MRI Techniques: Bilateral Findings and "Normal Findings"

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ABSTRACT: Magnetic resonance imaging (MRI) techniques allow for significantly better imaging of the temporal lobe compared to computed tomography (CT) or other non-invasive modalities. For detection of foreign tissue lesions, MRI surpasses CT. For the highest non-invasive yield for detection of mesial temporal sclerosis, optimal sequences that should be employed are a heavily T1-weighted volumetric acquisition (to enable both volumetric calculation of hippocampal volume, and, if needed, intracranial volume), T2-weighted coronal sequences, with or without T2-mapping, fluid-attenuated inversion recovery (FLAIR) and, to exclude subtle susceptibility effects from hematoma or cavernoma, gradient echo scans. Magnetic resonance spectroscopy (MRS) may show a decrease in N-acetyl aspartate (NAA) concentration, or NAA: Choline + creatine ratio. Functional MRI is a new and exciting tool that offers the promise of accurately localizing hemispheric functions; its role in the preoperative evaluation of temporal lobe seizures remains uncertain at present.

RÉSUMÉ: Techniques de RMN: observations bilatérales et "observations normales". Les techniques de RMN permettent de visualiser beaucoup mieux le lobe temporal comparé au CT scan ou aux autres modalités d'imagerie non effractive. La RMN surpasse le CT scan pour la détection de lésions tissulaires étrangères. Les séquences optimales qui doivent être employées pour avoir le plus de chances de succès par des méthodes non effractives dans la détection de la sclérose temporale mésiale, sont l'acquisition volumétrique lourdement pondérée en T1 (pour calculer le volume de l'hippocampe et, au besoin le volume intracrânien). Les séquences coronales pondérées en T2, avec ou sans cartographie T2, FLAIR (fluid-attenuated inversion-recovery) et, pour exclure des effets de susceptibilité subtiles dus à un hématome ou à un cavernome, écographie à gradients. La spectroscopie par résonance spectroscopique peut montrer une diminution de la concentraton du N-acetyl aspartate (NAA), ou du ratio NAA:Choline + créatine. La RMN fonctionnelle est un outil nouveau et prometteur qui offre la possibilité de localiser précisément les fonctions hémisphériques; son rôle dans l'évaluation préopératoire des crises temporales demeure incertain pour l'instant.

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Bilateral signal abnormalities, low hippocampal volumes (either by measurement, or as a ratio of intracranial volume), or abnormal T2-relaxation times are seen in 10% to 25% of patients with temporal lobe epilepsy (TLE). These patients present a problem for ratio, or difference-based quantitative measurements. However, these findings are not surprising given that between 31% and 80% of postmortem examinations in patients with seizures of temporal lobe origin show bilateral mesial temporal sclerosis (MTS). By imaging, the more atrophic hippocampus is usually the symptomatic one. The outcome after unilateral resection of hippocampus where bilateral abnormalities are present seems to be similar to that of patients with unilateral abnormalities, but limited patient data are available.

Despite the increased accuracy provided by volumetric and T2-relaxation techniques, there are still patients in all of the series reported who have normal imaging. Other modalities, including invasive recording, or possibly CT, magneto-encephalography, positron emission tomography (PET), or single photon emission tomography (SPECT), or functional imaging, may be helpful in localizing the seizure focus if conventional methods fail and should be employed as available.

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Sensitivity of MRI for mesialtemporal sclerosis (MTS)

The advent of MRI produced a significant improvement in diagnostic accuracy of noninvasive imaging tests in temporal lobe epilepsy. The ability to image in multiple planes, the increased sensitivity to abnormal water, and the absence of beam hardening artifacts made MRI significantly better than CT in overall lesion depiction. There was a significant improvement in the detection of lesions in the temporal lobe with MRI, especially foreign tissue lesions, where sensitivity at present approaches 100%.[1] However, the early literature showed difficulty in the reliable detection of MTS. Unfortunately, the early MRI literature described patients scanned at multiple field strengths (from 0.15 T to 1.5T), and the sign of increased signal in the hippocampus was not seen reliably in patients with MTS. However, recent literature has shown that it is seen in up to 86-93% of patients with MTS.[1,2,3] The work of several groups, most noticeably those from the Mayo Clinic, Montreal and Yale, USA, has shown that thin sections through the temporal lobe with calculation of the volume of the hippocampus, improves the detection of mesial temporal sclerosis.[4,5,6] All groups used heavily T1-weighted, thin sections (1.25 —3mm nominal slice thickness). The Mayo Clinic group, under Jack, emphasized the usual similarity in volume of the normal hippocampi; when the volume of the left hippocampus was subtracted from the right hippocampus, it was possible to differentiate left from right MTS with reasonable reliability.[4] The difference had high sensitivity and specificity in predicting side of MTS. The Montreal group has also shown the importance of measuring the amygdala,[5] as it may be atrophic in patients with temporal lobe originating seizures. These are all important. However, it is probably important not only to have control values of absolute hippocampal volumes, but also to relate the volume of the hippocampus, and possibly the amygdala, to total hemispheric volume. Current methods are relatively time-consuming, requiring manual outlining of the hippocampus and/or amygdala, either by the radiologist, or a trained technologist.

Jackson[7] has proposed measuring the T2-relaxation time in the hippocampus, a method which has shown high sensitivity and specificity for detection of MTS.[7] This technique requires multiple echoes (>8, typically 16) using a single slice through the hippocampus, obliquely orientated to be perpendicular to the hippocampus. Abnormality is present when the T2 relaxation time calculated from the multiple echoes, is over 108 msec. It should be noted, however, that T2 times may be site specific, and each centre performing T2-relaxometry should establish its own hippocampal T2 values. More recently, Woermann et al[8] have shown that a multi-slice double echo technique is also reliable, though their T2 values were lower (abnormal over 93 msec). In their paper, they show that there may be a localized increase in T2 which could be missed on single slice measurement.

Fluid attenuated inversion recovery (FLAIR) imaging has been described for depiction of MTS. In this technique, a long inversion time, of around 2000 msec – the T1 time of cerebro-spinal fluid (CSF) – is used. This technique has been described as being significantly better than T2-weighted MRI in showing abnormal signal in the mesial temporal structures.[9]

If there is a history of significant head injury, a gradient echo image with heavy T2* weighting may be useful to visualize shears or cortical contusions; these will be missed, even at high field, with standard, or, as is popular nowadays, fast spin echo techniques. In particular, fast spin echo techniques have less sensitivity to any sort of T2* effect.

Most authors use the head coil for imaging; newer techniques suggest using phased array technology and local surface coils, though only a few centres are doing this. There is little documentation of the overall efficacy of the improved signal to noise that the surface coils produce.

Bitemporal MTS

Several recent papers describe the problem of bilateral MTS. Subtraction of volumetric measurements, as proposed by the Mayo group, will not show a difference. Quigg et al,[10] in a series of 40 patients, showed that 10 of the 40 had normal hippocampal differences, despite having bilateral MTS by absolute volume measurement compared to controls. Other authors have also described this finding.[6,11,12] Obviously, the T2-relaxometry method, as well as the FLAIR technique, and even conventional T2-weighted techniques may show abnormal signal in the involved hippocampus (and in the case of bilateral MTS, hippocampi). Van Paesschen[13] described 15/100 patients with MTS who had increased T2 measurements in both hippocampi, but normal hippocampal volumes; they employed absolute hippocampal volume measurement, and either compared the volumes to controls, or used differences in volumes more than two standard deviations outside the norm. Conversely, in their series, there were 8/100 patients who had both normal T2 values by relaxometry, but decreased volumes by measurement. One of 100 patients in their series had normal T2 and volumetric measurements. In all, out of 100 patients, 19 had bilateral MTS using either increased T2, or atrophy as indicators. In the 19, only 12 had both increased T2 signal, as well as decreased hippocampal volume. In other papers,[14,15] this same group of investigators showed that 26/82 patients had bilateral MTS based on hippocampal T2 and volumetric changes. They used a ratio of the log of glial density to neuronal density rather than absolute neuronal or glial cell densities. Hippocampal sclerosis was associated with higher ratios than controls in all hippocampal regions. End folium sclerosis had only higher ratios in the granule cell layer of the dentate gyrus. Another recent paper by Woermann et al[8] showed 6/30 (20%) patients with bilateral findings; four patients had diffuse findings (both volume loss and T2 relaxation time increase), and two had diffuse T2 relaxation time increase with only unilateral volume loss. Another group has shown that the decreased volume correlates with a pathological reduction in neuronal density.[16]

Bilateral MRI changes do not necessarily portray an unfavourable outcome from unilateral temporal lobectomy.[10,12] However, severe contralateral atrophy may be associated with poor outcome.[17] As well, more diffuse hippocampal involvement histopathologically is known to have an even poorer surgical outcome.[18]

Normal MRI

Although uncommon, even in younger patients (age <20), all radiological measures of hippocampal pathology may be normal. It is more common in patients who have onset of epilepsy at an older age to have normal MRI parameters; thus any patient who

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has typical EEG and historical evidence of MTS, despite normal MRI, should still be investigated further.[14] The incidence of normal MRI in temporal lobe epilepsy in adults is between 3% and 10%.[8,10,15] This may be due to the fact that end folium sclerosis (also termed non-specific hippocampal sclerosis, dentate sclerosis, or mild hippocampal sclerosis) can appear normal on imaging.[15]

Magnetic resonance spectroscopy

Magnetic resonance spectroscopy (MRS), or magnetic resonance spectroscopic imaging (MRSI), has recently become more widely available for the evaluation of patients with temporal lobe originating seizures.[19-23] All reports have shown a decrease in N-acetyl aspartate, a neuronal marker, in the affected lobe(s), and a decrease in the NAA: choline + creatine compounds. Typical values for control subjects for NAA concentration were 11.6 ± 1.3 mmol/l, decreasing to 8.1 ± 1.5 mmol/l in patients with hippocampal atrophy, and 8.6 ± 1.4 mmol/l in patients with ipsilaterally originating seizures, but no atrophy.[22] Metabolite peak ratios for NAA/choline + creatine were 0.81 ± 0.06 in controls, decreasing to 0.59 ± 0.1 ($p<0.05$) to 0.61 ± 0.08 in the ipsilateral temporal lobe. Values were also decreased in the opposite temporal lobe in 50% of patients, being 0.72 ± 0.16 and 0.73 ± 0.1 respectively for atrophic and non-atrophic ipsilateral hippocampi. Unfortunately, in the study of Ende et al[22] 2/11 operated patients had normal hippocampal neuropathologic studies. The outcomes for the operated patients were felt to depend on a concordant degree of NAA and depression of the NAA/choline + creatine ratio, though five of seven patients also had significant hippocampal atrophy. A more recent study suggests that there is a relationship between surgical failure and creatine/N-acetylated compounds of the non-operated temporal lobe.[23] A ratio of above 1.21 in patients with bilateral abnormalities was associated with poorer outcomes — four of nine patients (45%) had ongoing seizures post-operatively, compared to only 16 % of patients in the other group who had either uni- or bilateral changes but with lesser decreases on the non-operated side. In other studies, a decrease in right-sided hippocampal metabolites was associated significantly with loss of non-verbal functions (performance IQ), while loss of verbal cognitive functions was associated with abnormal left-sided metabolites.[19] MRS sensitivity ranges from 75%[19] to 99%.[19,24] It should be noted, however, that one of these studies[24] had no controls. In the study on children, Gadian et al[19] had five of 22 patients with temporally originating seizures who had no lateralizing features, with normal metabolic maps.

Functional neuroimaging, using the blood oxygenation level dependent (BOLD) effect, has recently become popular for demonstrating brain activation. There are no papers in the literature documenting its efficacy in lesion localization in TLE, however, two papers have shown increased blood flow in seizure foci.[25,26]

Relative sensitivities of the various techniques have been evaluated: a recent paper[27] showed that visual analysis of highly T1-weighted images for hippocampal atrophy had sensitivity of 90% and specificity of 86%. Standard inversion recovery signal abnormalities had sensitivity of 86% and specificity of 81%. Volumetric analysis had sensitivity of 86% and specificity of 81%. Differential volumetric analysis had 97% sensitivity and 88% specificity. Finally, hippocampal T2 maps (single slice) had 79% sensitivity and 74% specificity.

London Health Sciences Centre MRI protocol

At the London Health Sciences Centre, we currently use T2-weighted coronal images, as well as highly T1-weighted thin section imaging through the brain, and FLAIR slices coronally through the hippocampus in standard temporal lobe imaging. Because we are comfortable with the sensitivity of our T2-weighted images (93% sensitivity, 83% specificity, positive predictive value 88% based on our experience with 115 patients over the last nine years[1]), we do not routinely measure hippocampal volumes provided there is concordance with the clinical and EEG findings. Where there is discordance, or where there is conflicting data, absolute hippocampal volumes are measured. Gradient echo sequences are added as needed.

The optimal imaging of the temporal lobe by MRI includes coronal T2-weighted imaging, FLAIR imaging, also coronal, and heavily T1-weighted images through the entire brain, to allow volumetric measurement of the hippocampus, and, also, the ipsilateral hemisphere. Where there is also a history of trauma, it is suggested that a T2* gradient echo image be added, to optimize detection of minor shear injuries. The role of MRS, given high rates of abnormality seen with conventional anatomic neuroimaging, is uncertain; it may be of prognostic value. Normal investigations are common in patients with later onset of TLE, and they should still be further investigated with other imaging modalities, including CT, PET and SPECT, as well as invasive recordings.

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