Apolipoprotein E and posttraumatic brain atrophy

It is unclear whether apolipoprotein E (ApoE) has a role in recovery from brain trauma. Isoniemi et al. report that in patients who had brain trauma 30 years earlier, the genotype of ApoE was not associated with the development of either hippocampal or ventricular atrophy.

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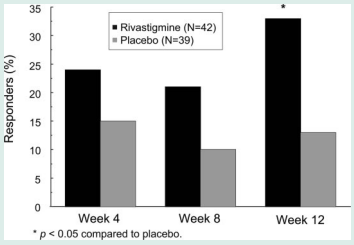
Effects of rivastigmine in patients with traumatic brain injury



In a double-blind, placebo-controlled clinical trial, Silver et al. studied the effects of rivastigmine (3 to 6 mg/day) in 157 patients with traumatic brain injury. Rivastigmine improved cognitive measures in the subgroup of patients with moderate to severe memory impairment at baseline.

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Damage control for traumatic brain injury

Commentary by John Adair, MD

Traumatic brain injury (TBI) remains one of the most common causes of neurologic morbidity. Estimates of TBI incidence, with 1.5 to 2 million new cases each year in America, make the condition at least twice as common as stroke.[1] Only about 1% of cases of TBI require neurosurgical intervention, making evaluation and management of such patients an important component of neurologic practice.

The clinical consequences of TBI result from focal neuroglial death and diffuse axonal injury (DAI). Both focal damage and DAI share similar pathobiology, with membrane failure and disrupted ionic homeostasis, elevated extracellular glutamate, mitochondrial dysfunction, and oxidative stress.[2] While the anatomic distribution of TBI varies widely, the proximity of the frontotemporal regions to adjacent bony structures may account for focal dysfunction predominating in these areas. Likewise, DAI most commonly impacts anterior structures, including the rostral corpus callosum. Accordingly, behavioral disorders observed during recovery include confusion and disorientation, both anterograde and retrograde amnesia, impaired attention with distractibility and poor concentration, executive dysfunction, and various forms of emotional dysregulation and altered personality.[3]

Until we have novel protective therapies directed at TBI's underlying mechanisms, clinicians must rely on symptomatic treatment strategies. Psychotropic agents can suppress specific noncognitive behavioral syndromes (i.e., affective disorders) and, if comorbid chronic pain or seizures complicate TBI, neurologists may be able to address multiple problems with anticonvulsants. Unfortunately, cognitive and conative deficits often cause the greatest disability and much less is known about their psychopharmacologic basis. It is also unclear whether genetic factors such as ApoE influence recovery from TBI, a topic addressed by Isoniemi et al.

Modification of specific neurotransmitters seems a rational adjunct to usual rehabilitation services. For example, the basal forebrain's location and their axonal course may render telencephalic cholinergic systems relatively vulnerable to trauma and, indeed, some evidence indicates cholinergic deficiency after TBI.[4] The same general region conveys ascending monoaminergic projections to neocortex and limbic structures via the medial forebrain bundle. Despite the considerable prevalence of TBI, however, there is little evidence for off-label use of currently available modifiers of cholinergic or monoaminergic function.

Only controlled trials can validate clinical experience based on individual cases. The Silver et al. clinical trial tests the effect of a cholinesterase inhibitor in recovered patients with TBI with cognitive residua. While overall results showed little benefit, one subset of patients demonstrated significant improvement in memory task performance. While this article leaves the clinical utility of cholinesterase inhibitors unclear, it is a first step in separating anecdote from evidence-based practice. TBI management must still be guided by cautious creativity and compassion.

References

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