Imaging Sheds Light on Lasting Effects of TBI

BY MICHELE SULLIVAN

BANGKOK, THAILAND — New imaging techniques may help to explain the disabling symptoms that can plague patients with traumatic brain injury long after their acute problems have resolved, and eventually guide the best choice for medical therapy.

Survivors of traumatic brain injury who complain of depression, irritability, and memory or cognitive problems may be written off as psychiatric cases or malingerers, Dr. Ramon Diaz-Arrastia said at the World Congress of Neurology. "This is the frustrating thing about TBI. The patients might look OK—they don't have paralysis, they are walking around. But their cognitive and behavioral problems are real."

Imaging techniques that are now well established in other areas of neurology—such as diffusion-weighted and susceptibility-weighted MRI—are now being used to show that brain injuries leave permanent, life-altering marks behind after the contusions and hematomas have healed.

These findings may have both immediate and long-range benefits, said Dr. Diaz-Arrastia, a professor of neurology at the University of Texas Southwestern Medical Center, Dallas. "Right now, imaging these patients has the primary value of providing a prognosis and perhaps helping them obtain the care that they need. In terms of reimbursement, it's useful to have an objective documentation of the injury when trying to convince insurers to cover rehabilitative service."

In the future, imaging the post-TBI brain may help guide medical treatment choices and monitor drugs' effectiveness. So far, nearly 30 drugs have provided effective neuroprotection in animal models of TBI, he said. However, no drug that has undergone testing in well-designed phase III trials has proven beneficial to humans.

Part of the problem may be the heterogeneity of human brain injury, Dr. Diaz-Arrastia said. There are many subtypes of TBI, yet "from the point of view of the clinical trials, all patients who present in a coma [after a brain injury] are treated the same way, even though the injuries can be very different, with very different prognoses."

TBI patients 'might look OK … but their cognitive and behavioral problems are real.'

DR. DIAZ-ARRASTIA

Susceptibility-weighted imaging (SWI) is one technique being studied in TBI patients. It measures the paramagnetic shift of intravascular deoxyhemoglobin and methemoglobin, amplifying the appearance of microhemorrhages and making them much easier to identify. "SWI picks up 640% more lesions and 200% more lesion volume than does gradient-recall echo," Dr. Diaz-Arrastia said, referring to work by Dr. Karen Tong from Loma Linda (Calif.) University.

SWI is very good at identifying diffuse microvascular injury, a marker for diffuse axonal injury that is usually invisible on computed axial tomography. "The only problem is that SWI may be overly sensitive," he said. "One patient with a lot of microhemorrhages might be complaining only of headache and dizziness, whereas another with a similar volume might have a lot more problems."

Diffusion-weighted imaging (DWI), which is well established in the stroke world, is understudied in TBI, probably because it's a challenge to perform MRI on these acutely ill patients. But this technique provides detailed information about the makeup of lesions, showing vasogenic and cytotoxic edema, as well as location in the superficial or deep structures in both gray and white matter.

Dr. Diaz-Arrastia and his colleagues performed DWI on 99 patients with TBI. Of these, the study identified corpus callosum lesions in 84%. It was able to differentiate between patients with primarily cytotoxic lesions (54%) and those with vasogenic lesions (46%). "We also found that the volume of these brain le-

Continued on following page

Continued from previous page

sions, irrespective of location, explained about 28% of the variance in outcome among these patients," he said. "It's a relatively modest correlation with outcome, but it shows that what we are measuring is something that is functionally important and affects outcome."

Diffusion tensor imaging shows how water tracks along the axons, giving a good view of white matter lesions. Follow-up scans on TBI patients have shown tantalizing clues to the possible causes of their long-term problems.

"When we scan patients within a day or two of injury, we may see subtle changes in the parameters. But if we come back 6 months later and rescan, we see much greater dropout of axons. Initially, the patient may be in a coma, and when they are scanned later they are usually much improved and walking around, albeit with problems with memory or executive function. So this tells us that something is happening weeks or months after the injury that results in white matter dropout," he said.

Quantitative volumetric assessment of the cortical field measures the thickness and volume of different regions, Dr. Diaz-Arrastia said. "In our patients, we have found that the brain shrinks overall after a severe traumatic injury, but that not all structures shrink at the same rate. Some cortical regions shrink very little, while others, like the hippocampus, appear particularly sensitive to injury." This makes sense given the cognitive and mood issues that TBI patients can experience.

On average, whole brain volume and both gray and white matter volumes decreased by 3%-10% in the first few months after severe TBI. In comparison, Dr. Diaz-Arrastia said, the rate of atrophy for patients with Alzheimer's disease is about 1%-2% a year.

Functional MRIs also provide some clues that the injured brain sustains long-term problems. The blood oxygen level dependent signal typically shows seemingly random fluctuations when the brain is at rest. But recent studies have shown that these fluctuations actually represent the communication between brain regions that work together. "In our patients, we found a very high indication that the functional connectivity between the hippocampi was greatly reduced," compared with controls, he said. ■

Daily Headache Develops in 20% After Blasts

PHILADELPHIA — About 20% of soldiers returning from Iraq or Afghanistan develop chronic daily headache after blast exposure or concussion, according to a preliminary study.

Dr. Brett Theeler and his colleagues found that newly returned soldiers who were exposed to blast explosions within 60 feet and those who suffered concussion injuries with or without loss of consciousness were likely to develop headache within 1 week of their experience. Chronic daily headache (CDH) was defined as headaches occurring at least 15 days per month.

In the cohort of 5,270 soldiers who completed a 13-question headache survey, 957 screened positive for any of the risk factors: 196 were classified as having CDH and 761 did not. The mean headache frequency was 23 days per month for the CDH group and 5 days per month for the non-CDH group. Headaches were migraine type in 66% of soldiers with CDH and 48% of soldiers without CDH. Most of those with CDH (55%) developed headaches within 1 week of having had a concussion, compared with 33% of those without CDH, Dr. Theeler reported at the International Headache Congress.

Soldiers with CDH were also exposed to more blasts on average than those without CDH (six vs. five, respectively). Although the average difference in blast exposure was small, there was a very wide range of exposures among those with CDH, "leading us to consider that there may be a dose-response relationship between blast exposure and headache," said Dr. Theeler, a neurologist and U.S. Army captain at William Beaumont Army Medical Center, El Paso, Tex.

More than twice as many solders with CDH also screened positive for post-traumatic stress disorder (40% vs. 17%).

Dr. Theeler said his data were preliminary. However, he published a recent article suggesting that a history of mild head trauma consistent with blast exposure was present in 50% of soldiers who screened positive for headache (Headache 2009;49:529-34).

The International Headache Society and the American Headache Society sponsored the congress.

—Michele G. Sullivan