Loss of digitations of the hippocampal head on high-resolution fast spin-echo MR: a sign of mesial temporal sclerosis.

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Loss of Digitations of the Hippocampal Head on High-Resolution Fast Spin-Echo MR: A Sign of Mesial Temporal Sclerosis

Catherine Oppenheim, Didier Dormont, Alessandra Biondi, Stéphane Lehéry, Dominique Hasboun, Stéphane Clémenceau, Michel Baulac, and Claude Marsault

PURPOSE: The purpose of our study was to determine the significance of the loss of visualization of digitations in the hippocampal head on high-resolution fast spin-echo MR images in the diagnosis of mesial temporal sclerosis (MTS).

METHODS: MR examinations of 193 patients with intractable epilepsy were evaluated retrospectively for atrophy and/or T2 signal changes of the hippocampi. On the basis of these two criteria, MTS was diagnosed in 63 hippocampi. Twenty-four patients had surgery, and MTS was confirmed in all cases. A control group included 60 hippocampi in patients with frontal seizures but no MR-detectable abnormalities. In a second step, visibility of digitations in the hippocampal head was evaluated in the two groups of subjects.

RESULTS: In the group of 63 hippocampi in which MTS was diagnosed, digitations were not visible in 51 cases, poorly visible in eight, and sharply visible in four. Twenty-two of 24 hippocampi in which MTS was confirmed histologically had no MR-visible digitations. In the control group, digitations were sharply visible in 55 cases and poorly visible in five. Statistical analysis showed a significant difference in the visualization of digitations between hippocampi with MTS and those in the control group.

CONCLUSION: With a sensitivity of 92% and a specificity of 100%, the finding of complete loss of digitations in the hippocampal head may be used as a major diagnostic criterion to establish the MR diagnosis of MTS. This morphologic sign may also be useful in the diagnosis of bilateral MTS or to validate the MR diagnosis of MTS when there is no obvious atrophy or changes in signal intensity.

Mesial temporal sclerosis (MTS) is the most common cause of medically intractable complex partial seizures (1–4). Preoperative studies of patients with medically refractory seizures include clinical examination, electroencephalography (EEG), video-EEG, positron emission tomography, and magnetic resonance (MR) imaging. Some patients are also studied with intracranially implanted electrodes. MR demonstration of MTS is important as it enables localization of the epileptic focus and has a prognostic value. The probability of a seizure-free outcome after surgery is significantly greater for patients with MTS than for patients with nonspecific histologic findings (2, 5–10).

The radiologic diagnosis of MTS is based on MR imaging findings of atrophy and/or T2 signal changes in the hippocampus. On the basis of these criteria, MR imaging has a sensitivity close to 90% in the detection of MTS (7, 11). Other signs of MTS include loss of visualization of the internal structures of the hippocampus (12, 13); unilateral atrophy of the mammillary body (14), the fornix, or the amygdala (15); thinning of the collateral white matter in the adjacent parahippocampal gyrus (16); diminished demarcation between gray and white matter in the temporal lobe neocortex (16); and temporal horn enlargement (6, 17). With continuing refinement of MR technology, finer anatomic details of the hippocampal anatomy will be identified.

Anatomically, the intraventricular part of the hippocampal head, called the digitations hippocampi, contains two or three digitations, which are sagittally oriented and separated by small sulci (18, 19). On
MR images obtained perpendicular to the long axis of the hippocampal head, the digitations are well delineated (20–22). During our work, we noticed the loss of digitations of the hippocampal head in patients with other patterns of MTS on MR images. We thus decided to test the significance of this sign for the diagnosis of MTS.

Methods

Patients

Between May 1993 and June 1996, 193 patients with a clinical diagnosis of medically intractable partial seizures were studied with MR imaging. The patients included 89 males and 104 females, ranging in age from 10 to 75 years (mean age, 32 years; SD, 12 years), with simple partial seizures, complex partial seizures, or secondarily generalized seizures. Analysis of ictal symptoms, EEG, and video-EEG abnormalities suggested a temporal origin of the seizures in 114 patients, a frontal origin in 30, and an occipital origin in 21. Lateralization could not be determined in 28 cases. Among those patients, 24 were treated with temporal lobectomy or amygdalo-hippocampectomy. Pathologic criteria for the diagnosis of MTS were substantial neuronal cell loss in the hippocampus and associated gliosis in the CA1 or CA3 ammonian fields. Histopathologic examination revealed findings consistent with MTS in all cases. Seven other patients with temporal or extratemporal lesion underwent lesionectomy.

Imaging Protocol

All patients were studied with the same protocol with a quadrature head coil on a 1.5-T unit. Sequences were performed successively, including a spin-echo T1-weighted sagittal acquisition (600/11/1 [repetition time/echo time/excitation]), T2-weighted axial sections through the entire brain (2800/30,90/1), and high-resolution T2-weighted fast spin-echo images (4600/100 effective/4) of the temporal lobe with 3- or 4-mm interleaved sections, a 512 × 256 matrix, a 24-cm field of view, an echo train length of eight, and a 32-kHz bandwidth. The direction of the frequency-encoding gradient was superior/inferior and orientation of the imaging plane was perpendicular to the long axis of the hippocampus, as determined on the first acquisition. Twenty-one sections were obtained in 8 minutes 30 seconds with this technique. Additionally, three-dimensional spoiled gradient–recalled acquisition at the steady state (SPGR) images (23/5/1) were obtained with 1.5-mm-thick sections, a 256 × 192 matrix, a 22-cm field of view, and a 35° flip angle. One hundred twenty-four contiguous sections were obtained in the frontal plane and reformatted along and perpendicular to the long axis of the hippocampus on an independent console. This last acquisition was repeated after injection of 0.1 mmol/kg of gadolinium tetra-azacyclododecane tetraacetic acid (Gd-DOTA, Guerbet Laboratories, Paris, France) in 27 patients with tumor or dysplastic lesions.

MR Evaluation

All 193 MR studies were reviewed retrospectively and independently by two neuroradiologists who were blinded to clinical and pathologic data. Visual analysis of the coronal fast spin-echo MR images and of the reformatted coronal views from the 3-D SPGR acquisition consisted of determining signal characteristics and of evaluating hippocampal atrophy, both previously validated criteria for the diagnosis of MTS (6, 7, 13, 16, 23–25). On the basis of these two MR criteria, the reviewers were asked to identify the normal hippocampal formation and then rate their level of confidence for the diagnosis of MTS (absent, questionable, definite). After consensus, hippocampi were considered normal in 77 patients and questionable in 14 (subtle size asymmetry) (Table 1). The diagnosis of MTS was classified as definite by visual inspection of MR images in 59 patients (63 hippocampi; four patients had bilateral MTS). Twenty-four of these 59 patients had a corticectomy (partial temporal lobectomy or selective amygdalo-hippocampectomy). The diagnosis of MTS was confirmed histologically in all 24 patients. The MR diagnostic criteria of MTS (atrophy and signal changes on T2-weighted MR images) for the 63 hippocampi with MTS, including the 24 that were surgically removed, are given in Table 2. Enlargement of the ipsilateral temporal horn was observed in 29 of 63 hippocampi with MTS and in 31 patients with normal or questionable hippocampi. Atrophy of the parahippocampal gyrus was observed in 23 of the 63 hippocampi with other patterns of MTS.

As indicated in Table 1, focal lesions (in a temporal or extratemporal location), including tumors, malformations, or sequelae, were observed in another group of 43 patients. Three of the 55 patients with unilateral MTS had an ipsilateral, associated lesion: a cavernoma in one case and nodular heterotopia in two cases.

To compare the visibility of digitations of the hippocampal head in patients with and without MTS, six groups were constituted. Patients with a temporal or extratemporal focal lesion and without MTS (n = 43) were excluded from the analysis. The definite- and doubtful- MTS group included all 63 hippocampi (59 patients) with an MR diagnosis of MTS classified as definite regardless of the surgical decision; the histologic- and no- MTS group included all cases of MTS that were proved histologically (24 hippocampi in 24 patients); the doubtfull- and no- MTS group included 14 hippocampi (14 patients) with questionable atrophy; the contralateral- and no- MTS group included hippocampi considered normal on the basis of MR findings but located contralaterally to a definite MTS (55 hippocampi in 55 patients); and the normal group included all hippocampi in the patients with no abnormalities visible on MR images (154 hippocampi in 77 patients). In this last group, a subgroup of patients with clinical, EEG, and video-EEG data suggestive of frontal epileptogenic focus was isolated. These 30 patients (60 hippocampi) constituted the frontal group, which was used as a control group. The MR images of the patients in these six groups were then mixed and submitted randomly to the reviewers. Only the sections in which the hippocampal heads were visible were submitted. The reviewers were asked to estimate the accuracy of visibility of the digitations of the hippocampal heads and to classify them into one of the three following categories: sharply visible (one, two, or three foldings could be well delineated at the level of

<table>
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<th>TABLE 1: MR diagnosis for the entire population (n = 193)</th>
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<tr>
<td>MR Diagnosis</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Unilateral MTS</td>
</tr>
<tr>
<td>Bilateral MTS</td>
</tr>
<tr>
<td>Questionable MTS</td>
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<tr>
<td>Focal lesion</td>
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<td>No abnormality</td>
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Note.—MTS indicates mesial temporal sclerosis.

<table>
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<th>TABLE 2: MR hippocampal patterns classified as definite mesial temporal sclerosis</th>
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<tr>
<td>Part of Hippocampus</td>
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</tr>
<tr>
<td>None</td>
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<tr>
<td>Head only</td>
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<tr>
<td>Body only</td>
</tr>
<tr>
<td>Head and body</td>
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<tr>
<td>Total</td>
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hippocampal head), not visible (the ventricular part of the hippocampal head, ie, its superior part, was completely flat), and poorly visible (intermediate configurations). For this analysis, high-resolution coronal fast spin-echo images and SPGR sections reformatted perpendicular to the hippocampal axis were both available.

Statistical analysis with nonparametric \( \chi^2 \) test was used to compare the aspect of the digitations in the definite-MTS, histologic-MTS, doubtful-MTS, and contralateral-MTS groups against the aspect of the digitations in the control (frontal) group. If one of the three categories of digitations included no observation, the \( \chi^2 \) test compared the two other categories (1 degree of freedom \([df]\)). Whenever the \( \chi^2 \) test was not valid because of insufficient theoretical values, the categories *not visible* and *poorly visible* were grouped and the \( \chi^2 \) test was performed with 1 \( df \). In other cases, the \( \chi^2 \) test was performed for all three categories of digitation patterns (2 \( df \)).

**Results**

The observed aspects of the digitations of the hippocampal head are shown in Figures 1 through 5. Interobserver agreement was excellent: there were no discrepancies for the criterion *not visible* and only three discrepancies, solved by consensus, between the criteria *sharply visible* and *poorly visible*. Table 3 lists the results of the analysis for all the groups.

Of the 24 patients with histologically proved MTS, the digitations were not visible in 22 (92%). In the definite-MTS group, the digitations were not visible in 51 (81%) of 63 hippocampi. Disappearance of the digitations was not observed in the 60 hippocampi of the control (frontal) group or in the 154 hippocampi considered normal (the normal group) on MR imaging analysis. Thus, there were no false-positive studies. Overall, if we consider only the histologically proved cases of MTS, observation of a complete loss of digitations of the hippocampal head had a sensitivity of 92% (22/24) for the diagnosis of MTS. Specificity, as based on the frontal (control) group, appeared to be 100%. If the normal group was taken as the control group, considering that there were no patients with MTS in this group, the absence of visible hippocampal digitations had a 100% specificity for the diagnosis of MTS. If we use the diagnostic criterion *poorly visible* or *not visible* in assessing the histologic-MTS group, the sensitivity reaches 96% and the specificity drops to 92%. There were four hippocampi with sharply visible digitations in the definite-MTS group (classified on the basis of atrophy and increased signal on T2-weighted images), including one histologically proved case. For two of these hippocampi, including the histologically proved case, increased signal and atrophy were located exclusively in the hippocampal body. For the other two hippocampi, the signs of MTS predominated on the body with abnormal, hyperintense signal extending to the head without evidence of head atrophy.

Statistical analysis showed a significant difference \( (\chi^2 = 95.8; \ P \ll 10^{-3}; \ df = 2) \) of the hippocampal digitations aspect observed in the definite-MTS and frontal groups. Similar statistical results were found when the histologically proved MTS (histologic-MTS group) was compared with the frontal group \( (\chi^2 = 75.1; \ P \ll 10^{-5}; \ df = 2) \). There was a statistically significant difference between the aspect of the digitations in the doubtful-MTS group and that of the frontal group \( (\chi^2 = 7.3; \ P = .007; \ df = 1) \). No significant difference was observed for the aspect of the digitations between the contralateral-MTS and frontal groups \( (\chi^2 = 2.45; \ P = .12; \ df = 1) \).
Detection of MTS is crucial in the preoperative appraisal of patients with medically intractable temporal lobe epilepsy. This was impossible before the advent of high-field MR units. MR diagnosis of MTS usually relies on two signs: atrophy of the hippocampal formation and increased signal intensity on T2-weighted images (6, 11–13, 26–28). Atrophy of the hippocampus can be detected qualitatively by comparing the size of the hippocampal formation on both sides or quantitatively by using volumetric methods (24, 29–34). Hippocampal volumetry is slightly more sensitive than qualitative methods (8, 23, 28, 31, 35, 36); however, because of the large range of normally sized hippocampal formations (21, 30, 36), most authors use asymmetry indexes to compare both hippocampal formations in the same subject, and not absolute volume measurements. Because qualitative and most quantitative techniques rely on the comparison of the size and volume of the two hippocampal formations in the same subject (12, 28), bilateral MTS, which represents up to 50% of cases according to autopsy studies (1, 37–39), is thus difficult to detect. The second sign of MTS is a hyperintense hippocampal signal on T2-weighted images (5, 11, 13, 17, 24–27, 40–42). Increased T2-weighted signal associated with an atrophic hippocampus is strongly suggestive of MTS. However, these signal changes may be subtle or may be caused by foreign tissue, such as a hamartoma, small glioma, or posttraumatic gliotic scar (12, 26). In addition, increased cerebrospinal fluid from an enlarged temporal horn, flow artifacts from the proximity of vessels (26), or a developmental cyst resulting from failure of closure of the hippocampal sulcus (43) can mimic signal abnormalities consistent with MTS. To increase the sensitivity of MR imaging in the diagnosis of MTS, other MR findings have been described, including loss of normal internal hippocampal architecture (12, 13), homolateral atrophy of the mammillary body or fornix (14) or temporal amygdala (15), thinning of the collateral white matter in the adjacent parahippocampal gyrus (6), loss of gray-white matter differentiation of the parahippocampal gyrus (16, 44), or temporal horn dilatation (6, 17). Although some of these signs are helpful in the diagnosis of MTS, most authors consider atrophy and hyperintense signal on T2-weighted images to be the most sensitive signs (16, 20, 33, 45), enabling the diagnosis of MTS by means of qualitative image analysis in up to 90% of cases (22, 25, 26).

To our knowledge, high-resolution fast spin-echo pulse sequences (ie, with a matrix size of 512 × 256)
have not been used in the appraisal of patients with intractable seizures. With the development of fast spin-echo techniques, it has become possible to obtain high-resolution T2-weighted images with thin contiguous sections (3 to 4 mm) within a clinically acceptable time frame. This results in excellent delineation of the morphology of the entire hippocampal formation and also allows assessment of signal abnormalities. Tien et al (11) used fast spin-echo pulse sequences to study patients with MTS, but these authors chose to use thinner sections (2 mm) rather than increase the matrix size (256 × 256). We preferred higher resolution (512 × 256) with thicker sections (3 to 4 mm), because high spatial resolution in the section-select direction was generated by the thin sections (1.5 mm) of the 3-D acquisition.

Our study showed that the lack of visible hippocampal digitations has a high diagnostic value, enabling the diagnosis of MTS with a sensitivity of 92% in pathologically proved cases. For this group, if we combine hippocampi that completely lack visible digitations with those in which visibility is decreased, diagnostic sensitivity for MTS reaches 96%.

To obtain a better understanding of the significance of the loss of digitations in MTS, we compared the anatomy of the hippocampal head with the data on histopathologic changes in MTS. Anatomically, the head of the hippocampus is bulbous and is crossed by several grooves that separate it into the digitations (18, 21). The hippocampal body lacks the digitations of the hippocampal head (18, 22). Digitations of the hippocampus have been compared with toes, thus providing the Latin name for the head of the hippocampus, pes hippocampi (18). On frontal MR views, these digitations correspond to the parasagittal infoldings of Ammon’s horn, which are responsible for small humps bulging into the inferior aspect of the temporal ventricular horn (18, 19). Fast spin-echo T2-weighted pulse sequences, obtained with high resolution and thin sections, afford excellent delineation of the digitations (22) because of the high contrast difference between the gray matter of the hippocampus and the bright signal of the cerebrospinal fluid in the temporal horn and choroidal fissure. The lack of choroid plexus at the level of the hippocampal head (18, 22) could also account for this excellent delineation. The foldings of the gray matter of Ammon’s horn, like the rest of the cortical ribbon, are of variable thickness (18). This could explain the various patterns of digitations on frontal MR images, seen as one to three small wavelets at the top aspect of the hippocampal head. According to Duvernoy (18), the digitations seen on the hippocampal head are mainly due to the foldings of CA1, the largest of the four ammonian fields. Pathologic studies of hippocampi with MTS have shown that neuronal loss and gliosis are observed preferentially in CA1 and CA3, with relative sparing of CA2 (1, 7, 45, 46). It is therefore likely that the loss of digitations in MTS is explained by the neuronal loss in CA1 at the level of the hippocampal head. This hypothesis is supported by our observation that for all but one hippocampal head considered as atrophic, digitations were absent or poorly visible. For the four hippocampi with MTS and sharply visible digitations, none had evidence of atrophy of the head, and the atrophy was limited to the body on MR images. These observations support the hypothesis that the loss of digitations is related to the regional atrophy of the head.

Our results should be interpreted with care given that only 24 (38%) of 63 hippocampi with MR-definite MTS underwent surgery. However, in all surgical cases, the diagnosis of MTS was confirmed histologically. This could suggest that in a large majority of cases diagnosed on the basis of MR studies, MTS would have been confirmed pathologically if the patients had undergone surgery. In regard to the fact that sensitivity of the MR finding of loss of hippocampal digitations for the diagnosis of MTS was lower in the definite-MTS group (81%) than in the histologic-MTS group (92%), we believe this could be due to a bias of selection, because candidates for surgery may have more severe hippocampal atrophy, which would explain the highest frequency of loss of digitations in the histologic-MTS group. False-positive cases in the definite-MTS group might also account for the lower frequency with which loss of digitations was observed in that group. Similarly, the doubtful-MTS group could have contained hippocampi with undiagnosed MTS on the basis of other MR criteria, which could explain the two cases in that group with complete loss of digitations.

Constitution of a control group enables the assessment of specificity. The ideal control group should contain no MTS. Among patients with MR images considered to be normal, there could be a few subtle cases of MTS that were undiagnosed by means of the classic criteria of atrophy and increased signal on T2-weighted MR images. We therefore decided to select within this group only those patients with clinical symptoms and EEG findings suggestive of a frontal focus. Although this subgroup was not composed of healthy subjects, the possibility of including any with MTS was minimized. Patients with other lesions, such as cavernoma, were excluded from this subgroup because they may have had an associated disease, such as MTS (47). Since there were no false-negative cases, specificity for the diagnosis of MTS reached 100% if we consider only the criterion of a complete loss of digitations, and 92% if we consider both a complete loss and poorly visible digitations of the hippocampal head. It must be stressed that evaluation of specificity was based on MR findings and not histologic criteria, because, in our series, hippocampectomy was not performed in patients with no MR signs of MTS.

Interpreting the significance of decreased visibility of digitations is difficult. Should it be considered a normal anatomic variant, or is it a sign of minimal MTS? If decreased visibility of digitations is a normal anatomic variant, this pattern should be found as often in normal hippocampi as in those with disease. In fact, this sign was found in 7% of cases in the normal group, in 8% in the frontal group, in 21% in
the doubtful-MTS group, and in 18% in the contralateral-MTS group (a hippocampus contralateral to one with MTS). A hypothesis of an underlying minimal MTS could explain these percentage differences. The normal and contralateral-MTS groups probably contained hippocampi with MTS that was undiagnosed on the basis of purely qualitative MR image analysis, for which sensitivity reached only 90%. The group labeled contralateral MTS was treated separately, because, according to autopsy results, bilateral asymmetric atrophy may be as high as 50% (1, 37–39). So, a theory of minimal atrophy could explain why diminished visibility of the digitations sometimes occurred in the normal group but more often in the contralateral-MTS group. The doubtful-MTS group included all patients in whom it was difficult to determine the presence of MTS solely on the basis of MR imaging. This group potentially contained the majority of hippocampi with discrete atrophy, which probably explains the high percentage of hippocampi with diminished visibility of digitations.

Conclusion

We have described another MR imaging finding in the qualitative diagnosis of MTS: a loss of visible digitations of the hippocampal head. As opposed to the search for atrophy, there is no need to compare this feature with findings in the contralateral hippocampus. This MR characteristic can be useful for the diagnosis of MTS when there is no obvious atrophy, and may be a strong indicator of the presence of bilateral MTS or of MTS involving principally or exclusively the hippocampal head (48, 49). The high sensitivity and specificity of this sign suggest that it could be used as another major diagnostic criterion to establish the MR diagnosis of MTS.

References

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