High resolution magnetic resonance imaging in adults with partial or secondary generalised epilepsy attending a tertiary referral unit

L M Li, D R Fish, S M Sisodiya, S D Shorvon, N Alsanjari, J M Stevens

Abstract
In the past the underlying structural abnormalities leading to the development of chronic seizure disorders have usually only been disclosed by histological examination of surgical or postmortem material, due to their often subtle nature that was beyond the resolution of CT or early MRI. The MRI findings in 341 patients with chronic, refractory epilepsy attending The National Hospital for Neurology and Neurosurgery and Chalfont Centre for Epilepsy are reported. Studies were performed on a 1.5 Tesla scanner with a specific volumetric protocol, allowing the reconstruction of 1.5 mm contiguous slices throughout the whole brain. Direct visual inspection of the two dimensional images without the use of additional quantitative measures showed that 254/341 (74%) were abnormal. Twenty-four (7%) patients had more than one lesion. The principal MRI diagnoses were hippocampal asymmetry (32%), cortical dysgenesis (12%), tumour (12%), and vascular malformation (8%). Pathological confirmation was available from surgical specimens in 70 patients and showed a very high degree of sensitivity and specificity for the different entities. The advent of more widely available high resolution MRI should make it possible to identify the underlying pathological substrate in most patients with chronic partial epilepsy. This will allow a fundamental reclassification of the epilepsies for both medical and surgical management, with increasing precision as new methods (both of acquisition and postprocessing) are added to the neuroimaging battery used in clinical practice.

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Keywords: neuroimaging; magnetic resonance imaging; epilepsy

About one in 40 people will have two or more non-convulsive seizures during their life and 1 in 200 will endure chronic epilepsy.1-4 The aetiological definition of epilepsy is crucial for management and advising on prognosis.5

Computed tomography allows the demonstration of certain tumours, vascular abnormalities, and other major structural or calcified lesions. These are, however, responsible for only a small proportion of cases with chronic partial epilepsy. Most have other diseases such as hippocampal sclerosis or cortical dysgenesis, which are not usually demonstrable with CT, or even early generation MRI.

Advances in neuroimaging have had a major impact in the evaluation and management of patients with epilepsy.6 High resolution MRI shows the underlying structural abnormality in a significant proportion of patients once labelled as having cryptogenic epilepsy, providing a more informed classification system.

In addition, MRI plays an indispensable part in the evaluation of candidates referred for surgical treatment of medically refractory epilepsy, because the nature of the underlying pathology and the extent of its removal are key prognostic factors.7

In the present study we report the MRI findings in a large group of patients with medically refractory epilepsy seen at a tertiary health centre. It is in this group currently, with their potential for surgical treatment, that MRI will be especially important.

Subjects and methods
During a three year period (1991 to 1994), a group of patients with medically refractory epilepsy seen at the National Hospital for Neurology and Neurosurgery and the Chalfont Centre for Epilepsy were referred to St Mary’s Hospital for MRI. Three hundred and forty one patients (172 male, 169 female) with a history of seizures with or without secondary generalisation were studied. The median age was 28 (range 8–84) years at the time of MRI. The patients were scanned on a 1.5 Tesla GE Signa unit (GE Medical Systems, Milwaukee, USA) by a standardised protocol.8 Volumetric imaging was performed in the coronal plane with a spoiled gradient echo technique providing T1 weighted images. Contiguous 1.5 mm thick slices were obtained of the entire head, with a 35/51 (TR/TE/NEX) pulse sequence, flip angle 35° and matrix size 256 × 128. In addition, sagittal T1 (500/10/2, TR/TE/NEX), axial T2 (2800/90/1, TR/TE/NEX), and proton density weighted (2800/30/1, TR/TE/NEX) series were obtained with a slice thickness of 5 mm, an interslice gap of 2.5 mm, and a matrix size of 256 × 192. Volumetric data could be reformatted in any plane. In addition, 50 normal adult subjects were scanned. All scans were reported by two dimensional visual analysis by one of us (JS), who looked specifically at the pattern of gyration, sulcal depth and cortical thickness, the pattern of the
Table 1 MRI Diagnosis of the 240 relevant lesions

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Location</th>
<th>FL</th>
<th>TL</th>
<th>PL</th>
<th>OL</th>
<th>ML</th>
<th>D</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippocampal asymmetry</td>
<td></td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>9</td>
<td>12</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Cortical dysgenisis</td>
<td></td>
<td>14</td>
<td>14</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Tumour</td>
<td></td>
<td>12</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Vascular malformation</td>
<td></td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Infarct/contusion</td>
<td></td>
<td>41</td>
<td>137</td>
<td>19</td>
<td>5</td>
<td>24</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

FL = Frontal lobe; TL = temporal lobe; PL = parietal lobe; OL = occipital lobe; ML = multilobar; D = diffuse.

grey-white interface, and asymmetry of hippocampal formation.

Results

Two hundred and fifty four (74%) scans were abnormal on direct visual inspection of the two dimensional images. Twenty four (7%) patients out of 341 had more than one lesion. Two hundred and forty lesions detected on visual inspection were considered to be relevant to the patients’ epilepsy (table 1), and 38 were thought to be probably coincidental (signal changes in white matter (20), cerebral vascular disease (seven), diffuse cortical atrophy (seven), changes suggestive of multiple sclerosis (two), grey matter heterotopia in the midbrain (one), and neuroma in the cerebellum (one)).

In the 24 patients with dual lesions, the commonest association was hippocampal asymmetry and cortical dysgenisis (11). Others included hippocampal asymmetry and infarct (four), cortical dysgenisis and tumour (two), tumours (two), tumour and infarct (two), cortical dysgenisis and vascular malformation (one), hippocampal asymmetry and tumour (one), and hippocampal asymmetry and vascular malformation (one).

In the control group, two of 50 scans were reported as abnormal (minor Chiari malformation and subependymal nodular heterotopia). Of the first 100 patients who were scanned by this protocol, CT had shown the relevant lesion in only six.

Seventy patients had surgical treatment with subsequent histopathology. Thirty one out of 70 had foreign tissue lesions. These were: astrocytoma (10), dysembryoplastic neuroepithelial tumour (nine), cavernoma (six), arteriovenous malformation (two), glioblastoma (one), oligodendroglioma (one), neurocytoma (one), and angiomata (one). Thirty eight out of 70 had mesial temporal sclerosis or temporal lobe gliosis (characterisation of the extent of these changes was dependent on the nature of the surgical specimen). One patient had perivascular inflammation. Table 2 summarises the correlation of two dimensional visual inspection of the MRI with histopathology. The presumptive MRI diagnosis of vascular malformation was wrong in two cases (two tumours); one other histologically established vascular malformation was not seen on the unenhanced images (subsequently seen on additional imaging with gadolinium enhancement), and another histologically established case was thought to have an old contusion on the MRI data. Diagnosis of tumour by MRI was wrong in one case (hippocampal sclerosis associated with microdysgenesis). All patients in this selected subgroup undergoing surgery with subsequent histopathology established hippocampal sclerosis had had this pathology identified on MRI, except for one case with dual pathology. This patient had a posterior temporal lesion (presumed dysembryoplastic neuroepithelial tumour) but underwent anterior temporal lobe surgery with histological evidence of hippocampal sclerosis that was not identified by visual inspection of the two dimensional images (although atrophy of the hippocampus was evident on subsequent quantitative volumetric analysis). One patient found to have temporal lobe gliosis and mild cell loss restricted to CA4 was thought to have asymmetric hippocampal sclerosis on visual inspection of the two dimensional MRI.

Discussion

The present results show that three quarters of patients with chronic and partial epilepsy may have lesions thought to be of aetiological significance detected by visual inspection on high resolution MRI using 1.5 mm thick slices. The lesions most often found were tumours and vascular malformations in the frontal lobe; hippocampal sclerosis and tumours in the temporal lobe; tumours and cortical dysgenesis in the parietal lobe; cortical dysgenesis and vascular malformations in the occipital lobe; and cortical dysgenesis in multilobar cases.

Classification of patients with epilepsy, using the syndromic classification proposed by The International League Against Epilepsy (ILAE) Commission 1989,10 is often a difficult task, and usually this can only be done retrospectively. The aetiology will remain unknown in 60% of patients even after six months of treatment.11 In the CT era,12–24 the pick up rate of relevant lesions was low; most abnormalities detected were gross or diffuse such as generalised atrophy, and few were surgically remeasurable (table 3). In the current series, a comparison between these two techniques in the first 100 patients showed MRI to be far superior to CT, which is in concordance with previous reports.24 27–34 It seems, at the present, that syndromic classification of epilepsy into cryptogenic, symptomatic, and idiopathic categories is of limited value without adequate MRI assessment.

The abnormalities better seen on MRI than...
on CT are hippocampal asymmetry, small tumours and vascular malformations, and subtle cortical dysgenesis.6 35-37 Computed tomography has a poor detection rate for the important structural abnormalities in the temporal lobes.35 Magnetic resonance imaging has proved to be highly sensitive and specific in visualisation of temporal lobe diseases, especially hippocampal sclerosis and tumours.36-40

An additional survey41 performed by one of us—of 186 patients with chronic partial epilepsy comparing CT with detailed MRI, including the coronal volumetric acquisitions—showed that the CT had detected only 60% of dysembryoplastic neuroepithelial tumour, 50% of vascular lesions, 40% of cortical dysplasia and 30% of subependymal heterotopias, and none of the cases of band heterotopia. The same survey compared routine MRI performed in non-specialised units (consisting of 5 or 10 mm axial slices with a 2-5 mm interslice gap, using T1, proton density and T2 weighted sequences, and only occasionally using coronal acquisition with 5 mm slice thickness and heavy T1 or T2 weighting) in 110 patients. It showed that routine MRI also had failed to diagnose all cases of hippocampal sclerosis, 50% of band heterotopias, 20% of subependymal heterotopias, and 20% of cortical dysplasias, but no differences were found in the detection of vascular and tumorous lesions.

The nature of the pathological lesion responsible for the development of the seizure disorder is the key component of the epileptogenic zone. Much of the variability in outcome relates to the extent to which it can be resected.1-4 Althonly previously in most cases the pathological substrate could only be defined on histological examination of surgical specimens, with high resolution MRI the diagnosis may be made preoperatively.8 33 35 48 One important issue concerned with presurgical evaluation is the presence of dual pathology.9-42 The commonest association found was hippocampal asymmetry and cortical dysgenesis, seen on visual inspection of two dimensional imaging in 3% of this series, but more often evident in quantitative studies.43 High resolution MRI is important in all presurgical patients not only to identify the responsible lesion, but also to try to rule out as far as possible the presence of other lesions, such as subtle cortical dysgenesis, which may adversely affect postoperative outcome.

The overall pick up in the present series represents that which can be achieved by simple two dimensional visual inspection of high resolution MRI alone. We accept that there is a selection and referral bias in this study for patients with chronic partial epilepsy seen at tertiary centres, who may be more likely to have an underlying structural pathology. The patients in our clinic were, however, similar to those seen at other tertiary centres, and form the group of patients in whom MRI is most likely to be applied. Furthermore, these are precisely the cases most likely to be referred for surgical evaluation.

There are various complex techniques which can be used to increase the yield of MRI in epilepsy further. These include quantitative volumetric assessment of the hippocampus.44-46 This technique provides more information than simple visual inspection.46 Studies47-49 showed that two dimensional visual inspection could miss subtle but important hippocampal asymmetry. Volumetric analysis of other cerebral structures has been shown to be a promising technique. In a group of patients with seizure semiology suggesting frontal lobe epilepsy, in whom two dimensional visual inspection of high resolution MRI was normal, Sisodiya et al50 showed relevant gyral abnormalities on three dimensional reconstruction in nine of 15 cases. Alternative methods of data acquisition can also increase the yield of MRI. Bergin et al51 reported the use of the fluid attenuated inversion recovery (FLAIR) sequence in 36 patients with partial seizures. In this selected group, the FLAIR sequence improved the yield of MRI by 30%. Quantitative T2 mapping has also been reported to show a good correlation with hippocampal sclerosis.42 52 53 Visual inspection can reliably detect T2 values when these are 115 ms or higher; however, five of 40 patients showed T2 quantitative abnormalities of 106–115 ms and were found to have hippocampal sclerosis.48 In addition, T2 and absolute volume measurement may be useful in bilateral hippocampal sclerosis.48 54
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In conclusion, the increasing availability of high resolution MRI should make it possible to identify the underlying pathological substrate in most patients with chronic medically refractory epilepsy. This will allow a fundamental reclassification of the epilepsies for both medical and surgical management, with increasing precision as research methods are added to the neuroimaging battery used in clinical practice.

46 Sioudyja SM, Raymond AA, Stevens JM, Fish DR, Shorvon SD. Demonstration of unsuspected gyriform abnormalities by three-dimensional reconstruction of magnetic resonance images [abstract]. Epilepsia 1994;35(suppl 7):S30.
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