

## WIDESPREAD NEURONAL DYSFUNCTION IN TEMPORAL LOBE EPILEPSY

### Reduced Extrahippocampal NAA in Mesial Temporal Lobe Epilepsy

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Epilepsia 2002;43(10):1210–1216

**PURPOSE:** Structural and metabolic abnormalities in the hippocampal region in medial temporal lobe epilepsy (mTLE) are well described; less is known about extrahippocampal changes. This study was designed to characterize extrahippocampal metabolic abnormalities in mTLE with magnetic resonance spectroscopy in combination with tissue segmentation and volumetry of gray and white matter.

**METHODS:** Multislice magnetic resonance spectroscopic imaging ( $^1\text{H}$ -MRSI) in combination with tissue segmentation was performed on 16 patients with mTLE and 12 age-matched healthy volunteers. The data were analyzed by using a regression-analysis model that estimated the metabolite concentrations in 100% cortical gray and 100% white matter in the frontal lobe and nonfrontal brain. The segmented image was used to calculate the fraction of gray and white matter in these regions.

**RESULTS:** mTLE had significantly lower *N*-acetyl aspartate (NAA) in ipsi- and contralateral frontal gray ( $P = 0.03$ ) and in ipsi- and contralateral nonfrontal white matter ( $P = 0.008$ ) compared with controls. Although there were no associated volumetric deficits in frontal gray and white matter, ipsilateral nonfrontal gray matter ( $P = 0.003$ ) was significantly smaller than that in controls.

**CONCLUSIONS:** mTLE is associated with extrahippocampal metabolic abnormalities and volumetric deficits, but these do not necessarily affect the same regions.

often a characteristic ictal semiology and electroclinical correlation. The pathologic findings underlying the epileptogenic zone in medial temporal lobe epilepsy may be restricted to the amygdalohippocampal complex. Magnetic resonance imaging (MRI) in these individuals commonly reveals hippocampal atrophy with volumetric loss and a signal-intensity alteration related to mesial temporal sclerosis. Magnetic resonance spectroscopy (MRS) may show a metabolic alteration in patients with medial temporal lobe epilepsy with a reduction of *N*-acetyl aspartate (NAA) in the hippocampal region. NAA is a reliable marker of both neuronal loss and neuronal function. Less is known about extrahippocampal volumetric or metabolic abnormalities in patients with medial temporal lobe epilepsy.

The present study by Mueller et al. evaluated extrahippocampal  $^1\text{H}$ -MRS and MRI in patients with medial temporal lobe epilepsy. The investigators obtained these neuroimaging procedures in 16 patients with medial temporal lobe epilepsy and in 12 age-matched healthy controls. Eleven of the 16 patients had unilateral hippocampal formation atrophy with or without a signal change that was concordant with the temporal lobe of seizure origin as determined by EEG. MRI was performed to assess ipsi- and contralateral frontal and nonfrontal volume loss. Bilateral and symmetrical extrahippocampal gray and white matter NAA reductions occurred in the patients with medial temporal lobe epilepsy. The extrahippocampal metabolic changes were not lateralized to the temporal lobe of seizure origin. There were no similar reductions in creatine/phosphocreatine and choline compound concentrations. Ipsilateral nonfrontal gray matter exhibited a volume loss compared with the normal controls. The metabolic abnormalities were not necessarily associated with volume loss, suggesting that the NAA reductions may be related to “neuronal-glial dysfunction.”

The present study indicated that metabolic and volumetric extrahippocampal changes occur in patients with medial temporal lobe epilepsy. This observation is profound and may objectively indicate the presence of a functional disturbance remote from the epileptogenic zone. This may have important implications in understanding several issues in patients with medial temporal lobe epilepsy, including co-morbidity. The pathogenesis for the widespread structural and metabolic abnormalities in patients with a localization-related epilepsy is

### COMMENTARY

Medial temporal lobe epilepsy is associated with partial seizure activity of mesial temporal lobe origin and



not known. As suggested by the investigators, the potential explanations include the underlying “epileptogenic process,” repetitive seizure activity, or antiepileptic drug therapy. Subsequent studies will be necessary to determine if the extrahip-

pocampal metabolic abnormalities “normalize” after successful surgical treatment for partial epilepsy.

*by Gregory D. Cascino, M.D.*