# New Methods Find TBI Missed by Standard Scans

BY JEFF EVANS
*Senior Writer*

WASHINGTON — Advanced imaging methods with MRI and magnetoencephalography may be able to detect mild traumatic brain injury with greater accuracy than can conventional imaging techniques, according to two prospective pilot studies.

Conventional MR and CT neuroimaging focus on the detection of bleeding, which is only indirectly related to axonal injury. These methods are not able to detect about 70%-80% of mild to moderate traumatic brain injuries (TBIs), according to Mingxiong Huang, Ph.D., of the University of California, San Diego, and his colleagues.

Dr. Huang and his coinvestigators are finding that the combination of diffusion-tensor imaging (DTI) and magnetoencephalography (MEG) can reveal axonal injury resulting from tissue shearing and stretching, which is a leading cause of persistent postconcussive symptoms in mild TBI patients.

MEG pinpoints the temporal and spatial activation of neurons in the brain based on the tiny magnetic fields created by neuronal currents in cortical gray matter. DTI measures the pattern and direction of the movement of water molecules through white matter fiber tracts, which become disturbed after a TBI.

Detecting mild TBI is clinically important, Dr. Huang said, because even though roughly 85% of patients with mild TBI will be symptom free by 6 months, the remaining 15% have lingering cognitive and behavioral problems, and have a higher risk for developing epilepsy, severe depression, and dementia.

He and his colleagues studied 18 civilian and military patients with a closed-head injury and mild to moderate symptoms of TBI, along with 17 healthy control patients. None of the patients had visible lesions on conventional MRI or CT. In the patients with TBI symptoms, the researchers found that the location of neurons generating abnormal low-frequency delta waves that were seen on MEG was significantly correlated with the deafferentation of the underlying white matter fiber tracts on DTI. These findings were consistent with the patients' symptoms and the results of neuropsychological exams, and they help to confirm the hypothesis that pathological low-frequency delta waves are caused by the shearing of white matter fiber tracts, Dr. Huang reported at the annual meeting of the Society for Neuroscience.

MEG may be a more sensitive measure for mild TBI than is DTI because in some instances MEG was able to detect pathological low-frequency delta waves when DTI signals in white matter fiber tracts were within normal range, according to Dr. Huang. He also noted that the two modalities could be used to objectively monitor the effect of an intervention and provide prognostic information.

The investigators hope to expand their research by performing a longitudinal study in children that compares their recovery from mild TBI with the recovery of adults. In military personnel, the researchers would like to know how to differentiate the signs and symptoms of mild TBI from those of posttraumatic stress disorder. Both conditions have similar signs and symptoms and coincide in a subpopulation of patients, but the treatments for them are different.

In another study presented at the meeting, Andrew Maudsley, Ph.D., of the University of Miami and his colleagues used magnetic resonance spectroscopic imaging (MRSI) to detect the changes in brain metabolism that are indicative of mild TBI in patients with postconcussive symptoms.

The researchers used a volumetric acquisition method to obtain data on the whole brain rather than on just a single area, which is beneficial in imaging diffuse brain injury, according to Dr. Maudsley.

"If you used a conventional MRS method, which is a single voxel method, you have to [focus on] one brain region. You could very clearly choose a brain region, especially with mild injury, that actually looks normal on spectroscopy," he said in an interview.

The investigators measured levels of *N*-acetylaspartate, creatine, and choline

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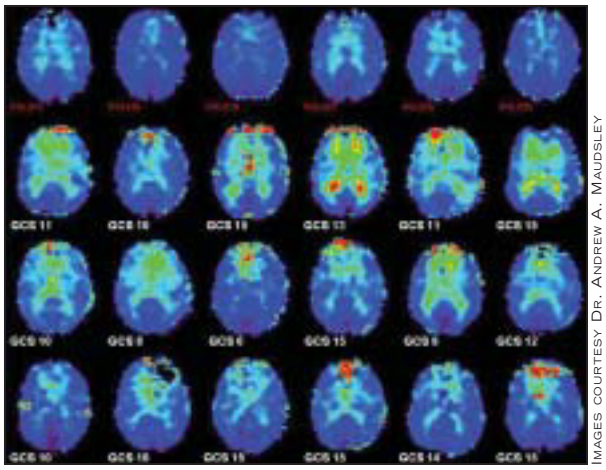

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**Magnetic resonance spectroscopic imaging of the brains of 18 traumatic brain injury patients (bottom three rows) show widespread alterations in the ratio of choline to *N*-acetyl aspartate (light blue to green color), unlike the brains of 6 control subjects (top row).**

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in the brain. The pilot study compared the average of all measured values from 22 patients who were classified as having mild brain injury with the average values from 67 age-matched controls. MRSI scans took place a median of 21 days after the patients' injuries, which were caused by motor vehicle accidents (17), falls (2), or assault (3).

Assessments of the group averages revealed that brain injury was associated with a significantly decreased level of *N*-acetylaspartate (a marker of neuronal and axonal viability), as well as an increased level of choline (a marker of membrane metabolism). The ratio of choline to *N*-acetylaspartate was the most sensitive marker for injury.

Overall, 90% of the patients had small and well-localized lesions on normal MRI, findings that are typical for mild TBI. But on MRSI, the researchers found widespread metabolite alterations throughout the cerebrum.

The patients' scores on neuropsychological tests were significantly correlated mostly with metabolite changes in the right frontal region. In one patient who underwent follow-up scans, the concentrations of *N*-acetylaspartate and choline continued to change significantly at 7 and 15 months post injury.

Dr. Maudsley said that he and his team hope to obtain longitudinal assessments of metabolite levels to determine if their short-term levels can predict future outcomes of patients with mild TBI. Outcomes at 6 months in close to half of the patients have shown some correlations between metabolite levels and scores on neuropsychological tests, he said.

"It's my feeling that these metabolites really take several days, if not a couple of weeks, to change. In the one example in which we had a more severe injury, things were actually worse at 6 months than they were at 5 weeks," he added.

The use of the 3-tesla MR scanners that Dr. Maudsley and his associates used in their study is beginning to extend beyond academic medical centers and into regular clinics, especially for brain MRI applications.

Neither Dr. Huang nor Dr. Maudsley had conflicts of interest to report. ■



### Corrections

There was an error in the article, "After Methotrexate, Glatiramer Acetate Improves MS Outcomes" that appeared on page 17 of the December 2008 issue of CLINICAL NEUROLOGY NEWS. The treatment described by the investigator involved mitoxantrone, not methotrexate.

There was an error in the caption for the image that appeared in a recent "Neuroscience Today, Neurology Tomorrow" column (November 2008, p. 14). The caption should have said that the neurons and dendrites were located in the dentate gyrus of the mouse's hippocampus, not in the CA1 area.

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