

ABNORMALITIES IDENTIFIED WITH T₂ RELAXOMETRY IN HIPPOCAMPI REMOTE FROM THE SEIZURE FOCUS: DO THEY MEAN ANYTHING?

Abnormalities in Hippocampi Remote from the Seizure Focus: A T₂ Relaxometry Study

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The aim of this study was to determine whether partial epilepsy is associated with abnormalities in hippocampi that are not the primary seizure focus. As hippocampal T₂ relaxometry is useful for identifying abnormalities that are not obvious on visual assessment of magnetic resonance imaging (MRI), this was the method used. Of 457 consecutive children and young adults from whom T₂ relaxometry data were obtained, 96 had well-characterized partial epilepsy and were enrolled, along with 27 control subjects. The patients were divided on the basis of clinical, video-EEG, and visual MRI assessment into three groups: those with (a) temporal lobe epilepsy (TLE) and mesial temporal sclerosis (MTS) (MTS-TLE); (b) lesional TLE (l-TLE); or (c) extratemporal epilepsy (ETE). A significant and similar prolongation of T₂ relaxation time was identified in hippocampi remote from the seizure focus in all patient groups when compared with control subjects. In the nonsclerotic hippocampus of patients with MTS, T₂ relaxation time was prolonged by a mean of 3.3 msec [95% confidence interval (CI), 0.8–5.9 msec; $P = 0.01$], patients with l-TLE had prolongation of T₂ relaxation time by a mean of 4.3 msec (95% CI, 1.8–7.1 msec; $P = 0.001$), and those with ETE had prolongation of T₂ relaxation time by a mean of 3.7 msec (95% CI, 1.6–6.6 msec; $P = 0.006$) compared with control subjects after adjustment for age. Unsurprisingly, in patients with MTS-TLE, T₂ relaxation time in the sclerotic hippocampus was prolonged by a mean of 19 msec (95% CI, 14.6–22.4 msec; $P < 0.001$). The similarity in the extent of prolongation of T₂ relaxation time in hippocampi that are not the primary epileptogenic focus, the wide variety of structural associations, and the varied sites of epileptogenic foci, considered together,

suggest that the abnormalities are likely to be caused by ongoing seizure activity rather than by underlying etiology or site of epileptogenic focus.

COMMENTARY

In the last decade, magnetic resonance imaging (MRI) technology has revolutionized the presurgical evaluations of epilepsy patients. The presence of a neuroimaging “target” on MRI that correlates with electrographic ictal data from video-EEG studies became a reassuring sign, predictive of a favorable postsurgical seizure outcome. Among the quantitative MRI techniques, T₂ relaxometry currently is considered a very sensitive diagnostic tool for the identification of hippocampal abnormalities (1,2). From the title of this article by Cross and colleagues, it is reasonable to expect that T₂ relaxometry would provide us with an explanation for some of our failed epilepsy surgeries, that is, to anticipate a prolongation of T₂ relaxation time in hippocampi remote from a seizure focus in patients with persistent seizures after surgery, but not in hippocampi of seizure-free patients. Alas, any anticipated excitement was soon proven to be premature! The data of this study raised several interesting questions, however.

A prolonged T₂ relaxation time was identified in three areas: the “uninvolved” hippocampus of some of the patients with unilateral mesial temporal sclerosis, in hippocampi ipsilateral to the seizure focus localized in an extra-mesial temporal lobe lesion, and in ipsilateral extratemporal cortex. Although the prolongation in the T₂ relaxation time in these hippocampi was significantly shorter than that identified in atrophic hippocampi (mean of 3.3 msec compared with 19 msec), it was significantly longer than the T₂ relaxation time of a control group. Yet such prolonged T₂ relaxation time did not distinguish patients treated surgically from those who were not surgically treated or patients who were seizure free after surgery from those with persistent seizures.

So what is the significance of such findings? Should the authors’ suggestions that this prolonged T₂ relaxation time is the expression of an abnormality caused by ongoing seizure activity be accepted? Before this explanation can be accepted, more studies must be performed to address the following key

issues. First, if the authors' conclusion is correct, a prolonged T_2 relaxation time should be identified in other neuroanatomic structures involved in the propagation of the ictal activity (e.g., the frontal lobe cortex or temporal lateral neocortex). Second, the issue of whether the magnitude of the prolongation of T_2 relaxation time identified in these hippocampi is an expression of a real abnormality of hippocampal tissue must be addressed. If that is the case, we may be able to identify an abnormal ratio in the *N*-acetylaspartate/creatine ratios (NAA/Cr) with magnetic resonance spectroscopy studies (3). Thus a magnetic resonance spectroscopy study of the region of interest should be added to this investigation. Third, it must be determined whether such prolongation of the T_2 relaxation time is irreversible, or does the prolongation normalize after the complete remission of seizures, in the same manner as abnormal NAA/Cr ratios, which are identified presurgically in hippocampi contralateral to resected sclerotic mesial temporal structures, normalize after

surgery. Clearly, attributing the findings of this study to ongoing seizure activity is premature!

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References

1. Jackson GD, Connelly A, Duncan JS, Grunewald RA, Gadian DG. Detection of hippocampal pathology in intractable partial epilepsy: Increased sensitivity with quantitative magnetic resonance T2 relaxometry. *Neurology* 1993;43:1793–1799.
2. Bernasconi A, Bernasconi N, Caramanos Z, Reuters DC, Andermann F, Dubeau F, Tampieri D, Pike BG, Arnold DL. T2 relaxometry can lateralize mesial temporal lobe epilepsy in patients with normal MRI. *Neuroimage* 2000;12:739–746.
3. Kuzniecki RI, Palmer C, Hugg J. Magnetic resonance spectroscopic imaging in temporal lobe epilepsy: neuronal dysfunction or cell loss? *Arch Neurol* 2001;58:2048–2053.