In this issue of the AJNR, Mamourian et al (1) assess the relationship between fornix asymmetry and mesial temporal sclerosis. While the authors have justifiably kept their focus narrow, their study raises several broader more important questions: What is mesial temporal sclerosis and why is it important to diagnosis? What imaging findings and techniques are necessary for diagnosing mesial temporal sclerosis and which combination of techniques is the most cost-effective? What is the significance of the secondary MR findings associated with mesial temporal sclerosis? Although there is insufficient information available to answer all aspects of these questions, there are enough data to review the importance of mesial temporal sclerosis, the types of imaging techniques used to diagnosis this entity, and the possible significance of secondary MR findings.

Mesial Temporal Sclerosis

Mesial temporal sclerosis, also known as hippocampal sclerosis, is the most common cause of temporal lobe epilepsy found at surgery. Histologically, it is characterized by a pattern of neuronal loss within the hippocampus affecting principally the pyramidal cell layers of the cornu ammonis and the granule layer of the dentate gyrus. A number of morphologic and cytochemical findings are associated with mesial temporal sclerosis, especially within the dentate gyrus. These changes include selective loss of inhibitory interneurons, abnormal spouting of axons, reorganization of neural transmitter receptors, alterations in second messenger systems, and hyperexcitability of the granule cells. The pathophysiology of these changes is not completely understood. It is postulated that an insult to the developing brain during childhood, such as a complicated febrile seizure or encephalitis, damages the dentate interneuron system. The damaged dentate gyrus becomes reorganized, leading to an aberrant hyperexcitable synaptic system. This is clinically manifested as recurrent seizures, or epilepsy (2–4).

Patients with medically refractory epilepsy due to mesial temporal sclerosis have only one reliable method for treatment: surgical resection of the hippocampus. Surgical resection of the hippocampus and anterior temporal lobe can cure epilepsy in as many as 90% of these patients, making it imperative that imaging techniques accurately show this disorder. Imaging has dramatically changed our ability to identify mesial temporal sclerosis before surgery (5–7).

Imaging Techniques

There is a wide range of imaging techniques available for diagnosing and locating mesial temporal sclerosis. These include MR imaging using simple visual inspection, MR hippocampal volumetrics, MR hippocampal T2 relaxometry, MR spectroscopy, single-photon emission computed tomography (SPECT), ictal SPECT, and positron emission tomography (PET). These methods all have high sensitivities. MR is the most extensively used imaging technique; it is widely available, and a trained observer readily detects mesial temporal sclerosis or other causes of epilepsy on MR (5–10). Quantitative techniques using either volume or T2 measurements of the hippocampus involve more sophistication and are labor intensive (11–13). MR spectroscopy is still in the early stages of evaluation, especially single-voxel studies of the hippocampus and temporal lobe (14). Interictal SPECT imaging is easily available but lacks the sensitivity and specificity of ictal SPECT imaging. The yield from ictal SPECT imaging can be very high but depends on the temporal relationship between seizure occurrence and injection of radiopharmaceutical, and ideally requires computer-assisted techniques that compare ictal with interictal SPECT imaging. PET is very sensitive but is not universally available (15). There is no consensus on the most cost-effective combination of techniques for diagnosing mesial temporal sclerosis and predicting postoperative outcome. The paradigm for assessing patients before epilepsy surgery varies widely and depends on institution philosophy (16).

The hallmark of mesial temporal sclerosis on MR imaging is an atrophic hippocampus associated with hyperintense signal on long-repetition-time sequences confined to the hippocampus (5–10). These findings, atrophy and hyperintensity, are often referred to as the two primary MR findings of mesial temporal sclerosis. Patients with these primary MR findings have a 70% to 90% probability of being free of seizures after temporal lobectomy (5, 17). On the
whether fornix asymmetry is linked more to lateral jects (22, 23). Mamourian and colleagues question asymmetries of these structures occur in healthy sub-
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18–21). One reason that these findings are relegated
smaller fornix; and an atrophic mamillary body (7,
temporal horn; narrowed collateral white matter;
dilatation of the spin-echo, or thin-section spoiled gradient-echo se-
sequences); temporal lobe volume loss; dilatation of the
temporal horn; narrowed collateral white matter;
other secondary findings are temporal horn dilatation
arrowheads and loss of the normal internal architecture of the
hippocampus. Compare the left hippocampus, which demon-
strates the normal hippocampal architecture due to alternating
U-shaped gray and white matter internally, to the right hip-
pocampus with loss of this internal pattern. The insert shows
atrophy of the ipsilateral mamillary body (mb) on a more anterior
image. CS indicates collateral sulcus.

other hand, if there are no primary MR findings, the
patient has less than a 50% likelihood of becoming seizure free after surgery. Although these yields are
impressive, they are selective. Some patients with mesial
temporal sclerosis have either absent or equivocal
primary MR findings of mesial temporal sclerosis.
The use of secondary MR features can help improve
the sensitivity and positive predictive value in this
group of patients, especially when used in conjunction
with other localizing techniques described above.

Secondary Findings of Mesial Temporal Sclerosis
What are the secondary MR findings of mesial
temporal sclerosis? Figure 1 provides an overview of
secondary findings, which include the following, all
ipsilateral to the side of mesial temporal sclerosis: loss
of the normal internal architecture of the hippocampus
(best seen on inversion-recovery, thin-section fast
spin-echo, or thin-section spoiled gradient-echo se-
quences); temporal lobe volume loss; dilatation of the
temporal horn; narrowed collateral white matter;
smaller fornix; and an atrophic mamillary body (7,
18–21). One reason that these findings are relegated
to the category of secondary findings is because mild
asymmetries of these structures occur in healthy sub-
jects (22, 23). Mamourian and colleagues question
whether fornix asymmetry is linked more to lateral
ventricular size asymmetry than to temporal lobe ep-
ilepsy (1). The authors show a statistically significant
relation between lateral ventricular size and mesial
temporal sclerosis, implying that an asymmetric
smaller fornix is due to the enlargement of the ven-
tricle rather than to the sclerosis. However, if enlarge-
ment of the ipsilateral ventricle and decreased size of the
ipsilateral fornix are both the result of mesial
temporal sclerosis, it would follow that there would
be an association between ventricular size and fornix
size. Unfortunately, the sample size of this study may
be too small to assess such relationships; thus we are
left with more questions than answers.

Most studies assessing secondary MR findings have
involved fewer than 50 subjects. The frequency of
secondary MR findings ipsilateral to temporal lobe
epilepsy has been reported as 3% of 33 patients for a
smaller mamillary body (19), 22% to 33% of nine for
temporal horn dilatation (24), 22% to 37% of 41
patients for temporal lobe atrophy (11), 67% of nine
patients for collateral white matter atrophy (24), 89% of
25 patients for disruption of the internal architecture
of the hippocampus (8), and 92% of 13 patients
(18) and 39% of 33 patients (19) for a smaller fornix.
At our institution, we have noted secondary MR find-
ings in about 40% to 60% of 65 patients with histo-
logically proved mesial temporal sclerosis.

Although there is a paucity of data on the signifi-
cance of the secondary MR findings, these might yield
important information in terms of the pathophysiol-
y, diagnosis, and prognosis of mesial temporal scle-
rosis. From a pathophysiologic perspective, MR find-
ings may further our understanding of mesial
temporal sclerosis. With MR imaging, we can assess
the entire brain and may be able to discover findings
and associations that can not be recognized at surgery
and pathologic examination because of limited brain
resection. Autopsy series of the brains of patients with
mesial temporal sclerosis are rare. Many of the sec-
ondary signs appear to be related to the afferent and
efferent pathways of the hippocampus (Fig 2). The
fornix and mamillary bodies are part of the major
efferent system of the hippocampus, while the ento-
rhinal cortex, temporal lobe, and collateral white con-
tribute to the afferent pathway. The presence of sec-
ondary MR findings indicates that one should think
about mesial temporal sclerosis as a process involving
diffuse regions of the brain rather than as one limited
to the hippocampus.

Secondary MR findings can help in the diagnosis
and lateralization of mesial temporal sclerosis. In
patients with subtle primary findings of unilateral
mesial temporal sclerosis, these secondary imaging
features help improve diagnostic confidence as dem-
strated in a recent abstract (25). In this study of 50
patients and 16 control subjects, the authors found
that while hippocampal volume alone was very sensi-
tive (94%), the combination of fornix volume plus
mamillary volume plus hippocampal volume was more sensitive (98%). Interestingly, the use of the fornix plus mamillary body volume without hippocampal volume proved to lateralize temporal lobe epilepsy correctly in 82% of patients.

In cases of bilateral hippocampal abnormalities, secondary findings can determine the more important side to resect. They might also provide clues for distinguishing those patients thought to have mesial temporal sclerosis before surgery, but who will be found to have hippocampal gliosis at surgery; as a group, these patients have poor postoperative seizure control.

Since mesial temporal sclerosis appears to be the end-stage process associated with a number of initiating insults (eg, childhood febrile seizures, encephalitis) it is possible that secondary MR signs could offer a way to categorize patients further according to cause and outcome. An important question is whether one or more of these signs can be linked to postoperative outcome. For example, do we know whether patients with mesial temporal sclerosis and ipsilateral temporal lobe atrophy more than two standard deviations below the norm have better outcomes than those patients with mesial temporal sclerosis but without temporal lobe atrophy?

Conclusions

Although the secondary MR findings associated with mesial temporal sclerosis are not sensitive predictors of this entity by themselves, they may offer clues in subtle cases, improve sensitivity in patients with bilateral findings, and further our knowledge of this entity. While Mamourian and colleagues (1) are to be commended for thinking about these issues, they have not gone far enough. Much more research is needed to define the exact role of secondary MR findings associated with mesial temporal sclerosis.

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References

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