



## Which Hippocampal Sclerosis is Imaged With 7-T MRI?

### Hippocampal Sclerosis in Temporal Lobe Epilepsy: Findings at 7 T<sup>1</sup>.

Thomas R. Henry, MD, Marie Chupin, PhD, Stéphane Lehericy, MD, PhD, John P. Strupp, MSEE, Michael A. Sikora, BS, Zhiyi Y. Sha, MD, PhD, Kâmil Uğurbil, PhD, Pierre-François Van de Moortele, MD, PhD. *Radiology* 2011;261:199–209.

**PURPOSE:** To determine if ultrahigh-field-strength magnetic resonance (MR) imaging can be used to detect subregional hippocampal alterations. **MATERIALS AND METHODS:** Subjects provided written consent to participate in this prospective institutional review board–approved HIPAA compliant study. T1- and T2-weighted 7-T brain MR images were acquired in 11 healthy subjects and eight patients with temporal lobe epilepsy (TLE). In all subjects, images were qualitatively examined for evidence of hippocampal atrophy, signal change, and malrotation with the Bernasconi definition, and digitations of the hippocampal heads were counted (agreement was measured with the *k* statistic). Data were analyzed quantitatively with manual subregional hippocampal body segmentation. Subregional data in individual subjects with TLE were compared with data in control subjects to detect deviation from the control range for volume measures on each side and with asymmetry indexes. **RESULTS:** All eight patients with TLE had hippocampal abnormalities on the epileptogenic side. Subregional analysis revealed selective lateral Ammon horn atrophy in six patients and diffuse Ammon horn and dentate gyrus atrophy in one patient. Paucity of hippocampal digitations occurred on the epileptogenic side in all patients with TLE and also on the contralateral side in three patients (interrater *k* value, 0.80). Hippocampal malrotation was observed in three patients with TLE and four control subjects. **CONCLUSION:** Ultrahigh-field-strength MR imaging permitted detection of selectively greater Ammon horn atrophy in patients with TLE and hippocampal sclerosis. Paucity of digitations is a deformity of the hippocampal head that was detected independent of hippocampal atrophy in patients with mesial TLE.

### Commentary

The hippocampus is the most frequent target of surgical treatment for epilepsy. Approximately 30% of patients with mesial temporal sclerosis (MTS) on surgical pathology, however, have normal findings on conventional MRI prior to surgery (1). Epilepsy specialists have hoped that ultra-high-field 7-T MRI might improve detection and characterization of MTS for pre-surgical screening (2). Henry et al. have shown that ultra-high-field strength 7-T MRI might be helpful in defining structural changes in hippocampal sclerosis (HS) that may not be visible on conventional MRI imaging. This study did not, however, evaluate whether 7-T MRI has a higher sensitivity for identifying MTS than does conventional MRI—all eight of the patients had MTS on 1.5- and 3-T MRI.

The authors did show that ultra-high-field MRI might be helpful in characterizing different subtypes of MTS in patients with temporal lobe epilepsy. Recently, Thom et al. (3) and others (4) have shown that several subtypes of MTS identified on histologic analysis may differ in their etiologies, associated clinical findings, and surgical prognoses. In 165 patients receiving medial temporal lobe resections for drug-resistant epilep-

sy, Thom et al. (3) identified six different pathologic patterns: 1) 36% had classic HS with neuronal loss in CA1, hilus, and CA3 regions of hippocampus, with sparing of CA2/subiculum. This is similar to Ammon's horn sclerosis, an older definition that includes mossy fiber sprouting from dentate granule cells; some patients with this type have granule cell dispersion; 2) 24% of patients had total HS with neuronal loss in all hippocampal subfields, including CA2/subiculum; 3) 3% had endfolium sclerosis (EFS), with neuronal loss in the hilus and portions of CA3 regions of hippocampus (i.e., the endfolium) but with sparing of CA1 and CA2 regions; 4) 6% of patients had primary CA1 atrophy (termed CA1p); 5) 21% had indeterminate HS with neuronal loss in CA3 and CA2 areas and with preserved CA4; and 6) and 10% of the patients had electroclinical syndromes of medial temporal lobe epilepsy but did not have HS.

In this current study, Henry et al. evaluated hippocampal sclerosis using 7-T MRI in a small group of eight patients, but they included controls and were able to identify classic HS (i.e., Ammon's horn sclerosis) in several patients. They also identified total HS in one patient and probable EFS in another. Henry et al. also demonstrated a common morphologic pattern in all the patients with HS: The head of the hippocampus had decreased digitations (none or one digitations) ipsilaterally, but several patients also had decreased digitations contralateral to the side of seizure onset. This demonstrates that ultra-high-field strength MRI may potentially help identify subtypes



of HS in patients with medial temporal lobe epilepsy and may show a marker of MTS (i.e., decreased digitations). The study is preliminary and did not address a number of key issues in imaging the hippocampus, including whether 7-T MRI improves detection of HS compared with conventional MRI; whether 7-T MRI can help identify MTS (i.e., HS associated with neuronal loss in adjacent parahippocampal/entorhinal and amygdala areas); and whether defining subtypes of MTS would be clinically useful and help to predict risks to memory and outcomes with medial temporal resection.

The 7-T MRI findings suggest that some of the clinical issues raised by surgical pathology series could potentially be evaluated prospectively with pre-operative ultra-high-field imaging. Thom et al. (3) reported, for example, that patients with primary CA1 (i.e., CA1p) neuronal loss or no HS had poorer outcomes than patients with EFS. Only a small number of patients, however, had these patterns. Van Paesschen et al. (5) reported a somewhat different outcome in a surgical series: patients with nonspecific HS, mild HS, and EFS often had later onset of seizures, no history of childhood convulsions, and less favorable surgical outcomes than did patients with classic HS. Patients with adult mid- to late-onset of seizures with MTS may lack typical clinical patterns of early childhood injury, a latency period, and later development of drug-resistant epilepsy, and they may potentially have non-classic HS subtypes. The 7-T MRI imaging might be potentially helpful in addressing several current controversies in surgical treatment of medial temporal epilepsy. Accurate structural imaging might help show whether patients with subtypes of HS could benefit from specific surgical approaches, such as relatively large medial temporal resections for patients with MTS and amygdalar-entorhinal atrophy. Patients with EFS might potentially respond to locally targeted treatment with stereotactic laser resection or local ablation. Improved structural imaging of hippocampus may help improve assessment of memory risks before and after surgery. For example, are patients with total HS or CA1 atrophy perhaps at reduced risk for memory loss with surgery

compared with those with EFS (6,7)? Ultra-high-field MRI appears to be helpful for characterizing anatomic abnormalities in hippocampus in patients with HS, but considerable work is needed on establishing clinical correlations with these patterns. Identifying subtypes of MTS preoperatively might improve our surgical selection of patients with medial temporal lobe epilepsy.

by Gregory L. Krauss, MD

#### References

1. Smith AP, Sani S, Kanner AM, Stoub T, Morrin M, Palac S, Bergen DC, Balabonov A, Smith M, Whisler WW, Byrne RW. Medically intractable temporal lobe epilepsy in patients with normal MRI: Surgical outcome in twenty-one consecutive patients. *Seizures* 2011;20:475–479.
2. Knake S, Triantafyllou C, WAlkd LL, Wiggins G, Kirk GP, Larsson PG, Stufflebeam SM, Foley MT, Shiraishi H, Dale AM, Halfren E, Grant PE. 3T phased array MRI improves the presurgical evaluation in focal epilepsies: A prospective study. *Neurology* 2005;65:1026–1031.
3. Thom M, Liagkouras I, Elliot KJ, Martinian L, Harkness W, McEvoy A, Caboclo LO, Sisodiya SM. Reliability of patterns of hippocampal sclerosis as predictors of postsurgical outcome. *Epilepsia* 2010;51:1801–1808.
4. Scharfman HE, Pedley TA. Temporal lobe epilepsy. In: *Neurobiology of Disease*. (Gilman S, ed.) Burlington:Elsevier, 2007:349–370.
5. Van Paesschen W, Revesz T, Duncan JS, King MD, Connelly A. Quantitative neuropathology and quantitative magnetic resonance imaging of the hippocampus in temporal lobe epilepsy. *Ann Neurol* 1997;42:756–766.
6. Bonilha L, Martz GU, Glazier SS, Edwards JC. Subtypes of medial temporal lobe epilepsy: Influence on temporal lobectomy outcomes? *Epilepsia* 2011;53:1–6.
7. Alhusaini S, Doherty CP, Scanlon C, Ronan L, Maguire S, Borgulya G, Brennan P, Delanty N, Fitzsimons M, Cavalleri GL. A cross-sectional MRI study of brain regional atrophy and clinical characteristics of temporal lobe epilepsy with hippocampal sclerosis. *Epilepsy Res*. 2012;99:156-166.



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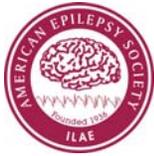
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