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Commentary

Quantitative MR For Epilepsy: A Clinical and Research Tool?

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An explosion in the use of quantitative magnetic resonance (MR) for the investigation of epilepsy has taken place during the last 5 years. Assessment of structural brain changes with MR-based volumetrics (1–7) or T2 relaxometry (8–10) is an ideal model for integrating research with clinical decision making. These techniques have furthered our understanding not only of brain dysfunction (in this case hippocampal sclerosis) but also of brain function (in this case the hippocampus). Quantitative techniques have found a place in the preoperative assessment of hippocampal sclerosis because of their increased sensitivity over visual inspection (11).

Most quantitative MR investigations for epilepsy have concentrated on measuring brain volumes rather than relaxation times. Using this method, the degree of hippocampal atrophy can be quantified and compared with other variables for both research and clinical purposes. Hippocampal atrophy already has been shown to correlate with hippocampal sclerosis, lateralization of the electroencephalographic abnormalities, degree of hippocampal neuronal loss, verbal memory performance, and postoperative seizure control (1–7, 12–14). The critical clinical question is whether these techniques offer enough additional information over visual inspection to warrant the increased investment in personnel, training, time, equipment, and normative data development. With current imaging techniques, volume measurements detect hippocampal sclerosis in about 80% to 100% (1–7, 13) of cases compared with 80% to 90% (1, 7, 11, 12, 15–18) with visual assessment. (These values are somewhat inflated because of the methods used, such as retrospective analysis, narrow inclusion criteria, and inconsistent bases for diagnosis.) In studies directly comparing these two methods, volumetrics has a small but increased sensitivity (7, 11). There is debate as to the need for volume quantitation in routine clinical work (11). We agree with others that visual assessment is very accurate if multiple features of hippocampal sclerosis are evaluated, such as hippocampal atrophy, morphometric findings, and signal changes (12, 16, 18). We have not compared visual inspection with volume measurements at our institution. However, we detected hippocampal sclerosis visually in 50 (88%) of 57 patients with pathologic verification. Ten additional patients with no significant hippocampal neuronal loss were all correctly categorized as not having hippocampal sclerosis. The problem with visual inspection is that it requires a well-trained observer to assess the hippocampus correctly when confronted with head rotation or subtle changes (15). We believe volumetric measurements have a clinical role because they can correct for rotation, are reproducible, and are slightly more sensitive than visual evaluation.

The manuscript by Grünewald et al (8) in this issue of *AJNR*, as well as a related paper by Jackson et al (9), describes a different quantitative technique for studying epilepsy. They found T2 relaxometry to be a reliable and sensitive method for detecting hippocampal sclerosis (for T2 values greater than 116 milliseconds). An older study by Matsuda et al also used T2 values to uncover hippocampal sclerosis (10). Although these findings are intriguing, one might ask why we should be interested in this quantitative technique for determining hippocampal sclerosis, when a reliable, sensitive, and specific method already exists? The answer lies with the biological factors that are the basis for the MR findings. The underlying mechanism for T2 prolongation may be independent of the mechanism producing the atrophic changes. This could have important implications for the following clinical and research questions:

1. Can T2 values help identify the additional 5% to 15% of patients with hippocampal

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sclerosis not discovered by visual analysis or volumetrics?
2. Can they distinguish temporal lobe epilepsy caused by hippocampal sclerosis from atypical cryptogenic temporal lobe epilepsy? Patients in the atypical group seem to have medial temporal lobe epilepsy based on electrical and clinical criteria but do not share the pathology, reorganization, or good postoperative outcome associated with hippocampal sclerosis (19).
3. Can this method improve preoperative identification of those patients who will have good surgical outcomes?
4. Can it improve surgical selection not only in the temporal lobe epilepsy syndromes, but in other syndromes (such as frontal lobe epilepsy associated with gliosis)?
5. Can T2 relaxation be altered without visually apparent signal changes on MR?
6. Can we use this as a research tool to probe the underlying structural changes responsible for T2 prolongation? Is it glial cell proliferation as thought by some authors (8, 9)?
7. Can T2 relaxometry be correlated with other biological variables to further our understanding of hippocampal function and hippocampal sclerosis? For example, is there a relationship between verbal memory scores and T2 values? Grünewald et al explore the relationship between T2 values and various clinical factors associated with hippocampal sclerosis, such as duration of seizures. Although a history of prolonged early childhood seizure was the only significant correlation found, there may be other variables not yet studied which are linked to T2 values.

Despite the importance of the work by Grünewald et al, there are flaws in making some correlations. There are only 10 pathologically verified cases of hippocampal sclerosis. This is a serious problem, because the diagnosis of hippocampal sclerosis in the other cases is based, in part, on visual MR signal changes; one would expect an increased T2 value in these cases. Thus, the findings are preliminary because of the small number of cases with proved pathologic and outcome findings.

There are a number of technical problems and practical issues related to the hippocampal relaxometry technique described by Grünewald et al that should be stressed. Signal changes (as well as volume changes) associated with hippocampal sclerosis are not uniform throughout the hippocampus (12, 15). There is usually regional or segmental involvement. As shown in the Table, the hippocampal body seems to be the segment most often affected by signal changes. If a single measurement of T2 value is performed, it should be at the level of the body, as Grünewald et al seem to have done.

The difficulties in making accurate T2 measurements with a multiecho sequence are well known (20). If the refocusing pulses do not produce a 180° flip angle for all the relevant spins, then the echo amplitudes reflect not only T2 relaxation, but also the exchange of transverse and longitudinal magnetization, which in turn exhibits a complicated dependence on T1, T2, and the details of the pulse sequence. A spatial variation of flip angle, which can result from off-resonance effects or nonuniformities in the B1 field, makes it impossible to refocus all spins accurately. Although shimming errors and eddy current fields can, in principle, affect the echo train in a Carr-Purcell-Meiboom-Gill imaging sequence, B1 effects are typically a larger source of error. Even in an ideal radio frequency coil, the electrical conductivity and dielectric constant of tissue make the B1 field vary as a function of position within the patient (21). This causes a variation of flip angle, and hence the apparent T2, across the field of view of an image.

A second effect becomes important in multisection, multiecho acquisitions, because the refocusing pulses must be section selective in this case. In practice, the selectivity of refocusing pulses is limited, so that spins near the center and those near the edge of a section will be subject to substantially different flip angles. This

Segmental signal changes associated with hippocampal sclerosis

Medial Temporal Lobe Segment	Number with Signal Changes
Amygdala	2
Amygdala-head junction	3
Hippocampal head	21
Head-body junction	39
Hippocampal body	46
Body-tail junction	31
Hippocampal tail	27

Note.—Signal changes represent hyperintensity seen on long repetition time images in 50 (88%) of 57 patients with pathologically proved hippocampal sclerosis. No signal changes were seen in 10 additional patients with epilepsy who underwent temporal lobectomy and had no significant hippocampal neuronal loss.

can produce a measurement error that is roughly uniform across the image. A common approach to minimizing this error is to make the thickness of the selected section somewhat larger for the refocusing pulses than for the excitation pulse. In this way, the spins that contribute to the MR signal (those in the excited section) are not near the edges of the refocused section, and hence are subject to more uniform flip angles. The drawback of this approach, of course, is that the intersection spacing must be larger than in this case, because the refocusing pulses partially saturate thicker planes on either side of the imaged section.

Despite these complications, with care it is possible to obtain T2 values reproducible to about 5% to 10% on different instruments (20, 22). A more accurate measurement can be made with a series of single-echo, single-section acquisitions. However, this entails an examination time that is usually unacceptable in clinical applications.

The most important practical dilemma involves determining which MR sequences to use for both clinical and research investigations of epilepsy. Use of all sequences suggested by various authors for imaging of the patient with epilepsy would involve an inordinate number of hours of scanning time (2, 7–9, 11, 16, 18, 23). The sequence advocated by Grünewald et al adds an additional 7.5 minutes. One possible solution might be to use a dual-echo multisection sequence for the dual purpose of clinical imaging and hippocampal T2 relaxometry. Dual-echo multisection T2 assessment has been used for determination of other disease (24, 25). Although absolute accuracy in T2 measurements is difficult to come by, much can be gained by making relative comparisons between tissue types and/or patients. Although a given patient group is likely to produce different mean T2 values on different scanners, the ratio of T2 values between groups is likely to be preserved. For example, Grünewald et al find a 10% difference in T2 between control subjects and patients with histories of prolonged early childhood convulsions (8). This difference is likely to be reproducible, even though the T2 values of similar groups may themselves vary by 10% among different institutions.

The articles by Grünewald et al and others describe a promising technique for the investigation of epilepsy (8–10). One advantage relaxometry has over volumetrics is that T2 relaxometry involves little additional investment in resources. Because T2 relaxometry and volumetrics may not be directly linked by their underlying biological mechanisms, T2 measurements may yield new information leading to advances in the treatment of epilepsy.

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