapy of Parkinson's disease centered on the spinal cord and brain stem. Tremors could be relieved, but the patient often paid the price with severe weakness and spasticity. After Spatz, the focus shifted to the basal ganglia and thalami. Neuroanatomic direction was still quite dependent upon contrast ventriculography or superficial landmarks, and even included ligation of the anterior choroidal artery to devascularize the ablation target. Some of these procedures had mortality rates of up to 41%. Stereotactic guidance changed this. Some groups, notably Lars Leskell's in Lund and Stockholm, performed carefully controlled interventions demonstrating that the optimal pallidotomy site was the posterior medial aspect of the medial globus palladus (1). As anatomic guidance became more precise, postoperative lesion size diminished and bilateral pallidotomies became safe. Despite such well controlled studies, ventral lateral thalamotomy became the preferred ablation target. Thalamotomies peaked in the 1960s, stopped only by the development of levodopa with its striking clinical benefits. By the mid 1960s and early 1970s, Parkinson's disease was rarely treated by functional neurosurgery. As clinical experience with dopaminergic agonist treatment of parkinsonism grew, however, 50% of treated patients were found to have significant motor complications. Medications developed to ameliorate motor complications increased the incidence of non-motor difficulties, especially psychiatric problems. These limitations of pharmacologic therapy in concert with the advent of much more sophisticated neuroanatomic guidance, especially MR imaging, have allowed the rebirth of functional neurosurgery. What is especially exciting about this neurosurgery now, however, is that ablation is not the only option. In fact, it may not even be the best. Spectacular results have been found with electrical stimulation devices, driven by work done by the Medtronic Corporation (Minneapolis, MN) of cardiac pacemaker fame. A strong proponent of electrical stimulation, Alim Benabid from Grenoble, France, reported favorable results in nearly 75% of tremor patients treated with this device. The excitement over neurostimulation has been noticed by a "journal" that is increasingly becoming "required reading" for the medical community, *The Wall Street Journal*(2). As would be expected, there is controversy over the ideal implantation site for this electrical stimulation device, with the globus palladus and subthalamic nucleus the two most favored. In fact, there is a blinded investigation in progress at the University of Oregon aimed at solving this controversy. Other investigators are considering the benfits of ablating one