Conflict of Interest Disclosures: Dr Jack has provided consulting services for Eli Lilly and owns stock in Johnson and Johnson.

REFERENCES


Status Epilepticus and Brain Atrophy

Shrinkage Is a Growing Problem

Andrew J. Cole, MD

There is general agreement among neurologists, emergency physicians, and intensivists that status epilepticus is a medical emergency; that the longer status goes on, the more difficult it is to stop; and that as the status moves up the severity spectrum from simple status to refractory status requiring treatment with an anesthetic to super-refractory status requiring more than 1 course of anesthetic treatment, the lower the likelihood of successful treatment and the higher the mortality.1 In this issue of JAMA Neurology, Hocker and colleagues2 present a retrospective study demonstrating the evolution of apparent brain atrophy in a series of adult patients treated at the Mayo Clinic with so-called super-refractory status epilepticus (SRSE). Patients with an overt anoxic ischemic etiology, epilepsy partialis continua, and absence of status were excluded. This series of 19 patients, culled from 42 who met the authors’ diagnostic criteria for SRSE, were selected for study based on the availability of magnetic resonance imaging (MRI) scans at prespecified points in time. The authors use a straightforward metric, percentage change in the ventricular brain ratio (ΔVBR), to quantify change in brain volume between 2 scans, one obtained within 2 weeks of onset of SRSE and the second within 6 months of resolution of SRSE but at least 1 week after the initial scan. The main findings stated by the authors are that in all patients studied, measurable brain atrophy developed between the 2 scans obtained, and amount of atrophy was positively correlated with duration of anesthetic therapy, negatively correlated with patient age, and not correlated with functional outcome. Curiously, no table of case-wise data are provided, making it difficult for readers to inspect the case-by-case association between degree of ΔVBR and duration, etiology, treatment, or even age of the specific patients.

This study reaffirms that prolonged status epilepticus is bad for the brain. On its face, the study suggests that there should be an urgency to resolving SRSE and so limiting the exposure to anesthetics and associated insults with the hope of lessening fixed structural decline in brain volume. Any such conclusion, however, must be tempered by the lack of control for premorbid function, etiology, and specific treatment, especially in the context of studies cited by the authors describing potential toxicity of various anesthetic and antiepileptic agents.3 It is particularly surprising that there is a poor correlation of ΔVBR with the modified Rankin Scale score as a measure of outcome. Two possibilities are that extrinsic variables such as etiology or specific anesthetics used, or intrinsic patient-specific characteristics are more powerful determinants of functional outcome than the degree of observed apparent relative brain atrophy compared with baseline assessment. The authors freely admit that the number of patients studied is small, and the spectrum of etiologies and treat-
Do ω-3 Fatty Acids Regulate Cerebral β Amyloid?

Joseph F. Quinn, MD

Numerous epidemiologic studies suggest that dietary consumption of fish or of ω-3 fatty acids (the putative “active ingredient” in fish) may reduce the risk of late-life dementia including Alzheimer disease (AD). However, clinical trials have failed to demonstrate disease-modifying effects in mild to moderate AD,1,2 diminishing enthusiasm for ω-3s for brain health during aging. A study in this issue of JAMA Neurology by Yassine et al3 revisits this topic with a clinical study aimed at testing the hypothesis that the ω-3 fatty acid docosahexaenoic acid (DHA) has clinically relevant “antiamyloid” effects in the aging brain.

Docosahexaenoic acid has received particular attention because it is the most abundant polyunsaturated fatty acid in the brain, playing an important structural role in synapses while also modulating a number of signaling pathways. Brain DHA levels are also modulated by dietary intake, so it is plausible for dietary DHA to alter brain concentrations and affect downstream targets including brain pathology and function. Transgenic mouse studies from 2 different laboratories using 2 different strains of mice previously showed that DHA administration was associated with lower cerebral β amyloid.4,5 These preclinical data, combined with the epidemiologic data, motivated a large multicenter National Institute on Aging-funded trial of DHA to slow the progression of AD. Sadly, DHA failed to slow cognitive decline during an 18-month period in nearly 400 patients with mild to moderate AD.6 In light of the view that any antiamyloid therapy may need to be initiated prior to the onset of dementia to be clinically effective, it will come as no surprise that DHA, a putative antiamyloid agent, failed to modify the disease course in a study population that had dementia at baseline. The idea of “earlier” intervention with DHA has been discussed, but it is challenging to reinvigorate interest in a failed treatment strategy, regardless of the viability of the argument, because clinical trials are such expensive and labor-intensive ventures.

However, the Yassine et al study3 has the potential to rekindle interest in the therapeutic potential of DHA by presenting clinical evidence in support of the transgenic mouse studies indicating that DHA consumption is associated with reduced cerebral amyloid. Yassine and colleagues took advantage of an