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A new clinical application of MR spectroscopy in hepatic encephalopathy.

R N Bryan and P Barker

AJNR Am J Neuroradiol 1998, 19 (9) 1593-1594

<http://www.ajnr.org/content/19/9/1593.citation>

This information is current as
of April 18, 2024.

terminology might be as futile as Sisyphus' eternal attempt to roll a boulder up a hill only to see it tumble down again. In the case of CCFs, perhaps with next month's Journal.

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A New Clinical Application of MR Spectroscopy in Hepatic Encephalopathy

One of the first disease processes shown to have an abnormal proton MR spectrum was hepatic encephalopathy (HE), in a study in which Ross et al found decreased *myo*-inositol (mI) (1). Subsequent studies of HE further documented the changes in mI as well as increases in glutamine/glutamate (Glx) and decreases in choline (Cho). However, the clinical role of MR spectroscopy in this condition, as well as others, has only slowly evolved for a number of reasons, technical as well as clinical. Initially, proton MR spectroscopy was limited to single-voxel methods and long-TE techniques; the former factor limiting spatial sampling, the latter factor limiting spectral analysis. Single-voxel techniques have now been supplemented by chemical-shift imaging techniques, which better allow the study of localized and heterogeneous lesions such as ischemia and tumors. Short-TE techniques, necessary for mI and Glx detection, are now widely available and increase the ability to study brain metabolism in more detail.

With technological advances, it is the search for useful applications that is now being pursued. In this issue of *The American Journal of Neuroradiology*, Haseler et al (page 1681) push MR spectroscopy nearer to being a necessary clinical tool. The utility of a medical technique may derive from a variety of attributes. The technique could provide new insight into the pathophysiology of a disease, improve diagnosis, or, as proposed in the article by these authors, better direct therapy. The use of imaging techniques to better direct or monitor therapy is becoming increasingly important in the clinical arena. For example, imaging findings as indicators of treatment outcome have recently played a critical role in the evaluation, and eventual FDA approval, of multiple sclerosis drugs (2). Haseler et al show that lactulose treatment of HE causes MR spectroscopic changes to return to normal. Specifically, a week of lactulose therapy increased mI and decreased Glx, coincident with improvement of clinical HE grade. Good-quality

spectra clearly illustrate the differences between control subjects and HE patients before and after treatment. All articles on spectroscopy should include plots of primary data of this type. Importantly, the results suggest that MR spectroscopy may provide more sensitive markers of therapeutic response, at least in part because of the statistical advantage of using continuous variables instead of categorical clinical grades. The concordance of the MR spectroscopic and clinical response to therapy also suggests that the spectral changes, while incompletely understood, are not insignificant correlates of HE but rather reflections of metabolism related to cerebral dysfunction.

While these MR spectroscopic results are encouraging, more work is needed to solidify this clinical application. The use of spectral peak ratios, rather than absolute metabolic levels, remains suboptimal. Numerous publications have demonstrated the feasibility of metabolite quantitation with the use of proton MR spectroscopy, and these techniques should be applied in clinical studies. The sample size in the present study was small, only eight subjects actually completed the week of lactulose therapy. In addition, the possibility of sample bias exists, as only subjects with HE grade II/III were included in the treatment group. This restriction is appropriate for a pilot study, but MR spectroscopic findings of therapeutic response in a larger group of patients, including those with HE grades I through IV, are needed. A comparison of MR spectroscopic values with other HE-related variables, such as ammonia, is also needed. And longer follow-up studies are essential to determine the persistence of the MR spectroscopic mI and Glx findings and to ascertain whether this therapy can reverse the more subtle but longer lasting Cho changes.

If the MR spectroscopic responses to therapy presented in the present article are indeed corroborated by larger studies, then not only may the technique be

useful for directing and monitoring lactulose therapy but, perhaps more important, it may be useful for evaluating other treatments, such as TIPS and new medical therapies for HE.

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Spine Imaging: Should We Take This Lying Down?

The purpose of this editorial is to advocate further experimental work such as that which Muhle et al describe in this issue of the *American Journal of Neuroradiology* (page 1763).

For spine imaging, patients are placed in a supine position, often with supports or cushions to enhance their comfort. This position, which minimizes the patient's discomfort, may diminish any visible effect of spinal cord or spinal nerves. Weight-bearing, flexion, extension, or lateral bending change anatomic relationships, especially in the neural foramina and central spinal canal. Therefore, the application of some force to the spine during imaging may improve the detection of significant pathologic changes.

Kinematic and functional imaging studies of the spine have been reported in the neuroradiologic and orthopedic literature. Prolonged standing diminishes the size of the neural foramina and central spinal canal because disks lose water and height whenever the load on the spine is increased. Axial loading of the spine decreases the disk height measured on MR images, and axial compression of the spine causes bulging of the intervertebral disk and narrowing of the diameters of the neural foramen and central canal. In imaging studies, flexion or extension significantly narrows the neural foramina in relation to the neutral position. Flexion, extension, or axial rotation forces applied to the spine narrow the neural foramina at spinal levels with degenerating disks enough to cause mild compression of spinal nerve roots. One CT investigation in adult volunteers with disk degeneration has shown that a bulging disk, and to a greater extent a herniated disk, increases the amount of rotation that will occur at that level when a rotatory force is applied (Johansen JG, Nork M, Fleming G, "Torsional Instability of the Lumbar Spine," poster exhibit at the annual meeting of the American Society of Neuroradiology, Philadelphia, May 1998). The effect of weight-bearing, load, and disk degeneration on spinal nerves needs more study to clarify the relationship between disk degeneration and back pain.

While disk degeneration is widely considered to be a major cause of back pain, the precise relationship between disk degeneration and back pain has been poorly characterized. Degeneration in the intervertebral disk is blamed for many cases of lower back and sciatic pain, and yet intervertebral disk degeneration is found in up to 50% of asymptomatic persons at MR imaging. The effect of disk degeneration on spinal stiffness may explain some discrepancies in the clinical significance of degenerating disks. Disk degeneration reduces the stiffness of the disk so that any force applied to the spine produces a greater motion and therefore greater stress in the other connective tissues, such as the anterior longitudinal ligament, posterior longitudinal ligament, and capsule of the facet joint. The motion produced by a specific force depends on the type of degenerative change in the intervertebral disk. Therefore, kinematic spine imaging technique may help us to understand the motions of the spine and to distinguish clinically significant disease.

The spine, which appears immobile in our static images, is far from a rigid structure. The neural foramina and central spinal canal, which appear immutable in images, undergo constant change as a result of the loads they sustain during daily activities. Thus, the function of the spine can be better understood if it is imaged in various load conditions. Muhle et al have devised a method of imaging the cervical spine in flexion and extension and have attempted to quantify the resulting anatomic changes. While their classification system may not receive immediate acceptance, their techniques may stimulate new kinematic imaging studies of the spine.

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