REVIEW

Frontal lobe epilepsy: seizure semiology and presurgical evaluation

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INTRODUCTION

John Hughlings Jackson reflected that the frontal lobe is the brain's 'most complex and least organized centre' (Jackson 1931) and, despite subsequent advances in neuroscience, even by the late 20th century the frontal lobe was still considered to be an 'uncharted province of the brain' (Goldman-Rakic 1984). For epileptologists today, frontal lobe epilepsy (FLE) remains the most challenging of all the epilepsies, both in terms of understanding how seizures are organized and how they should be treated. This is very evident in comparison to the now well-defined syndrome of mesial temporal lobe epilepsy (TLE).

Important advances have been made in recent decades, especially in correlations between the clinical and electrical expression of seizures, permitting better understanding of FLE. Together with major developments in the field of neuroimaging, these advances are changing the approach to management, particularly in making curative surgery a real possibility for many more patients than ever before.

Understanding FLE, it can be argued, will also help us understand more about the cerebral processes that underlie normal higher brain functions such as the interaction between emotion and decision making (Damasio 1995). Indeed, frontal lobe epilepsy has been described as 'the next frontier' (Niedermeyer 1998). From historical observations to futuristic developments: what does all this mean for our routine clinical practice?

AIMS OF THIS REVIEW

We have chosen to focus on the approach to the electroclinical diagnosis and localization of FLE, in other words the combined analysis of the clinical features of seizures (semiology) and electroencephalographic (EEG) data. This approach is particularly important when assessing those patients who may be candidates for epilepsy surgery: the 20% or so of all patients with partial epilepsy who are pharmacoresistant. In addition we will briefly discuss recent developments in other aspects of presurgical evaluation.

WHY ARE ELECTROCLINICAL CORRELATIONS SO IMPORTANT IN FRONTAL LOBE EPILEPSY?

In epilepsy, as in all neurological practice, the history and physical signs are of paramount importance and cannot be replaced by a single test,

no matter how sophisticated. Just as the presence of a right hemiparesis alerts the clinician to look for a lesion in the contralateral motor pathway, so too can the clinical features of a seizure point to the activation (or inhibition) of certain brain regions. At its simplest level, this allows us to relate a sign such as a focal clonic contraction in the hand with seizure activity in the contralateral motor cortex. However, in FLE the observed symptoms or signs may be complex, subtle and often occur simultaneously or in rapid succession, frequently reflecting the activation of different structures within a dynamic system, with rapid and unpredictable propagation patterns.

Not only is it challenging to determine from which part of the frontal lobe the seizure arises, but also it is often difficult to assess whether a particular attack is indeed a frontal lobe seizure at all. Frontal lobe seizures are particularly prone to misdiagnosis as psychogenic non-epileptic seizures, due to their sometimes bizarre or atypical appearance, as well as to the fact that surface EEG does not necessarily show interictal or ictal abnormalities (Bautista *et al.* 1998).

Another possible misdiagnosis of FLE is of a sleep disorder, particularly as a large proportion of frontal seizures arise from sleep. For example, the nocturnal attack disorder originally identified as a form of movement disorder – 'paroxysmal nocturnal dystonia' (Lugarasi & Cirignotta 1981) – was subsequently recognized to have an epileptic basis in most cases (Meierkord *et al.* 1992). The syndrome of autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) was later described; this is a monogenic disorder with high penetrance, characterized by brief hyperkinetic nocturnal seizures.

Because of these diagnostic difficulties, caution must be exercised, and an epilepsy specialist rather than a general neurologist or general physician should ideally make the diagnosis.

The localizing value of specific semiological features is, in general, less well-understood in FLE, compared with TLE. For this reason, as well as other issues related to the limitations of EEG in FLE, diagnosis and localization are well recognized to be more difficult than in other localization-related epilepsies (Manford *et al.* 1996). Indeed, it is likely that some epilepsy 'surgical failures', including cases operated for presumed TLE that do not become seizure-free post-operatively, reflect incorrect presurgical localization, rather than suboptimal resection (Walsh & Delgado-Escueta 1984). FLE forms the second largest group of potentially operable localiza-

tion-related epilepsies after TLE. The reliable electroclinical diagnosis of FLE, as well as the identification of subtypes, is therefore particularly important in terms of optimal selection of candidates for epilepsy surgery.

Despite the complex nature of most frontal seizures, certain semiological patterns are reproducible and can help to define the likely region(s) involved. The occurrence of localized tonic posturing (face, upper limb, lower limb), emotional behaviour (such as fear) and complex motor activity, may direct the clinician towards a particular part of the frontal lobe, as will be discussed later. This becomes crucial when a more precise sublobar understanding of localization is required.

FRONTAL LOBE ANATOMY AND RELATION TO SEMIOLOGY

The frontal lobe is the largest lobe in the brain (accounting for about 40% of cerebral cortex) (Fig. 1). This large size contributes to diagnostic difficulties. There are multiple diverse propagation patterns, and there is the problem of limited EEG sampling, particularly from relatively 'hidden' regions such as medial and basal (orbitofrontal) cortex (Bautista *et al.* 1998). The functional anatomical divisions of precentral, premotor and prefrontal cortex provide a useful model for thinking about semiology and will be briefly described:

- The precentral region consists of primary motor cortex, Brodmann's area 4.
- The premotor cortex consists principally of the lateral and medial components of area 6, the latter corresponding to the supplementary motor area (SMA).
- There is some representation of language (including the region formally known as Broca's

area) within the premotor cortex, particularly in the dominant hemisphere (area 44).

- The frontal eye fields, which can contribute to ictal versive head and eye movement, lie within the dorsolateral cortex (area 8) in the boundary where the premotor and precentral cortex meet, and may therefore be involved in seizures arising from either of these regions.

The organization of the prefrontal cortex, which is predominantly made up of heteromodal association areas, is extremely complicated and incompletely understood. It has complicated and long association connections with other brain regions, including limbic and paralimbic areas, which involve a continuum of temporal and frontal lobe structures (particularly the cingulate gyrus and the posterior orbital region) (Fig. 2). Incoming sensory information from these areas may be processed, taking account of motivational and emotional states, and used to influence decision-making and many aspects of behaviour (Pandya & Yeterian 1985). Patients with prefrontal epilepsy may demonstrate interictalbehaviouralorpsychiatricabnormalities, such as lack of spontaneity and poor planning (frontal abulic syndrome), or impulsivity and socially inappropriate behaviour (frontal disinhibition syndrome), which may improve following surgery (Devinsky *et al.* 1995).

ATTEMPTS TO CLASSIFY FRONTAL LOBE EPILEPSY

Although the approach of separating temporal from extra-temporal epilepsy is now established, and most extra-temporal epilepsies have their origin in the frontal lobe, a widely accepted classification of FLE has not yet been reached. Indeed the nomenclature used by different groups to describe frontal seizure types has var-

Figure 1 Cytoarchitectonic diagram of the frontal lobe (prefrontal cortex shown in colour), with Brodmann's areas (Petrides & Pandya 1994). (a) Lateral view, (b) Medial aspect. Reprinted from *The Frontal Lobes, Computational Modelling and Neuropsychology: Handbook of Neuropsychology*, Vol 9, Boller F, Spinnler H, Hendler JA, 1994, with permission from Elsevier.

ied markedly over the years. Trying to advance our understanding of all this is important, because FLE must be regarded as a variety of seizure patterns originating from different regions of the frontal lobes rather than a disease *per se* (Wieser & Swartz 1992).

Important progress has been made recently by the proposed system of electroclinical patterns based on the functional anatomical divisions of the frontal lobe (Bartolomei & Chauvel 2000; Chauvel 2003). This recognizes central, premotor and prefrontal seizure types with distinction between predominantly dorsolateral and medioventral types within each of these categories. This model is clinically useful because it reflects the tendency for postural and tonic motor activity to be seen in the most posterior subtypes (central, precentral) and more complex motor behaviours with autonomic and emotional manifestations to be associated with prefrontal seizures. Distinction between dorsal and medial patterns is also possible to some extent, this having been already well-documented in motor area seizures. There is some evidence to suggest that prefrontal seizures may be similarly separable. This classification will be discussed later.

ANATOMO-ELECTRO-CLINICAL CORRELATIONS

Detailed study of FLE electro-clinical correlations has been possible since the advent of

Figure 2 There are extensive functional connections between the prefrontal cortex and other frontal lobe structures as well as other lobes of the brain. The long length of these connections is a contributing factor to the highly variable propagation patterns and the diverse, complex semiology that may occur with frontal lobe seizures. The more highly integrative (and more anteriorly situated) the association area, the longer these projections are. (a) Lateral view, (b) Medial view. AS, arcuate sulcus; CC, corpus callosum; CF, calcarine fissure; CING S, cingulate sulcus; CS, central (Rolandic) sulcus; IOS, inferior occipital sulcus; IPS, intraparietal sulcus; LF, lateral (Sylvian) fissure; LS, lunate sulcus; PS, principal sulcus (Pandya & Yeterian 1985, permission sought.)

video-EEG recording, enabling correlation of detailed clinical observations of seizures with simultaneously recorded electrophysiological data. The development of depth electrode EEG recording, especially the technique of stereo-electroencephalography (SEEG), developed by the French team of Bancaud and Talairach in the 1960s–1980s, has been crucially important in this respect (Chauvel 2001). SEEG involves the stereotaxic placement under general anaesthetic of depth electrodes that record EEG from deep brain structures. It has certain advantages over other intracranial recording methods (such as subdural grids or strips placed on the cortical surface), in that it permits simultaneous recording from superficial and deep structures, allowing better spatial definition of the likely region of seizure onset, or epileptogenic zone (EZ). Morbidity is also lower. Ictal and interictal SEEG recording with simultaneous video is generally obtained over a period of 4–10 days, during an

Figure 3 Stereo electroencephalographic (SEEG) intracerebral recording of a dorsolateral prefrontal seizure. (a) This patient had seizures characterized by semipurposeful behaviour, proximal tonic posturing and vocalization. The combination of clinical, electrophysiological and imaging data suggested likely involvement of the dorsolateral prefrontal region. (b) The electrical onset of the seizure is clearly seen in his ictal SEEG recording, with a build-up of high amplitude rhythmic spikes (red arrows) followed by a high frequency rapid discharge (blue arrows). The electrodes involved lie within a localized part of the dorsolateral prefrontal region. (c) Representation of propagation patterns as recorded with SEEG, superimposed on a 3D MRI reconstruction. The patient subsequently underwent localized cortical resection, with no postoperative neurocognitive deficit, and remains seizure-free at 1-year follow-up. With thanks to the staff of the Epilepsy Unit, Hôpital de la Timone, Marseille, France.

inpatient stay in a specialist videotelemetry unit. The decision about where to place the electrodes is based on the hypotheses regarding the likely brain structures involved in the EZ. These hypotheses are formed by the epilepsy team and are based on the ensemble of all the available non-invasive data [standard EEG and video-EEG, MRI, single photon emission computerized tomography (SPECT), positron emission tomography (PET), etc.], and including detailed semiological observations. This technique can be very useful in those patients with FLE who are potential surgical candidates, but where standard non-invasive investigations are insufficient to allow localization of the EZ (for example normal or nonlocalizing MRI). Potential contra-indications to surgery (e.g. involvement of language areas) can also be studied during the recording. The method is well-established in several European countries for epilepsy pre-surgical evaluation, but remains much less used elsewhere, including in the UK and US. An example of this electroclinical approach is shown in Fig. 3.

GENERAL FEATURES OF FRONTAL SEIZURE SEMIOLOGY

Recent reviews have revealed the diversity of presentation of frontal seizure semiology and some have sought to define clinical or electro-clinical subtypes (Bancaud & Talairach 1992; Talairach *et al.* 1992a; Chauvel *et al.* 1995; Williamson & Engel 1997; So 1998; Swartz *et al.* 1998; Bartolomei & Chauvel 2000; Jobst *et al.* 2000; Kotagal *et al.* 2003). Those (relatively few) series with confirmation of frontal lobe origin by depth studies and/or subsequent surgical cure by frontal resection have been particularly useful.

Frontal seizure semiology is extremely diverse, but certain features are agreed to suggest frontal lobe origin. Seizures may be brief with sudden onset and termination; often arise from sleep; may occur in clusters; have a tendency to rapid secondary generalization; and produce minimal postictal confusion (Williamson *et al.* 1985; Williamson & Engel 1997). Clonic activity and asymmetric tonic posturing are typical of frontal seizures and of all the possible frontal seizure symptoms and signs, motor manifestations remain the most frequent and important, observed in 90% of patients (Chauvel *et al.* 1995).

Complex gestural manifestations or patterns of behaviour seem to be particularly characteristic of certain FLEs and are increasingly recognized (Williamson *et al.* 1985; Bancaud & Talairach 1992; Chauvel *et al.* 1995; Manford *et al.* 1996; Jobst 2000). Gestural automatisms include fumbling or exploratory movements with the hand directed toward self or environment, such as tapping or grabbing of objects or bedclothes; more complex behaviours might include snapping the fingers, crossing and uncrossing the legs, or more dramatic pedalling movements, thrashing or hitting. Some of these complex manifestations may seem to be to a greater or lesser degree adapted to the environment, indicating a degree of retained awareness and autonomy. Although the term 'hypermotor seizures' was proposed by the Cleveland group to describe such seizures characterized by motor agitation associated with an emotional quality, this has not been uniformly accepted as a useful description (So 1998).

DIFFICULTIES OF ELECTROCLINICAL CORRELATION IN FLE

Unlike TLE, where the sites of epileptic discharge likely to be responsible for certain ictal clinical signs are relatively well-recognized, the neurophysiological organization of many types of frontal lobe seizure remains poorly understood.

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Several recent FLE studies have attempted to demonstrate a consistent sublobar localization for given ictal symptoms or signs but have found limited correlations (Manford *et al.* 1996; Jobst *et al.* 2000; Kotagal *et al.* 2003). This has led some authors to question whether it is possible to rely at all on semiological analysis when attempting to localize frontal seizures (Manford 1996).

However, such conclusions may to some degree reflect the limitations of using statistical cluster analysis to try to correlate an isolated clinical sign with a 'focus' of epileptic activity, rather than considering patterns of clinical signs and the concept of an epileptic 'network' that involves several sites and which gives rise to ictal phenomena depending on the interplay of a dynamic system.

The underlying mechanism of the complex ictal behaviour patterns seen in FLE remains an interesting and disputed question. One theory, proposed by Jackson and being revisited today, is that epileptic activity may disrupt the control normally exerted by higher brain centres, thus allowing the 'release' or disinhibition of more primitive, stereotyped behaviours. Such release phenomena might be comparable with the forced grasping or 'utilization behaviour' first described by Lhermitte (1983) in patients with bilateral frontal lesions, now recognized to form part of the spectrum of abnormal motor responses that occur in the context of imbalance between internally generated control of movement and response to environmental cues (Archibald *et al.* 2001). The stepping reflex is another example of such release phenomena, and the kicking movements or pelvic thrusting during frontal seizures may be interpreted as relating to this. Recent electrophysiological data supporting the role of epileptic networks in frontal lobe ictal phenomena argue in favour of a 'functional uncoupling' of this nature (Wendling *et al.* 2003; Gavaret *et al.* 2004).

This area therefore remains one of the most important for further study if we are to advance in our ability to understand FLE, and successfully select FLE patients for surgical treatment.

ANATOMIC-FUNCTIONAL CLASSIFICATION OF FRONTAL LOBE SEIZURES

While the recent anatomical and functional categorization of frontal seizure subtypes proposed by Chauvel and colleagues remains preliminary, it provides a useful way to consider the localizing value of certain patterns of seizure semiology (Fig. 4)

Figure 4 Summary of elements of frontal seizure semiology in relation to precentral, premotor and prefrontal regions. (a) dorsolateral view (b) medial view. BA, Brodmann's area; SMA, supplementary motor area.

Pre-central seizures

The best-defined frontal seizure type was recognized by Jackson over 100 years ago (in Jackson 1931). His description of focal seizures with contralateral clonic movements arising from the precentral (primary motor) region remains valid today. The characteristic feature is the slow progression from one body part to another adjacent segment – the 'Jacksonian march'. The body part involved in the seizure indicates the region of motor cortex activity according to the somatotopic representation in the motor cortex, so that it is possible to distinguish dorsal from medial precentral seizures.

In the light of depth electrode data, it is now recognized that seizures arising from the precentral cortex may also appear rather different to the classical Jacksonian focal clonic seizure. For example, contralateral clonic movements may be accompanied by more complex bilateral tonic posturing, or predominantly distal partial myoclonus (Chauvel *et al.* 1992).

Another form of epilepsy associated with the Rolandic (central) region, in other words motor (frontal precentral) and also sensory (parietal postcentral) areas, is reflex epilepsy. (Vignal *et al.* 1998). This rare phenomenon (about 1% of partial epilepsies) manifests as seizures that are triggered by cutaneous stimulation or movement of a specific body part. They may manifest as tonic posturing (often asymmetric), clonic jerks or a combination of both; sometimes there is also a sensory component (e.g. tingling in the arm followed by clonic jerks in the same territory). The aetiology may be related to hyperexcitability of the sensorimotor Rolandic cortex.

In the related but separate entity of startle seizures, a sudden or unexpected sensory stimulus, usually a noise, can provoke a motor startle response characterized by tonic motor signs, such as bilateral upper and lower limb posturing, that is often asymmetric. Such seizures were classically described in the context of infantile hemiplegia due to a cortical lesion involving the motor area, and their cortical origin in the precentral and premotor region has been demonstrated (Chauvel *et al.* 1992).

Another specific type of seizure more rarely arising from central regions is *epilepsia partialis continua*, a form of 'partial somatomotor status epilepticus'. This can remain focal for hours, days, weeks or even months because of long-loop reflex mechanisms in the sensorimotor cortex (Biraben & Chauvel 1997). Its cortical origin has

been shown by stereo-electroencephalography (SEEG) and by scalp-EEG using back averaging techniques. The underlying cause in some is an autoimmune process, which is now recognized to be the mechanism for Rasmussen's encephalitis; vascular lesions and tumours may also be responsible.

Premotor seizures

This region includes the supplementary motor area (SMA). Seizures arising in the SMA were originally described on the basis of the results of electrical stimulation of normal cortex. However, the spectrum of semiology for seizures involving the SMA is now recognized to be wider than originally suggested (Bancaud & Talairach 1992; Chauvel *et al.* 1992). Premotor seizures are characterized by postural and tonic signs, which are predominantly proximal, usually bilateral and asymmetrical. The upper limbs are most often involved, producing the classical 'fencing posture' or a variety of other tonic postures (Fig. 5). Adversion (turning) of the head and eyes is often associated with this, due to involvement of the frontal eye fields. The direction of adversion may be ipsilateral or contralateral to the site of epileptic activity, depending on its timing within the seizure, and is therefore not a consistently reliable guide to lateralization of

Figure 5 This patient has seizures arising from the left supplementary motor area in the premotor frontal region. Note the characteristic asymmetric tonic posturing of upper limbs during one of her typical seizures. With thanks to Dr JP Vignal, Nancy, France.

the epilepsy. Speech arrest or vocalization (characteristically palilalia) may also occur if there is involvement of the speech area in the frontal operculum. Spread to involve the operculum and the lower central region may also give rise to facial clonic jerks and salivation. More complex movements of all four limbs can follow these main signs. Initial subjective sensations or 'auras' occur infrequently in this seizure type, but some patients describe sensory symptoms such as ill-defined tightness or tingling, which may be generalized or localized (Williamson & Engel 1997). Secondary generalization is infrequent.

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Prefrontal seizures

Prefrontal seizures remain the least well-characterized of all frontal seizures. In fact distinguishing between prefrontal and premotor origin can be difficult, as seizures may involve both areas. Seizure patterns that arise from the prefrontal region reflect its highly complex organization, so that in comparison with the relatively simple elements of more posterior frontal seizures, prefrontal semiology is extremely diverse and may be highly idiosyncratic.

The first observations of prefrontal seizures were published in the 1970s (Tharp 1972; Ludwig *et al.* 1975). These were described as brief attacks typically occurring in clusters, often at night, and characterized by a frightened appearance, agitation, repetitive semipurposeful behaviour and vocalizations that could be non-verbal (screaming) or verbal (expletives). It was initially speculated that these were of orbito-

frontal origin, although whether it was possible to distinguish them electroclinically from temporal lobe seizures was disputed for a decade or so. A frontal lobe origin for this pattern of seizure was later confirmed by depth EEG recordings (Williamson *et al.* 1985). Subsequent workers developed distinctions between those with a dorsal origin from those arising from anterior cingulate, orbitofrontal, and frontopolar areas (Bancaud & Talairach 1992).

Currently available data suggest that the clearest differentiation can be made between ventral and dorsal patterns.

Ventro-medial prefrontal seizures

Seizures arising from ventral or ventro-medial regions appear to correspond to those initially described as 'complex partial seizures of frontal lobe origin' (Williamson *et al.* 1985), as described above. Some begin with what appears to be a dramatic reaction to fear, with a frightened facial expression, screaming and abrupt agitation (Fig. 6). This intense behavioural reaction to fear is very different from the pattern of temporal lobe seizures that include a subjective sensation of fear. There may be complex, apparently purposeful gesticulation, such as kicking or punching, bipedal cycling movements or attempts to escape. Autonomic signs such as mydriasis, tachycardia and facial flushing are common, as well as peri-ictal urination. It appears that a consistent role for a ventro-medial epilepsy network can be demonstrated for those seizures involving ictal fear-related behaviour (Biraben *et al.* 2001).

Dorso-lateral prefrontal seizures

Certain clinical features suggest the involvement of the dorsal prefrontal region, notably tonic deviation of the eyes preceding head version, and gestural automatisms that may be directed towards the same location as the gaze. These movements may appear semipurposeful, for example a patient may appear to be reaching towards something in their visual field. There may also be a compulsive element to the behaviour ('forced acting'). Motor patterns in this seizure type are usually complex, such as semirhythmic tapping of the hands or feet, or grasping motions. They are often associated with asymmetrical tonic or dystonic posturing of upper and/or lower limbs. Vocalization may occur; unlike the pattern seen in medioventral seizures, this often does not appear to have an initial emotional modification. Such vocalizations may be non-verbal (e.g. groaning,

Figure 6 Some prefrontal seizures may manifest as extreme motor agitation and emotional behaviour during the ictal period. This pattern appears to be associated with a ventromedial epileptic network, as in this patient who had epilepsy affecting the left ventromedial prefrontal region. With thanks to staff of the Epilepsy Unit, Hôpital de la Timone, Marseille, France.

humming) or verbal (e.g. palilalia, jargon, swearing, singing). Visual hallucinations may also be reported in seizures from this region; these can include dimming or blurring of vision and more rarely actual hallucinations, either simple, such as coloured shapes, or what have been described as 'psychical' illusions (e.g. images of a familiar person) (Chauvel *et al.* 1995). 'Forced thinking' may occur, consisting of a recurrent intrusive thought or an overwhelming impulse to perform a certain act (e.g. to open the eyes, or to grab something).

Another form of dorsolateral seizure is that associated with a spike-wave, rather than a tonic discharge, which manifests clinically as a 'frontal absence' with arrest of activity (Bancaud & Talairach 1992). This seizure type may appear electroclinically similar to the classical 'petit mal' absence seizures that occur in the context of idiopathic generalized epilepsy; indeed the nature of the differences between the two has been the topic of some debate. The absences of FLE tend to be more variable in their clinical expression, with a longer duration and/or the presence of associated features such as automatisms. The 'atypical absences' of the Lennox–Gastaut syndrome could be included in this category.

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premotor and motor regions, secondary generalization is frequent.

This proposed classification remains somewhat theoretical and is the subject of ongoing study but progress in the identification of electroclinical patterns has the potential to greatly advance the surgical treatment of FLE.

DEVELOPMENTS IN THE PRESURGICAL EVALUATION OF FRONTAL LOBE EPILEPSY

When considering the overall evolution of surgery for epilepsy, the importance of developments in neuroimaging over the past 15 years cannot be overestimated – these have revolutionized the optimum selection and treatment of potential epilepsy surgical candidates (Duncan 1997). Given the difficulties in the diagnosis and localization of FLE as described above, imaging plays an extremely important role. Magnetic resonance imaging (MRI), including techniques such as diffusion tensor imaging, has developed to the point where the great majority of patients with localization-related epilepsy can be shown to have an underlying cortical lesion (Fig. 7). Many authors emphasize the correlation between the presence of a visible focal lesion and good surgical outcome (Mosewich *et al.* 2000).

However, there remain around 20% of patients with localization-related epilepsy who have no lesion visible on current optimum MRI with expert review, and others with dual or multifocal pathology. Moreover, even when a

single lesion is seen on MRI, it is necessary to understand its relation to the epileptogenic zone, as the two do not necessarily fully overlap (Talairach *et al.* 1992b). Anatomic-electro-clinical correlation carried out using SEEG as devised by Talairach, which was developed well before the era of MRI, does not necessarily depend on the presence of a visible lesion on neuroimaging. In addition, some series have reported good outcomes in patients with normal imaging, based on presurgical evaluation incorporating semiological analysis and intracerebral recording as well as other noninvasive data (Talairach *et al.* 1992a; Zentner *et al.* 1996; Swartz *et al.* 1998; Siegel *et al.* 2001).

Much current research is therefore being directed towards the detection of focal lesions that are not visible with currently optimal MRI (Knowlton 2004). It seems likely that the small surgical series reporting successful outcomes despite normal imaging reflect those patients with 'invisible' focal lesions, many of which are focal cortical dysplasias, and which the ensemble of clinical data including intracerebral EEG have correctly identified. It is clear that development of less invasive methods that might permit the confident detection of such lesions is an important area for future work. Such methods include functional imaging, of which positron emission tomography (PET) appears particularly promising. Although most work relates to medial temporal epilepsy, a recent study has highlighted the potential importance of [^{11}C] flumazenil PET, which appears to have better

Figure 7 Brain MRI demonstrating the presence of a small dysplasia (arrow) in the left medial frontal lobe (prefrontal region). (a) Coronal inversion-recovery sequence, (b) Coronal FLAIR, (c) Axial T2.

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sensitivity and specificity in detecting metabolic abnormalities than 2-[^{18}F] fluoro-2-deoxy-d-glucose (FDG) PET in neocortical epilepsy and which may be useful in helping to detect extra-temporal epileptogenic zones even when MRI is normal (Hammers *et al.* 2003).

Developments in non-invasive neurophysiological techniques include magneto-electroencephalography (MEG), which, though limited to a few centres, seems to be particularly useful in neocortical compared with temporal epilepsy and has been validated by intracranial comparison studies (Barkley & Baumgartner 2003). Source localization techniques using high-resolution scalp EEG also appear promising (Gavaret *et al.* 2004) (Fig. 8).

Figure 8 High resolution EEG can be superimposed on a patient's MR scan to represent the region of greatest interictal activity and this can be particularly useful where imaging is non-localizing. This figure shows interictal spikes recorded from a 27-year-old woman with medioventral frontal lobe epilepsy. (a) Interictal spikes occurred in brief runs with maximal amplitude over electrodes FP1, F7 and FPZ (left fronto-polar region), (b) Source localization was then performed using a technique called MUSIC (Mosher *et al.* 1992), which showed the maximal contribution to be in the anterior part of the left cingulate gyrus. This localization was later validated during a depth EEG recording that demonstrated both interictal and ictal epileptic activity arising from this region. Cortectomy was subsequently performed and histopathology showed Taylor's dysplasia. The patient was seizure-free at 2 years post-operatively. With thanks to Dr Martine Gavaret, Hôpital de la Timone, Marseille, France.

The notion of 'totally non-invasive presurgical epilepsy evaluation' in the future (Knowlton 2004) is also supported by the potential of functional MRI for localization of language and memory function prior to deciding on surgical resection. This may eventually be able to replace tests such as the WADA and mapping by direct cortical stimulation.

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CONCLUSIONS

- The study of the semiology and electro-clinical correlation of frontal seizures continues to hold an important place in the understanding of frontal epilepsy and cerebral function.
- This type of detailed study has been made possible largely because of modern video-EEG techniques, especially those using depth recording, and those that have correlated electroclinical data with postoperative outcome.
- Recent years have seen major advances in classifying FLE: by establishing the tendency for frontal seizure types to be related to functional divisions of the frontal lobe and to be organized along antero-posterior and dorso-ventral gradients.
- There can be few treatments for chronic disease with the potential to make as huge an impact on an individual's quality of life as curative epilepsy surgery. This treatment has the potential to transform a young person's life from one with intractable seizures and the inevitably associated risks of increased mortality, social disadvantage and psychological vulnerability, to a normal existence.
- Although FLE remains in general more difficult and less common than TLE, thanks to the major developments in electroclinical correlation and neuroimaging, it is becoming possible to envisage surgery as a possibility for many future FLE patients
- A multimodal approach, combining electro-clinical methods with the best available imaging techniques, allows complex FLE cases to be tackled in centres with appropriate expertise
- The ultimate aim will be to achieve a reliable, non-invasive presurgical approach in as many patients as possible.
- One of the biggest challenges remains the surgical treatment of those patients with normal imaging. It seems likely that current developments in electroclinical correlation and functional imaging techniques will permit advancement in the near future.

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