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Whole-Brain N-Acetylaspartate: A Marker of the Severity of Mild Head Trauma

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Whole-Brain *N*-Acetylaspartate: A Marker of the Severity of Mild Head Trauma

Most of us have experienced some minor head trauma (MHT), sometimes due to ineptitude, sometimes as a purely accidental event. Also, as parents, we are always worried about head trauma (even minor) and its consequences in our children. Most patients with MHT have a Glasgow Coma Scale (GCS) of 13–15 on arrival at a hospital; they are generally confused and/or showing localizing pain at most.¹ However, the GCS was designed to evaluate adults, and a different scale exists for children under 4 years of age. In the medical literature, minor head trauma is also called “mild traumatic brain injury” or “concussion.” According to the International Symposium on Concussion in Sport, a “concussion” includes the following: 1) a direct blow to the head or to any body part with the force transmitting to the head; 2) immediate and short-lived deterioration of neurologic functions; 3) acute clinical symptoms that reflect a functional, rather than an anatomic, disorder; 4) various clinical symptoms that may or may not imply loss of consciousness; and, most important for neuro-radiologists, 5) normal findings on structural neuroimaging studies.² This last point has been debated in the literature, and several articles report lesions in as many as 9% of patients with MHT.¹ Skull fractures, subdural hematomas, and dural sinus thrombosis have all been reported in these patients.^{3,4} The only clinical symptoms due to MHT that predict significant structural lesions are seizures and loss of consciousness. Age, sex, headache, scalp lacerations, and vomiting are generally not associated with significant structural lesions. It appears, however, that these clinical observations are less consistent for patients under 2 years of age; thus, these young children need to be imaged with CT acutely, regardless of clinical symptoms.⁵ Although guidelines exist for the acute management of MHT, in many countries, they are not followed and patient management depends on individual physician preferences.⁶

What happens to patients after MHT? Recent literature supports the observations of some investigators who believe that even mild forms of brain injury may have considerable detrimental effects. Acutely, postconcussive symptoms may be somatic (headache, dizziness, blurry vision), emotional (irritability and anxiety), and/or cognitive.⁷ We all have heard of the individual “who has never been himself/herself again after getting hit on the head.” Deficits in the registration and retrieval processes, decreased quality of mnemonic memory, decreased story recall and verbal fluency, and so forth all have been noted after MHT. Fortunately, many patients recover some, if not all, of their function. Apart from these acute symptoms, remote effects have been observed after MHT. Children between 10–13 years of age with a history of MHT may develop hyperactivity, inattention, and conduct disorders.⁸ Posttraumatic seizures after MHT are said to develop in 3%–6% of children. A recent study shows that in concussed athletes, auditory information processing is abnormal.⁹ Repeated head injury (called the “second impact syndrome”)

may have dire consequences, such as brain edema, increased intracranial pressure, or herniations and death, though these are rare.¹⁰ It is thus obvious that MHT is not a benign process, despite its normal findings on structural imaging studies. As neuroradiologists, what can we do to document (and possibly predict) significant brain injury? How can we quantify the amount of brain damage induced by MHT?

Posttraumatic atrophy is a well-known sequela of head trauma, no matter how mild. Inglese et al¹¹ found prominent perivascular spaces after brain MHT. These enlarged spaces seem to develop early in the course of the injuries, may reflect permanent brain damage, and may be a marker of cerebral volume loss. Thus, it appears that with our advanced neuroimaging techniques, we neuroradiologists do have some tools to assess the effects of injuries on the brain. In this issue of the *AJNR*, Cohen et al¹² report the use of proton MR spectroscopy to study patients after MHT. In their study, the focus of attention was *N*-acetylaspartate (NAA), which is assumed to be a marker of neuronal well-being and viability. Their study is unique because whole-brain NAA was studied (reflecting global brain injury). Volumetrics in their patients showed decreased volume of gray matter, which, in combination with low whole-brain NAA, strongly suggests damage to the neurons and their axons. Cortical contusions and shearing injuries also lead to neuronal damage. Hemorrhagic shearing injuries could conceivably introduce enough susceptibility artifacts into the spectroscopic analysis to artificially lower the global concentration of NAA. This was taken into account by Cohen et al, who found “tiny foci of suspected shearing injuries” in only 6 of 20 patients and concluded that these lesions were far too small to account for the global decline in all patients. They repeated their analysis after the exclusion of older patients (in whom NAA may be low due to other reasons) with large bifrontal hemorrhagic contusions and still found a trend toward significance between patients and controls. Although the study of Cohen et al is not without problems, it at least offers preliminary objective evidence in vivo of neuronal damage after MHT. How do their results compare with those obtained by using other techniques?

Alterations in magnetization transfer and apparent diffusion coefficients have also been documented in the injured brain.^{13,14} Diffusion tensor imaging shows reduced fractional anisotropy (FA) in certain white matter tracts (such as the corpus callosum) that correlates in severity with GCS and Rankin scores, implying loss of fiber integrity in these regions.¹⁵ Because other tracts (ie, corticospinal) are relatively spared, it is probable that white matter involvement is either segmental or varies from patient to patient.

Cerebral perfusion is also affected in brain injury. Abnormal cerebellar perfusion has been noted in patients with post-MHT vertigo, whereas frontal hypoperfusion has been documented in patients with personality changes after MHT.¹⁶ In patients with severe head trauma, perfusion CT shows abnormal vascular autoregulation (high and low cerebral blood volume). Because the gray matter receives a higher amount of blood flow and volume, circulatory alterations may lead to ischemia and neuronal damage.

All these studies place neuroradiologists in an important position, not only in their traditional role of diagnosing acute and surgically treatable brain injuries but also in being able to

predict and play a role in the management of patients with MHT. Low whole-brain NAA and loss of FA seem to portray a poorer prognosis and, if identified early, may lead to changes in patient's rehabilitation. Regional perfusion abnormalities seem to be associated with discrete clinical symptoms. It is also possible that these advanced imaging techniques help to monitor "futuristic" treatments such as neuronal regeneration, tissue engineering, neuromodulation, and neural monitoring, as accomplished by nanotechnology and nanoneurosurgery. Nevertheless, no treatment will be more important than simple preventive measures. As our understanding of the physiology of brain trauma continues to evolve, it is clear that no such thing as "minor" head trauma exists.

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