An analysis of clinical seizure patterns and their localizing value in frontal and temporal lobe epilepsies

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Summary
The differentiation of frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE) is a clinical problem of major theoretical and practical importance. Current electroclinical classification is based on retrospective studies of highly selected patients. When applied to the presurgical evaluation of patients, it has poor specificity. The current study adopts a different and prospective approach to the analysis of ictal clinical manifestations and their value in differentiating FLE and TLE. Two hundred and fifty-two patients with partial epilepsy were selected according to criteria of focal abnormality on imaging, ictal EEG or interictal EEG or highly focal clinical pattern. A witnessed seizure description was obtained for each of their habitual seizures and the sequence of manifestations encoded and entered into a statistical cluster analysis to form a clinical classification of the 352 seizures identified, which comprised 14 clinical groups. Neuroimaging abnormalities were measured, using a template technique, and graded 0–3 according to extent of involvement of each region in the lesion, using standard anatomical divisions. A \( \chi^2 \) analysis of lesion location against seizure type was performed to assess the strength of association of seizure types with specific cerebral regions. The distribution of interictal EEG spikes and ictal EEG onsets were assessed qualitatively. An independent analysis was also performed, comparing clinical seizure manifestations associated with lesions restricted to either frontal or temporal lobes. Of the 14 clinical groups, four were predominantly related to temporal lobe abnormalities: fear/olfactory/gustatory; absence with no focal symptoms; experiential and visual. Within these groups, 45 out of 58 lesional cases involving this region (\( P < 0.001 \)). Two other groups were related to the frontal lobes; version/posturing and motor agitation. Early focal tonic activity or head turning were associated with lateral premotor lesions (\( P < 0.001 \)) and ictal and interictal EEG showed strong frontal predominance. Seizures characterized by general motor agitation were associated with lesions of the orbitofrontal (eight out of 13 cases) and frontopolar (six out of 13 cases) cortices (\( P < 0.001 \)). Location of interictal EEG spikes and ictal EEG onsets were generally consistent with lesion sites and where there were discrepancies, EEG localization tended to be more diffuse than lesion localization, rather than frankly discordant. Analysis of manifestations associated with pure frontal and pure temporal lesions supported the results of the cluster analysis and also showed a significant association of oro-alimentary automatisms with temporal lobe abnormalities. There were no consistent differences between groups with different localizations in terms of seizure frequency or other characteristics of seizure timing, although very high seizure frequencies were seen more often in association with frontal lesions. Only one combination of different seizure types in the same patient occurred with statistical significance: absence and generalized motor seizures and pseudo generalized epilepsy. The results of this study suggest that relatively few seizures can be localized reliably on clinical grounds and that even in those seizure types where there is a statistically significant association with specific cortical areas, an important minority do not share the same associations. Analysis of the seizure evolution as well as initial symptoms may be of value in localizing some cases, but even here wide variation occurs. These findings lead us to question the value of classifying partial epilepsy using electroclinical criteria, particularly in trying to infer anatomical localization. Possible mechanisms for blurring of the distinctions of clinical seizure types are discussed.

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Introduction

Frontal lobe epilepsy is probably the largest subgroup of extratemporal partial epilepsy, representing 20–30% of partial epilepsies (Bhatia and Kollevoed, 1976; Manford et al., 1992). The recognition of FLE and its differentiation from TLE are of importance both in understanding the pathophysiology of ictal mechanisms and, clinically, in optimizing selection of patients for epilepsy surgery.

The most recent International League Against Epilepsy (ILAE) electroclinical, syndromic classification (Table 1) (Anonymous, 1989), also suggests seven anatomically and clinically distinct regions of seizure generation within the frontal lobes. This classification derives from the experience of a panel of experts and interpretation of data especially from video-EEG-telemetry (VET) and the widely applied gold-standard of seizure localization by post-surgical remission. This states that if a technique identifies a region resection which produces permanent relief from seizures, then it correctly identified the maximally epileptogenic cortex (Smith et al., 1989). The patient group is, however, highly selected, as <1% of patients undergo surgery for epilepsy. Moreover, individuals do not usually undergo VET unless they are surgical candidates, with appropriate concordance of clinical, interictal EEG and imaging investigation, introducing substantial bias into any classification based on this group. Even applying these criteria, up to 60–80% derive limited benefit or no benefit from FLE surgery (Rasmussen, 1991), much worse than for TLE, suggesting particular problems in the classification FLE by this method. Our experience is that clinical seizure patterns are much more difficult to define, both in terms of temporal versus extratemporal and in terms of intrafrontal localization than is suggested by this apparently clear-cut classification.

The evolution of techniques in the analysis of partial seizures is important in understanding the limitations of current views in the classification of partial epilepsies. Hughlings Jackson first made a systematic analysis of seizure manifestations and their relationship to structural pathology (Taylor, 1958), recognizing classical patterns of clinical seizures, associated with pathological lesions identified post mortem. Early surgery targeted frontal central lesions since their motor sequelae were the clinical manifestations most readily lateralized on clinical grounds (Horsley, 1886). The introduction of EEG 60 years ago, allowed an extra dimension of pre-operative and intra-operative investigation, enabling the localization of seizure types that could not be established on clinical criteria alone and following this development, TLE was considered predominant. During these phases, the pathology underlying an individual’s epilepsy usually could not be determined pre-operatively. Indeed, the basis of the current classification of epilepsy is electroclinical (Anonymous, 1989), predating the ability to identify anatomico-pathological abnormalities by modern imaging techniques. With the advent of CT scanning, foreign tissue lesions were identified in up to 20% of cases (Theodore et al., 1986; Cordes et al., 1990), but the majority of partial epilepsies remained ‘cryptogenic’ until the development of modern, high resolution MRI. This has resulted in the pre-operative identification of the aetiology of the epilepsy and its location in an ever-increasing number of cases, with sensitivity of up to 90% (Cook et al., 1992; Cendes et al., 1993). Whilst the pathophysiological relationship of the site of the lesion and the expression of epileptic seizures is not certain—Hughlings Jackson originally pointed out that foreign tissue could not itself be involved directly in the propagation of seizure discharges (Taylor, 1958)—the site of the aetiological lesion is the most critical for seizure expression, even if its electroclinical presentation appears to be at a remote site (Engel et al., 1981; Sammaritano et al., 1987; Wyler et al., 1989; Palmini et al., 1991; Cascino et al., 1992; Salanova et al., 1993). This has resulted in a substantial shift in emphasis of investigation that has not yet been reflected in a reassessment of the standard classification.

Two-thirds of TLE is due to mesial temporal sclerosis (Babb and Brown, 1987), which is anatomically highly circumscribed and pathologically well defined, whereas the aetiologies of extratemporal epilepsy are more diverse and extratemporal lesions frequently cross the anatomical boundaries of the ILAE classification. These regions also have widespread connectivity (Pandya and Barnes, 1987) that may be of importance in the analysis of seizure dynamics (Spencer, 1988).

In the current study we aim to address the classification of partial epilepsies using a novel prospective method of relating clinical seizure manifestations to investigative results, taking into account the importance of modern neuroimaging. The patient selection and methods of analysis aim to eliminate much of the bias inherent in previous retrospective analyses of surgical series, allowing evaluation of the classification of epilepsy in a more representative population. In the first part of the study, a purely clinical classification of seizures is formed and this classification is related to EEG and neuroimaging abnormalities, to assess the predictive value of ictal symptoms. In the second part of the study, clinical seizure manifestations are compared between two groups defined by localized abnormalities on neuroimaging; those with pure frontal lesions and those with pure temporal lesions.
Patients were selected from records at the National Hospital for Neurology and Neurosurgery from August 1990 to December 1991, on the basis of epilepsy with strong evidence of focal onset. This hospital specializes in adult neurology and has general neurology as well as tertiary epilepsy services. Out-patient casenotes, EEG reports and CT and MRI scan reports were searched over this period for patients with evidence of focal seizure onset according to one or more of the following criteria [those with characteristics of occipital seizures were excluded as they are the subject of another study at our institution (Sveinsbjorndottir et al., 1992): (i) a demonstrable focal epileptogenic structural lesion on CT or MR scan; (ii) an ictal EEG recording suggesting focal electrographic seizure onset; (iii) an interictal EEG showing focal paroxysmal spike activity; (iv) clinical ictal onset with ictal symptoms suggesting focal epileptic activity.

Selection criteria were applied sequentially, in the order above, such that some patients had evidence of partial onset according to more than one criterion and in some cases, as investigations were undertaken, additional evidence of partial onset emerged. The initial selection criterion was clinical in 84 cases; imaging in 94 cases, interictal EEG in 47 cases and ictal EEG in 27 cases. Of 252 patients, 92 were seen in a specialist epilepsy clinic and 160 in general neurology clinics. Cases were ascertained by ongoing surveillance of EEG and imaging records and by referral into the study by colleagues. These selection methods were designed to include a broad base of patients from general neurology as well as specialist epilepsy practice. Because a proportion of patients may have focal seizure manifestations without any abnormalities on investigation, not to include this group would artificially restrict the study. Its inclusion does, however, risk the selection criteria introducing a bias into the analysis of clinical seizure patterns. In order to offset this risk, it is important to note that those selected according to EEG or imaging criteria were chosen irrespective of associated seizure pattern. In addition, those chosen according to clinical criteria were included irrespective of the site of any lesion or EEG abnormality identified subsequently. Unlike post-surgical series, selection criteria were independent, with concordance deliberately not considered in the initial selection, so it could be assessed later in relation to the identified seizure patterns.

Of 278 patients originally contacted, 252 were included and 26 excluded; 18 because no accurate eye-witness account of their seizures could be obtained; four because the patient had been seizure-free for >2 years and it was felt that time may have eroded the accuracy of the seizure description and four because re-examination of their investigations did not support the focal abnormality that had been their original selection criterion.

A witnessed seizure account was obtained prospectively from the patient and observer in all cases, using a semi-structured questionnaire designed especially for the study. In 176 cases the independent description was from an eye-witness, in 26 from video-telemetry recording and in 50 cases both sources were available. Some patients reported more than one seizure type. Where the early symptoms were very different the seizures were considered separately. If early symptoms were very similar in the two seizure types, suggesting that they represented variations in subsequent seizure evolution, the seizure was classed as a single type and recorded as its fullest expression, for example a patient with auras and complex partial seizures that were always preceded by the same auras. Only where a
seizure habitually became secondarily generalized, was the
generalized phase included in the description of the seizure.
Generalized seizures were only considered a separate type
where there was no evidence of the patient's habitual partial
seizure prior to secondary generalization. Three hundred
and fifty-two discrete seizure types were documented in
252 patients.

The definition of seizure manifestations is given in
Appendix 1. Ictal manifestations were coded in seven
categories, according to their sequence of occurrence during
the seizure, the first manifestation being given the highest
number. Manifestations not occurring at any stage of the
seizure were coded 0. This coding provided an ordinal
measure of the sequence of different manifestations, but did
not give an absolute measure of their timing.

Questionnaire validation was performed on 15 seizures
where both a witnessed account and video telemetry were
available. Many variables were coded 0 in any one seizure
and only 10% of the 780 variables encoded for the 15 patients
differed between historical and telemetry accounts. In nearly
half of these, this was only a difference of relative timing.
This low figure is well within the expected variability of
seizure manifestations.

Cluster analysis of seizure manifestations
Statistical cluster analysis was performed by Ward's method
on 346 seizure descriptions using Statistics Package for
the Social Services (SPSS)-X, utilizing Euclidean squared
distances with 52 variables (Appendix 2). Many of these
were clinically related manifestations grouped together. For
example, automatisms were divided into two types; those
characterized by simple repetitive motor activity, e.g. tapping
and those with more complex behavioural components, most
commonly exploratory behaviour. Six cases of complex
partial status epilepticus were excluded from this analysis,
because it was impossible to determine the sequence of
manifestations with this type and they were classed separately.
Each seizure type, rather than each patient, was entered as a
separate case in the statistical analysis; patients with more
than one habitual seizure type were entered more than once.
The variables included in the cluster analysis were the clinical
manifestations occurring during the seizure, rather than any
characteristics of timing or frequency, since the former were
felt to be more likely to be determined by the functions and
connectivity of the seizure-generating region. The gradient
of the cluster coefficient rose abruptly when the number of
groups fell below 15, suggesting that the minimum reasonable
number of groups was 13–15.

The localizing value of some symptoms, e.g. olfactory
aura, is undoubtedly greater than for others, e.g. cephalic
aura (Penfield and Jasper, 1954). To account for this, ictal
symptoms would have to be given different weights, but
there are no data with which to calculate appropriate
weightings. For this reason the cluster analysis could be seen
as generating general groupings; the aggregation of cases
into ever larger clusters was stopped at 25 groups, prior to
achieving the minimal reasonable number of groups, and the
final 14 groupings were created by the combination of
statistically defined groupings. Because this final definition
required some recombination of those derived from the cluster
analysis, independent validation was sought. Validation of
cluster analysis was at two levels; internal validation of the
statistical technique and external validation of the results.
Internal validation was undertaken by comparing results of
a different cluster technique; ‘quick-cluster’ on SPSS-PC+,
specifying the number of clusters as 25 (Hair et al., 1987).
By this method a validation of 65.5% was achieved. The
number of cases that would re-cluster to the same groups by
chance is a function of the number of groups and their size;
for 25 groups a figure of over 60% is highly significant and
previous studies, usually using smaller numbers of groups
have quoted acceptable validation figures of 40–70% (Hair
et al., 1987). External validation was provided by the separate
analysis of seizure manifestations due to pure temporal and
pure frontal lesions undertaken by an independent clinical
method (see below). The cluster technique also defined
seizure types generally recognized as clinically important,
supporting its clinical validity. Subsequent modifications to
the cluster analysis to produce 14 final groupings were
predictable in terms of the variables included in the analysis.
For example, olfactory and gustatory seizures were combined
into one group and generalized tonic, tonic–clonic, and clonic
seizures were recombined into subgroups of one overall
grouping. Jacksonian clonic seizures and isolated jerks were
separated into different groups; the cluster analysis had not
identified them separately because of the absence of a
seizure duration variable. It is important to note that these
modifications were made purely on the basis of clinical
seizure pattern without reference to results of investigations.

Interictal EEG analysis
At least one interictal EEG was available for 226 (89%) of
patients (median two EEGs per patient). The number and
location of up to the first 100 spikes were assessed on all
available routine, interictal EEGs for each patient. This gave
a good sample size and for 93% of patients included all
available interictal spikes. Spikes were selected as the most
easily defined and localized and unequivocally epileptic EEG
abnormality. Structural lesions were common in this series
and slow wave abnormalities might just have reflected these
lesions without having the same significance in relation to
epilepsy. Consequently, other EEG manifestations were not
assessed and spikes occurring during overbreathing were also
excluded since this is a generalized activation. No case had
spikes occurring only during hyperventilation. EEGs during
sleep were available in a minority of cases and there was no
systematic distinction drawn between spikes when awake
and when asleep. Spikes were classified as in Appendix 1.
Ictal EEG analysis

Ictal scalp EEGs were available in 77 patients; in 74 obtained during VET recording, enabling correlation with clinical manifestations and in three obtained by chance during routine EEG recording, without accurate timing of clinical accompaniments. The distribution of EEG onsets was described as in Appendix 1 and the temporal relationship to clinical onset and the pattern of discharge were also recorded, using definitions described previously (Quesney and Gloor, 1985).

CT scan analysis

Abnormal CT scans were documented in 51 patients. A stereotactic technique was used to plot lesions onto a standard atlas (Talairach et al., 1967) from bony landmarks, modified from previous methods (Cail and Morris, 1979; Greitz and Bergstrom, 1981). Separate multiplication factors from the maximum measurements in each dimension were calculated to plot the candidate CT scan onto the atlas template, thus allowing adjustment for individual variation in brain shape. CT scan slices passing through the superior orbit and through the superior petrous temporal bone were identified and from the interslice distance between these two bony landmarks, the slice orientation was calculated and the slices mapped onto the template. Lesions were then mapped onto each slice on the template. Correlation of a similar template technique, utilizing Talairach’s atlas, with the most recent MRI delineation of anatomy has confirmed the accuracy of the technique to within 5–10 mm.

MRI

Standard images

Standard images were performed using coronal and axial slices with a sagittal scout image on 0.5 Tesla or 1.5 Tesla machines. CNS landmarks were identified and the relationships of the lesion to these were analysed utilizing the stereotactic atlas as a guide. In most cases, the position of the lesion could be read directly from anatomical structures on the scan.

Volumetric studies

The methods of volumetric MRI and stereological measurement of hippocampal volume have been described previously (Cook et al., 1992). Scans were performed on a GE 1.5 Tesla Signa unit (GE Medical Systems, Milwaukee, Wis., USA) and lesions plotted as above. Anatomical structures were extremely well visualized on these scans and it was easy to correlate the location of foreign tissue lesions with the atlas, directly from the scan. In some cases, no foreign tissue lesion was seen but there were abnormalities of the cortical ribbon, representing dysplasia.

Anatomical localization

In all cases, the maximum extent of the lesion was mapped, including perilesional oedema. Of 126 lesions, 18 (15%) were tumours but these did not change significantly on serial imaging. Lesion locations were related to functional cerebral regions, using standard definitions (Williams et al., 1989) and were coded according to the extent of involvement of each region: Grade 3, >50% involvement of the region or a small lesion entirely within the region (heavily involved); Grade 2, 11–50% involved (partial involvement); Grade 1, 1–10% involved (possible involvement); Grade 0, uninvolved. Regions considered were: orbitofrontal, frontopolar, prefrontal, lateral premotor, supplementary motor area (SMA), anterior cingulate, primary motor, parietal, hippocampal and extrahippocampal temporal.

Validation of lesion analysis

A random sample of 20 scans (12 MR and eight CT) was selected and lesion location assessed by inspection by a consultant neuroradiologist, who was blinded to the previous assessment. There was 95% agreement in regions graded 3, and 80% agreement in regions graded 1–2, with the template technique deliberately tending to be more inclusive, in order to maximize the significance of any associations identified.

Clinical study of pure frontal versus pure temporal lesions

In 91 patients there was a demonstrable focal epileptogenic structural lesion on CT or MR scan restricted to frontal or temporal lobes. In 70 cases this lesion was the patient selection criterion for the study and in 21 cases it emerged during the course of further investigation. The 91 lesions were associated with 119 seizure types. For this analysis, ictal manifestations were considered ‘early’ if the first manifestation of the seizure or else preceded only by a non-specific phenomenon, recognized to have little localizing significance, e.g. a vague light-headedness or cephalic sensation. In 11 cases in the pure frontal group and 19 cases of the pure temporal group, VET was available. Of pure temporal abnormalities, 25 were pure hippocampal atrophy, 14 extrahippocampal foreign tissue lesions and three involved both hippocampus and other temporal structures. Foreign tissue abnormalities accounted for 35 pure frontal lesions and a cortical dysplastic appearance on MRI for 14 cases.

Statistical analysis

A $\chi^2$ analysis with Yate’s correction was used to assess whether involvement of particular regions on neuroimaging was significantly associated with the groups of clinically defined seizure types from the cluster analysis and to determine the association of clinical manifestations with pure frontal and pure temporal lesions.
Table 2 Summary of clinical seizure groupings

<table>
<thead>
<tr>
<th>Group (no. of cases)</th>
<th>Distinctive features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: fear behaviour and olfactory/gustatory (31)</td>
<td>Frequent prodrome; frequent vegetative changes, olfactory/gustatory (31) especially pupillary; verbal expressions of fear; rare secondary generalization</td>
</tr>
<tr>
<td>2: absence (57)</td>
<td>Predominantly waking; frequent behavioural automatisms</td>
</tr>
<tr>
<td>3: experiential (33)</td>
<td>None</td>
</tr>
<tr>
<td>4: visual (16)</td>
<td>None</td>
</tr>
<tr>
<td>5: version/posturing (74)</td>
<td>A proportion of this group with frequent, brief seizures, no aura, rapid recovery and retained awareness, but these timing characteristics were not true of the whole group</td>
</tr>
<tr>
<td>6: somatosensory (26)</td>
<td>Often evolve to simple motor activity but rare behavioural automatisms</td>
</tr>
<tr>
<td>7: Jacksonian clonic (12)</td>
<td>Rare vegetative symptoms or automatisms; Todd's paresis common</td>
</tr>
<tr>
<td>8: motor agitation (30)</td>
<td>High seizure frequency; mainly nocturnal; bizarre vocalization; frequent vegetative symptoms (often facial flushing rather than pallor)</td>
</tr>
<tr>
<td>9: generalized motor (47)</td>
<td>Low frequency; incontinence common; other vegetative symptoms rare</td>
</tr>
<tr>
<td>10: auditory (2)</td>
<td>None</td>
</tr>
<tr>
<td>11: hypotonic (6)</td>
<td>Brief duration; low seizure frequency</td>
</tr>
<tr>
<td>12: focal paresis (2)</td>
<td>None</td>
</tr>
<tr>
<td>13: complex partial status epilepticus (6)</td>
<td>Generally low frequency, usually associated with other seizure types</td>
</tr>
<tr>
<td>14: isolated jerks (8)</td>
<td>Rapid recovery by definition; usually associated with other seizure types</td>
</tr>
</tbody>
</table>

Table 3 Summary of investigation results for each seizure group

<table>
<thead>
<tr>
<th>Group (no. of cases)</th>
<th>Lesion location</th>
<th>Interictal EEG spikes</th>
<th>Ictal EEG onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: olfactory/gustatory/fear (31)</td>
<td>Temporal 10, frontal 2</td>
<td>Temporal 11, frontal 1</td>
<td>Temporal 8</td>
</tr>
<tr>
<td>2: absence (57)</td>
<td>Temporal 16, frontal 6</td>
<td>Temporal 11, frontal 10, frontotemporal 4</td>
<td>Temporal 2, frontal 3</td>
</tr>
<tr>
<td>3: experiential (33)</td>
<td>Temporal 14, mesial frontoparietal 4</td>
<td>Temporal 7, frontotemporal 5</td>
<td>Temporal 4, frontal 1</td>
</tr>
<tr>
<td>4: visual (16)</td>
<td>Temporal 6, frontal 2</td>
<td>Temporal 2, frontal 1, mixed 4</td>
<td>Frontotemporal 2, frontal 1</td>
</tr>
<tr>
<td>5: version/posturing (74)</td>
<td>Lateral premotor 18, frontoparietal 4</td>
<td>Frontal 19, central 4, mixed</td>
<td>Frontocentral 7</td>
</tr>
<tr>
<td>6: somatosensory (26)</td>
<td>Pericentral 7, lateral frontal 4</td>
<td>Temporal 3, frontal 2, central 4</td>
<td>Central 1</td>
</tr>
<tr>
<td>7: Jacksonian clonic (12)</td>
<td>Frontal 4, parietal 1</td>
<td>Frontocentral 3</td>
<td>Frontocentral 1</td>
</tr>
<tr>
<td>8: motor agitation (30)</td>
<td>Orbifrontal 7, frontopolar 7</td>
<td>Frontal 4, central 2</td>
<td>Frontal 1</td>
</tr>
<tr>
<td>9: generalized motor (47)</td>
<td>Temporal 5, frontal 9</td>
<td>Temporal 3, frontal 11</td>
<td>Frontal 7, frontotemporal 2</td>
</tr>
<tr>
<td>10: auditory (2)</td>
<td>Temporal 1</td>
<td>None</td>
<td>Temporal 1</td>
</tr>
<tr>
<td>11: hypotonic (6)</td>
<td>Temporal 1, frontal 1</td>
<td>Widespread 4</td>
<td>Not available</td>
</tr>
<tr>
<td>12: focal paresis (2)</td>
<td>Lateral frontal 2</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>13: complex partial status epilepticus (6)</td>
<td>Temporal 1, frontal 1</td>
<td>Frontal 2, frontotemporal 1</td>
<td>Widespread 3</td>
</tr>
<tr>
<td>14: isolated jerks (8)</td>
<td>Frontal 1</td>
<td>Fronto central 2</td>
<td>Generalized 1</td>
</tr>
</tbody>
</table>

Results

Table 2 shows the 14 clinical seizure types resulting from the cluster analysis, their identifying clinical characteristic and any additional distinctive features of the group. The results of investigations for each group are summarized in Table 3. Of these groups, nine were sufficiently large to allow statistical analysis and are discussed below; four were associated predominantly with temporal lobe abnormalities, with 47 out of 58 temporal lesional cases falling into these groups and four with frontal or perirolandic abnormalities, and with 47 out of 82 lesional cases in these groups (P << 0.001). Flow charts 1–9 in Appendix 3 show the evolution of seizure manifestations for all cases in each of these groups.
Predominantly temporal lobe associated seizure types

Group 1: olfactory/gustatory and fear behaviour
This group contained 31 seizures in 30 patients. Fifteen seizures were characterized by profound fear and epigastric sensation (subgroup 1a). Most had no other specific sensations but, in four, the feeling was associated with sensations in various modalities. In all except one case, fear led to 'fear behaviour', including verbal expressions of fear, appropriate facial expressions and clutching observers for emotional support. In half the seizures this was followed by rapid recovery, but a variety of motor manifestations ensued in the remainder.

Seizures characterized by olfactory and gustatory auras formed subgroup 1b. These auras were also frequently associated with other sensory modalities and with epigastric sensations. The commonest evolution of these seizures was to absence (44%), then usually to motor activity.

A non-specific prodrome occurred in 42%, somewhat more commonly than in other groups. Characteristics of seizure timing, including range of seizure frequency, seizure duration, postictal recovery time, diurnal variation and maximum seizure frequency were similar to other groups, but two cases in subgroup 1a had experienced seizure frequencies in excess of 100/day. Colour change, usually pallor was noted in 61% and pupillary dilatation (47%) was especially common in the fear subgroup (P < 0.001). Secondary generalization was similar in the two subgroups and was significantly less likely than in other groups (P < 0.001), 63% never having experienced generalized convulsive seizures.

Ten of 12 lesional cases were restricted to the temporal lobe; in the fear subgroup all four were hippocampal and in the olfactory subgroup, two were hippocampal and four extrahippocampal. The two frontal lesions were medial prefrontal/SMA and lateral prefrontal/lateral premotor. Interictal EEGs were available in all cases and in 16 (53%) interictal spikes were identified. In all 11 cases, where there were focal spikes, they predominated at the temporal electrodes. Regional and bilateral spikes were mostly frontotemporal in distribution. Widespread or generalized spikes occurred in only two cases. Ictal EEG abnormalities were documented in eight out of 10 cases undergoing recording and were focal or regional in five; all at temporal or frontotemporal electrodes. The EEG pattern was of rhythmical slow activity, varying from 3 to 7 Hz, in three cases and focal attenuation in the temporal region in two cases.

Group 2: absence without specific warning
Absences without warning or with non-specific physical or abdominal auras accounted for 57 (16%) of seizure types in 54 patients. In 11 seizures, the features were clinically indistinguishable from classical petit mal: no warning, no focal features, duration <30 s and immediate recovery. In the others, clinical features varied after the absence phase.

Characteristics of seizure timing were similar to other groups but habitual secondary generalization was uncommon, occurring in only three cases (5%).

Sixteen lesions involved the temporal lobes: 10 hippocampal and six extrahippocampal. Of six cases with absences and pure frontal lesions, five involved the mesial frontal cortex and the other lesion was restricted to the orbitofrontal cortex. Where there were focal interictal EEG spikes, they were predominantly temporal in 11 cases, frontopolar in four cases and frontocentral in six cases. Simultaneous bilateral spikes were more commonly bifrontal (eight cases) than bitemporal (one case). Symmetrical generalized spikes occurred in only one case, but spikes were multifocal in 13 cases. Five seizures (9%) were recorded. Ictal EEG abnormalities were identified in all cases but varied in location, including bifrontal, mesial frontal and focal temporal onsets.

Group 3: experiential
Thirty-three seizure types (9.4%) in 30 patients were characterized by initial experiential phenomena. The commonest seizure evolution was to absence, seen in 15 cases (45%) of which eight then recovered rapidly without further manifestations. Evolution directly to tonic posturing occurred in 12 cases (36%), of whom 10 developed other motor manifestations. Vegetative symptoms were common, especially colour change, noted in 15 cases (45%). Seizures tended to be less frequent than in other groups, with less inclination towards seizure clustering.

Temporal lobe lesions predominated, occurring in 13 cases: seven hippocampal, four extrahippocampal and two involving both subdivisions. Of three pure frontal lesions associated with experiential phenomena, all had medial frontal involvement including the anterior cingulate, which in one case, extended to frontopolar and orbitofrontal regions. Four further cases had frontoparietal involvement; two including the cingulate region and two the lateral suprasylvian region. There was a suggestion that the quality of sensations differed between extratemporal and temporal cases: déjà vu commoner with temporal and out of body experience or the feeling of a presence with extratemporal lesions, but numbers were small. Interictal EEG spikes were infrequent in most patients, and were generally temporal or frontotemporal. A localized ictal scalp EEG onset was identified in five out of eight seizures recorded; in four restricted to one temporal lobe and in the other bilateral frontotemporal in distribution.

Group 4: visual
Sixteen seizure types in 15 patients were characterized by visual symptoms: unformed hallucination in four, formed hallucination in six, micropsia/macropsia in three and other visual abnormalities in three. The commonest pattern of seizure evolution was to absence, associated with oral automatisms and progressing to posturing/version, irre-
perioral in three, mesial prefrontal or SMA in four, significantly associated with this seizure type. In those cases (29 lesional cases \( P < 0.001 \)), the only region that was.

Only results of investigations in this subgroup of very brief seizures differed from the rest of the group.

A subgroup appeared to have very frequent, brief seizures induced by startle stimuli, 10 fell into this group uncommon (9%). Of 19 patients in the whole study with temporal lobes. Analysis of the second symptom in these groups showed that in those cases associated with frontal lobe lesions, seizure progression was to version/posturing, without intervening absence in 10 out of 11 cases. By contrast, 29 temporal lobe cases that progressed to version and posturing, 24 had an intervening absence \( P < 0.001 \).

**Predominantly extratemporal associated seizure types**

**Group 5: version/posturing**

There were 74 seizures (21%) in 69 patients, in which version or posturing was the first localizing manifestation of the seizure. Progression to other motor manifestations occurred in 78%, simple automatisms being the commonest sequel to posturing (40%). By contrast, behavioural automatisms were uncommon (9%). Of 19 patients in the whole study with seizures induced by startle stimuli, 10 fell into this group \( P < 0.005 \). A subgroup appeared to have very frequent, brief seizures with rapid recovery, giving a bimodal distribution of these timing characteristics within the group but the overall spectrum was similar to other groups. There was no suggestion that results of investigations in this subgroup of very brief seizures differed from the rest of the group.

The lateral premotor cortex was involved in 18 out of 29 lesional cases \( P < 0.001 \), the only region that was significantly associated with this seizure type. In those cases where the premotor cortex was not involved, the lesion was perioral in three, mesial prefrontal or SMA in four, frontopolar or orbitofrontal in two and widespread in the rostral frontal cortex in two. Only one case with a pure temporal lesion (mesial temporal sclerosis) had this seizure type. The interictal EEG in this case showed widespread spikes, ipsilateral to the sclerosis, ranging from P3 to Fp1, including some in the region Fp1–F3–Fz.

Focal frontal spikes was the commonest pattern (19 cases), with central spikes in four cases. Bifrontal and transcenral spikes were also common, but in only one case there was a single focal temporal spike. Widespread or generalized spikes were also noted in 14 cases (37%). Of 21 cases with ictal recordings, one-third were masked by artefact throughout each seizure and in two-thirds an early abnormality was identified. This was unlocalized in five cases and localized in nine, all to the frontal or central region. In three seizures, however, the discharge appeared symmetric about the midline and could not be lateralized. The commonest ictal EEG seizure manifestations were spikes or fast activity, rather than slow wave activity usually seen in other groups.

**Group 6: focal somatosensory**

A focal somatosensory onset was reported in 26 seizure types (7.4%) in 26 patients, in 12 of whom there was a typical Jacksonian progression. Of the 20 in which the seizure evolved further, the commonest progression was to tonic posturing and head version (13 cases). Jacksonian clonic motor activity was seen in five cases, and occurred in both Jacksonian sensory and non-Jacksonian sensory subgroups. A Todd’s paresis was observed in five out of nine cases that had experienced focal clonic activity at any point in the seizure, irrespective of whether this was obviously Jacksonian and in one case with no focal clonic activity. Automatisms were uncommon and mostly simple in type; exploratory behaviour occurred in only one case. Five cases showed clear sensitivity to startle stimuli, all progressing to tonic activity. Characteristics of seizure timing and diurnal variation were unremarkable; five patients commonly woke from sleep to experience their aura. In nine cases, recovery from the seizure took longer than 5 min and six of these were explained by Todd’s paresis; other aspects of recovery were generally rapid. Vegetative symptoms (27%) and vocalizations (8%) were uncommon.

Of 15 lesional cases in this group, the perirolandic cortex was involved in 14 \( P < 0.001 \), irrespective of whether the sensation had a typical Jacksonian progression, and the strongest association was with parietal involvement. The single case which did not include either of these regions, was a large lesion spreading across anterior frontal and temporal regions. There was no suggestion that the size of the lesion correlated with the tendency of the seizure to progress and in three cases pure sensory seizures and pure motor seizures were seen at different times from the same pericentral lesion.

One case showed consistent interictal EEG spikes at one medial frontal electrode, but in others the location of spikes...
was very variable, including frontal, temporal and central regions. In only one of four cases, in which an ictal recording was obtained, was there an identifiable seizure discharge; overlying the pericentral region, contralateral to the clinically affected limb.

**Group 7: Jacksonian motor**

Fourteen seizures (4%) in 14 patients were characterized by focal clonic activity with Jacksonian progression. The majority progressed to hemiclonic activity, usually accompanied by ipsilateral head turning, without secondary generalization, and often leading to a Todd’s paresis. Characteristics of seizure timing were similar to other groups. Postictal duration was >1 min in eight cases, in five due to Todd’s paresis. In five cases respiratory abnormalities were noted; clonic jerking interfering with the pattern of respiratory movements.

In seven out of nine Jacksonian motor seizures associated with a structural lesion, there was involvement of the primary motor cortex in the lesion ($P < 0.001$) and, in the other two cases, the premotor and parietal cortices were involved. Only the prerolandic cortex was significantly associated with this seizure type. In only three cases were interictal EEG spikes recorded, and with this small number it was impossible to discern a distinct pattern. In one case, with a seizure captured fortuitously on routine EEG recording, there was an evolving discharge over the pericentral region, contralateral to the clinically affected side. In the other recorded case, there was continuous pericentral spiking and it was difficult to discern any change in scalp EEG pattern in association with the clinical seizure onset.

**Group 8: motor agitation**

Thirty seizures (8.5%) in 29 patients were dominated by early motor agitation. The seizure typically started with simple repetitive activities, such as tapping, which became more frenetic until the patient appeared in a state of general motor agitation, sometimes developing extremely rapidly. The pattern of this activity was often bizarre; violent striking, thrashing or bicycling movements or throwing themselves against the bed. Half the cases recovered rapidly and the others went on to a variety of other motor manifestations. Exclusively nocturnal occurrence was commonest in this group, occurring in 40% ($P < 0.001$). Although average seizure frequency differed little from the study group as a whole, clustering of seizures was common (60%) and patients tended to have suffered higher maximum seizure frequencies. Postictal recovery was often rapid, although sometimes this was difficult to judge, as the patient went straight back to sleep. Prominent vocalizations were common and often bizarre: piercing cries in six, laughing and crying in two, singing in five and ‘Donald-Duck speech’ in one case. Vegetative symptoms were common, especially colour change, in 14 cases (47%), which unlike other groups, was facial flushing more often than pallor.

Of 13 lesional patients in this group, seven involved the orbitofrontal cortex. Half of 14 patients in the study with structural lesions with orbitofrontal involvement had a seizure type falling into this category, making this region strongly associated with this seizure type ($P << 0.001$). In seven cases with this seizure type, the frontopolar cortex was affected, in six of whom, the orbitofrontal cortex was also involved. The six cases with motor agitation involving neither of these regions showed no consistent localization: hippocampal, extrahippocampal temporal, SMA, anterior cingulate, perisylvian and lateral prefrontal/premotor in one case each. Of six cases with >10 focal interictal EEG spikes, these were at frontal electrodes in four and at temporal and central sites in the other two. In one case focal activity predominated at the supraorbital electrode, but this electrode was used rarely in other patients. Spikes with a diffuse distribution were seen in only one case. Ictal electrographic discharges were seen frequently in this group and were localized in 10 cases; in seven they were frontal or bifrontal, with frequent involvement of frontopolar electrodes. Of the other three, discharges were frontotemporal in two and temporal in one case.

**Seizures without specific localization**

**Group 9: generalized motor activity**

Forty-seven seizures in 42 patients comprised bilateral motor activity without prior focal symptoms: twenty were generalized tonic seizures (subgroup a), 21 tonic-clonic seizures (subgroup b) and six bilateral clonic seizures with preservation of awareness (subgroup c). The only progression that was seen after the initial phase was to postictal automatisms, most frequently after generalized tonic seizures. The median seizure frequency was $<1$/month, less than for any other group ($P < 0.001$), and seizures only ever occurred very frequently ($>5$/day) in the tonic seizure category. Incontinence was commonest in this group, occurring in 36% ($P < 0.001$) but other vegetative symptoms were rarely reported. Vocalizations usually comprised a shout at seizure onset, although one patient appeared to giggle briefly at the onset of hypertension. In subgroup c, vocalizations mostly comprised speech with varying degrees of clarity, from individual words to coherent sentences, spoken during the period of bilateral clonic activity.

Lesions in this group were frontal in nine, hippocampal in two and extrahippocampal temporal in three. All three lesions associated with seizures with bilateral clonic activity with preserved awareness were frontal and two were parasagittal meningiomas, but the distribution of other frontal lesions showed no clear pattern with all regions being involved. Ictal spikes were observed only in relation to subgroups a and b and there were no clear differences between them. Spikes tended to be more multifocal or diffuse than in other
groups. Bilateral, simultaneous spikes (50%) and generalized spikes (30%) were also common, generally having a frontal preponderance. No ictal recordings were available in this group.

**Combinations of seizure types**

One hundred and sixty-seven individuals suffered one habitual seizure type, 70 two types and 15 three types. The only association of different seizure types in the same individual, reaching statistical significance, in 13 cases, was between groups 2 and 9; absences without focal onset and generalized motor seizures, mostly of tonic-clonic type ($P < 0.001$). Patients with these generalized seizure patterns tended to have more seizure types but this was an artefact of selection methods, as clinical selection criteria were for seizures with a focal pattern of onset and generalized tonic or tonic-clonic seizures were patients’ second or third seizure type in 26 cases (63%). Interictal EEG showed spikes in nine out of 12 cases in which it was available: four bifrontal, two unilateral frontal, one bitemporal and two centrotemporal. Widespread or generalized spikes were seen in only one case. Imaging was abnormal in four; two temporal (associated with frontal spikes in one) and two frontoparietal lesions.

**Clinical manifestations associated with pure frontal and pure temporal lesions**

Table 4 shows the seizure manifestations in the two groups of patients. Most manifestations occurred with similar frequency in frontal and temporal groups and, although some rarer symptoms appeared to have possible associations, e.g. olfactory and gustatory hallucinations, with temporal lesions, numbers were too small to analyse statistically.

Oral automatisms were significantly associated with temporal lobe lesions ($P < 0.001$), irrespective of other associated seizure manifestations. Overall, experiential symptoms were also commoner with TLE than with FLE ($P = 0.001$).

Although clonic movements and head turning per se were not strongly associated with one or other lobe, if they occurred early in the seizure there was a significant association with frontal lobe lesions ($P < 0.001$). A similar, but weaker, association was seen for early tonic movements ($P < 0.01$) but not for tonic movements as a whole.

No measures of seizure frequency, duration or postictal duration showed any significant difference between frontal and temporal lobe seizures, although, if seizures were very frequent ($>50$/day) or very short ($<10$ s) with rapid recovery, they were more likely to be associated with frontal than temporal lesions (Figs 1–4). Sensitivity to startle stimuli was seen in four cases with pure frontal lesions and in no pure temporal cases. There was a trend for complex behaviours to be commoner with temporal lesions but no difference between frontal and temporal lesions for simple automatisms.

Analysing individual behaviours yielded numbers too small to detect significant results.

**Inter-relationships of investigations**

Of 121 patients with localized imaging abnormalities, 102 had undergone interictal EEG recording and in 53 spikes were detected. There was a close concordance between these investigations in 10 cases. The EEG was discordant but ipsilateral in six and contralateral in five. In 32 cases, the spikes appeared more diffuse than the imaging abnormality, but not frankly discordant. Of 31 cases with an ictal EEG recording and no interictal spikes, a localizing ictal abnormality was observed in 11 (35%). Of 46 cases where both ictal and interictal abnormalities were present, there was no pattern as to which showed a more clearly focal abnormality. Frank discordance was seen in only two out of 35 patients with both ictal EEG abnormality and lesions on neuroimaging and, as with interictal EEG, the commonest pattern was for the EEG abnormality to be more diffuse than the lesion. There was no suggestion that concordance between investigations was greater for temporal or frontal lesions.

**Discussion**

**Study methods**

A central issue is how to define the localization of epileptic seizures and what emphasis to place on the most widely used investigations of EEG and neuroimaging. There are fundamental differences in the nature of the information available from MRI, compared with EEG. Extracranial EEG is a dynamic test but suffers from low anatomical resolution, whereas intracranial EEG samples only limited regions. MRI samples the whole brain with high resolution but provides a static image and it is impossible to know where the epilepsy is generated; from which part of an identified lesion, or indeed if the lesion induces seizure activity at a remote site. Where there has been discordance between EEG and MRI in previous studies, the latter has consistently been shown to be more predictive and removing the aetiology of the epilepsy is most likely to render the patient seizure-free, irrespective of where the electrical activity appears to occur (Engel et al., 1981; Sammaritano et al., 1987; Wyler et al., 1989; Palmini et al., 1991; Cascino et al., 1992; Salanova et al., 1993). In the current study, in which patients were selected without reference to concordance of investigations, frank discordance between EEG and neuroimaging was uncommon; rather the EEG abnormalities tended to be more diffuse than the extent of the lesion. For these reasons most emphasis has been placed on the aetiological definition of localization, as defined by neuroimaging.

The independence of patient selection criteria avoided the bias of concordance of investigations, introduced in studies of patients taken from a programme of presurgical assessment. Recognizing that some patients may have clinically localized
Table 4: Comparison of seizure manifestations between cases with pure frontal and pure temporal lesions (61 frontal and 58 temporal seizures)

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Frontal</th>
<th>Temporal</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clustering</td>
<td>23</td>
<td>18</td>
<td>None</td>
</tr>
<tr>
<td>Diurnal variation</td>
<td>See Fig. 1</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Average frequency</td>
<td>See Fig. 2</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Maximum frequency</td>
<td>See Fig. 3</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Seizure duration</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Postictal duration</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Secondary generalization</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Prodrome</td>
<td>16</td>
<td>12</td>
<td>Temporal (P = 0.001)</td>
</tr>
<tr>
<td>Frequent purely subjective seizures</td>
<td>14</td>
<td>29</td>
<td>Temporal (P = 0.001)</td>
</tr>
<tr>
<td>Abdominal symptom</td>
<td>11</td>
<td>20</td>
<td>None</td>
</tr>
<tr>
<td>Rising epigastric</td>
<td>3</td>
<td>6</td>
<td>None</td>
</tr>
<tr>
<td>Cephalic or general body sensation</td>
<td>17</td>
<td>12</td>
<td>None</td>
</tr>
<tr>
<td>Olfactory or gustatory sensation*</td>
<td>1</td>
<td>6</td>
<td>None</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>2</td>
<td>6</td>
<td>None</td>
</tr>
<tr>
<td>Somatosensory symptoms</td>
<td>4</td>
<td>10</td>
<td>None</td>
</tr>
<tr>
<td>Vegetative symptoms</td>
<td>31</td>
<td>31</td>
<td>None</td>
</tr>
<tr>
<td>Incontinence</td>
<td>10</td>
<td>4</td>
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<tr>
<td>Pallor</td>
<td>13</td>
<td>12</td>
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</tr>
<tr>
<td>Facial flushing</td>
<td>9</td>
<td>10</td>
<td>None</td>
</tr>
<tr>
<td>Experiential symptoms</td>
<td>9</td>
<td>22</td>
<td>Temporal (P = 0.001)</td>
</tr>
<tr>
<td>Fear</td>
<td>9</td>
<td>7</td>
<td>None</td>
</tr>
<tr>
<td>Generalized hypertonia</td>
<td>19</td>
<td>12</td>
<td>None</td>
</tr>
<tr>
<td>Clonic movements</td>
<td>35</td>
<td>17</td>
<td>FrONTAL ? (P &lt; 0.005)</td>
</tr>
<tr>
<td>Early clonic movements</td>
<td>21</td>
<td>4</td>
<td>FrONTAL (P &lt; 0.001)</td>
</tr>
<tr>
<td>Tonic movements</td>
<td>23</td>
<td>16</td>
<td>None</td>
</tr>
<tr>
<td>Early tonic movements</td>
<td>20</td>
<td>7</td>
<td>FrONTAL ? (P &lt; 0.01)</td>
</tr>
<tr>
<td>Head turning</td>
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<td>19</td>
<td>None</td>
</tr>
<tr>
<td>Early head turning</td>
<td>26</td>
<td>6</td>
<td>Frontal (P &lt; 0.001)</td>
</tr>
<tr>
<td>Oral automatisms</td>
<td>9</td>
<td>23</td>
<td>Temporal (P &lt; 0.001)</td>
</tr>
<tr>
<td>Simple automatisms</td>
<td>28</td>
<td>31</td>
<td>None</td>
</tr>
<tr>
<td>Behavioural automatisms</td>
<td>10</td>
<td>18</td>
<td>None</td>
</tr>
<tr>
<td>Motor agitation*</td>
<td>9</td>
<td>2</td>
<td>None</td>
</tr>
<tr>
<td>Non-verbal vocalization</td>
<td>12</td>
<td>6</td>
<td>None</td>
</tr>
<tr>
<td>Verbal vocalization</td>
<td>10</td>
<td>10</td>
<td>None</td>
</tr>
</tbody>
</table>

*Number of cases too small to analyse.

Fig. 1: Comparison of diurnal variation of seizures associated with lesions restricted to the frontal and temporal lobes.

seizure patterns without focal investigative abnormality, these too were included and, in some cases, focal EEG or imaging abnormality emerged later in the study, representing a truly prospective group. Bias was also minimized in the definition of seizure patterns: a standard protocol was used for recording clinical features, all seizure histories taken prospectively by

one observer and standardized methods were used to delineate seizure groupings. Only then was the localizing evidence for each pattern analysed to establish which seizures share similar abnormalities on investigation, pointing to similar cortical
rendered seizure-free by the same resective surgery are rarely epilepsy by this method? In addition, those patients with apparently similar electroclinical characteristics, yet not is the seizure pattern in defining the region of onset of patterns? If their seizure patterns are the same, of what value differ from those who are and do they have different seizure surgical resection, several questions need to be answered. In generalizing from patients who have undergone remission. In generalizing from patients who have undergone assessed by the extent to which they predict post-operative what way do those patients who are not surgical candidates which represent highly selected and uncontrolled case series. These methods differ significantly from those of most previous investigators who attempt to resolve the problems of case selection by describing a cohort of patients where seizures remitted after similar cortical resections (Rasmussen, 1963, 1983; Delgado-Escueta and Walsh, 1985; Quesney and Olivier, 1988; Engel et al., 1990; Salanova et al., 1995), which represent highly selected and uncontrolled case series. In these series pre-operative investigations are generally assessed by the extent to which they predict post-operative remission. In generalizing from patients who have undergone surgical resection, several questions need to be answered. In what way do those patients who are not surgical candidates differ from those who are and do they have different seizure patterns? If their seizure patterns are the same, of what value is the seizure pattern in defining the region of onset of epilepsy by this method? In addition, those patients with apparently similar electroclinical characteristics, yet not rendered seizure-free by the same resective surgery are rarely reported in detail. Yet these form an important group of false positives that must be included in the assessment of any predictive test of post-surgical outcome and any more general consideration of localization of seizure patterns. Moreover, the outcome of epilepsy surgery is a complex end-point with various outcomes, since patients may have a partial or late response or a late relapse (Engel, 1987), the pathophysiological bases of which are uncertain and which have implications for localization by this method.

Many patients have more than one seizure type and another important feature of this study is the differential consideration of patients and seizures. In contrast to ictal EEG, imaging and interictal EEG abnormalities are the same for all the patients’ habitual seizure types. There is no a priori justification in considering one habitual seizure type more representative of the underlying cause than another on grounds of, for example seizure frequency. Any localizational scheme must explain all the seizure types arising from a given lesion in order to be of practical value and have pathophysiological significance. For this reason all patients’ habitual seizure patterns were analysed against imaging and interictal EEG, rather than selecting one type, which would have ignored important data, and each seizure type was given equal weighting as a single data point. This contrasts with studies of seizures recorded on VET, which sometimes give every seizure recorded equal weighting, resulting in a bias in favour of patients with high seizure frequency and many recorded attacks (Delgado-Escueta et al., 1982, 1987; Swartz et al., 1991). The decision whether a patient's seizures represent variations on a theme or separate seizure types is difficult. In this study, differences in the initial manifestations were taken to represent different seizure types and differences in later manifestations as variations, perhaps due to differences in seizure spread. The fullest, habitual expression of each seizure was used as likely to give the most information regarding seizure spread. This technique resulted in some individuals having more than one seizure type in a particular clinical group, but the number for whom this occurred was small (4.5%) and was similar in all groups and, therefore, is unlikely to have influenced the results. Alterations in drug treatment made on admission for telemetry are recognized to influence recorded seizure patterns (Theodore, 1993). The high concordance between telemetry and historical accounts in those cases in which they were compared, suggests this is not a major source of bias.

Cluster analysis (Hair et al., 1987) is a non-parametric multivariate statistical technique, that may be applied to non-metric data and occasionally has been used by psychologists to define symptom complexes (Fish and Rourke, 1973; Mezzich, 1978). It has also been applied to the identification of relationships between clinical seizure manifestations (Kotagal, 1993) and to the definition of preferential routes of seizure spread on intracranial EEG (Wieser, 1981). Critical issues are the selection of the clustering technique; the choice of variables to be entered into the analysis and the method of calculation of inter-variable distance. The choice of clustering
paradigm is empirical (Hair et al., 1987) and there are, as yet, no reliable theoretical guidelines. Variables entered into the analysis were only those relating to the clinical manifestations of the seizure itself. It was felt that these were likely to be fundamental properties of the seizure-generating region and its connectivity, whereas other considerations of, for example, seizure frequency, duration and tendency to secondary generalization, might rather be functions of the severity of the underlying pathology and could have corrupted the statistical analysis. This is supported by the relatively benign prognosis of partial seizures in a general population, irrespective of localization (Manford et al., 1992). These variables were considered subsequently in analysis of the results. The number of potential seizure manifestations is so large that, were each to be entered as an independent variable into the statistical analysis, no groupings would ever be found. A further problem with statistical analysis is the weighting of data to allow for related variables. For example, swallowing and lip smacking automatisms are more closely related to each other than they are to clonic jerks and it would be inappropriate for the analysis to treat all three as equidistant. In order to minimize these problems, categories of variables have been analysed, using groupings of related symptoms. The aim of these modifications was to use existing knowledge in order to enhance data entry and make the cluster analysis as clinically meaningful as possible. It is important to appreciate that whilst these modifications may be viewed as seeding the data with preconceived relationships, they were kept to a minimum, are consistent with current views, and were applied equally to all cases in the analysis. The use of group variables reduces the number of variables entered into the statistical analysis, making patterns easier to discern and the cases were then analysed according to individual manifestations within the groups. Notwithstanding the groupings, the number of variables used, at 52, was still large.

The acid test of cluster analysis is whether the clusters produced have any clinical relevance. External validation showed consistent identification of well recognized, clinically meaningful groupings, e.g. absences with no focal features, focal clonic seizures, focal sensory seizures, seizures with olfaction and gustation, experiential seizures and differentiating generalized tonic from focal tonic or generalized tonic–clonic seizures. In addition, a separate analysis was undertaken, comparing manifestations associated with pure frontal and pure temporal lesions, which provided results clinically supporting the cluster analysis, by a completely independent technique.

**Clinical seizure types**

We looked at seizure classification in terms of clustering of clinical symptoms, evolution of clinical manifestations and the association of individual symptoms with frontal and temporal lobes. Cluster analysis gave 14 distinctive clinical types, but these proved to have limited localizing value with the exception of perirolandic seizures. Analysis of sequential manifestations showed early divergence in all seizure groups and was of little localizing value. The analysis of individual symptoms gave only five that differentiated between frontal and temporal lobe lesions with statistical significance. Thus, we conclude that reliable localization by electroclinical criteria is not possible and that the ILAE classification of partial seizures into a large number of distinctive types, with highly localizing clinical patterns is not tenable.

**Seizure patterns associated with the temporal lobes**

The seizure types associated with temporal lobe lesions were those characterized by absences and those with subjective onsets: fear, experiential and sensory modalities excluding somatosensory. These associations have been observed previously (Penfield and Jasper, 1954; Gloor et al., 1982; Delgado-Escueta and Walsh, 1985), were supported by the analysis of pure frontal versus pure temporal lesions. These seizure types were frequently accompanied by oralimentary automatisms and the separate analysis of these automatisms suggested that they were independently associated with temporal lobe lesions.

It is, however, important to note that in each clinically defined group, there was an important minority with lesions outside the temporal lobe. In most cases the initial subjective symptom was indistinguishable between frontal and temporal lobe associated cases. Our results suggest that, in these cases, analysis of the subsequent evolution of the seizure may be of value in determining localization, in that, where the onset was followed by motor activity without an intervening absence phase, a frontal lesion was more likely. The reason for this difference may be the more immediate relationship of the frontal lobes to motor outflow pathways. Of note, was that seizures with a somatosensory onset usually proceeded directly to motor activity without an absence phase and this is the only sensory modality to project directly onto motor cortex, bypassing association cortex (Pandya and Barnes, 1987). There were some recurrent patterns in the frontal lesions that were associated with these predominantly temporal lobe seizure types, in that they were commonly in regions with very close connections with the temporal lobes, e.g. cingulate gyrus for experiential phenomena (Sanides, 1970; Pandya and Barnes, 1987; Wada, 1989) and orbitofrontal cortex for visual and gustatory phenomena (Schneider et al., 1961; Leichnetz and Astruc, 1975).

**Seizures associated with extratemporal regions**

The close association of simple clonic and simple somatosensory seizures with the perirolandic region is well known (Penfield and Jasper, 1954) and it is recognized that both seizure types may occur from the same lesion at different times (Lehman et al., 1994). The probable anatomical
substrate of this association is that the corticospinal tracts arise from both precentral and postcentral gyri (Ghez, 1985) and that there are close connections between these regions (Pandya and Barnes, 1987). There was no evidence from these data that somatosensory seizures with and without Jacksonian progression had different localizations, as has been suggested previously (Penfield and Jasper, 1954; Quesney et al., 1992).

Two seizure types with prominent, early motor manifestations appeared to be especially associated with frontal lobe abnormalities on investigation. Seizures characterized by version and posturing are generally thought to be associated with the frontal lobes (Penfield and Jasper, 1954; Fegerstein and Roger, 1961; Cotte-Rittaud and Courjon, 1962; Geier et al., 1977; Williamson et al., 1985; Delgado-Escueta et al., 1987; Waterman et al., 1987; Quesney et al., 1990) and our findings strongly support this, in relation to interictal EEG, ictal EEG and neuroimaging in both analyses. This association only occurred, however, if the posture was early in the seizure, according with previous observations (Cotte-Rittaud and Courjon, 1962). Within the frontal lobes there was a strong statistical association of this seizure type with lesions of the lateral premotor region. This seizure pattern has been associated more frequently with the SMA but clear differences between the lateral premotor and SMA regions have been difficult to define (Quesney et al., 1990). Different investigators have favoured different regions as the site of onset of adverse seizures (Penfield and Jasper, 1954; Morris et al., 1988). This divergence may be explained by the stereotactic EEG finding, that spontaneous seizures restricted to either SMA or lateral premotor cortex are rare, and they are likely, therefore, to share similar clinical features (Chauvel et al., 1992). In addition, although there are some differences in connectivity and physiological functions between SMA and lateral premotor regions (Goldberg, 1985), there is considerable overlap between them (Maclean, 1987; Halsband et al., 1993).

Where ictal EEG abnormalities were recorded in this group, they were noteworthy for the predominance of high frequency discharges. This pattern is said to be characteristic of a discharge close to the electrode (Quesney and Gloor, 1985) and again would be more consistent with a laterally placed discharge than one in the mesial SMA, which would usually only manifest as slow waves on scalp EEG and frequently be missed altogether (Morris et al., 1988; Quesney, 1991). The especially low success rate of SMA surgery for adverse seizures (Rasmussen, 1991) also casts doubt on current criteria for localization to this region.

The presence of an abdominal or other physical aura did not confer any differences in the pattern of associated abnormalities on investigation, supporting the contention that these symptoms are non-specific, with little localizing value. This is consistent with the ‘temporal lobe auras’, previously reported from the anterolaterodorsal region (Quesney et al., 1992) and the association of abdominal sensations with posturing (Penfield and Jasper, 1954).

This seizure type has been described as typically characterized by very frequent, brief seizures with rapid recovery occurring mainly during sleep (Tinuper et al., 1990). In the current study, these timing characteristics were exhibited by a minority of cases. Although these cases have a striking clinical picture, it was the early occurrence of version or posturing that was the frontal lobe feature, irrespective of these other aspects of seizure timing, which did not differentiate between frontal and temporal-associated seizure types with statistical significance.

Seizures characterized by motor agitation was the only group in which a substantial proportion (40%) of cases had the timing characteristics often attributed to FLE (Anonymous, 1989; Wada, 1989), high seizure frequency, predominantly nocturnal attacks with short duration and rapid recovery. Even in this group only a minority conformed to this pattern. This group had strong evidence supporting a frontal localization in the majority of cases, most especially to the frontopolar/orbitofrontal region. Similar seizures have been reported previously from this area (Tharp, 1972; Ludwig et al., 1975; Wada, 1989) and motor agitation can be produced by stimulation of this cortical region cortex in animals (De Bruin, 1990). An aura of olfaction/gustation was recognized in some of these cases and has been described before from the orbitofrontal region (Munari and Bancard, 1992). It is recognized that lesions of the orbitofrontal region can impair olfactory and gustatory discrimination (Potter and Butters, 1980). It may not, therefore, be necessary for seizures to spread to the temporal lobe to produce these sensations, even though TLE is more characteristically associated with them (Daly, 1958). Spread between orbitofrontal cortex and temporal lobes may, however, occur extremely rapidly, via the uncinate fasciculus (Daly, 1957; Peretti et al., 1989) and has been recorded by stereotactic EEG in spontaneous seizures (Munari and Bancard, 1992).

Additional features were prominent in this group and have been recognized previously in seizures dominated by frenetic motor activity, including bizarre vocalization and autonomic changes (Tharp, 1972; Ludwig et al., 1975; Wada, 1989; Munari and Bancard, 1992). The importance of the orbitofrontal cortex in control of autonomic function is supported by anatomical and physiological studies (Neafsey, 1990).

Generalized tonic and tonic–clonic seizures were not associated with particular lesion sites. This may partly be due to patient selection criteria, in that generalized seizures were commonly the patient’s second or third seizure type. Many patients had long-standing epilepsy and generalized seizures may develop late in the course of localization-related epilepsy with various origins (Purves et al., 1988; Gambardella et al., 1994). Some studies have suggested these seizures are more characteristic of frontal lesions, especially of mesial frontal cortex (Ralston, 1961; Purves et al., 1988). In this study, if there was significant asymmetry of the initial tonic posture then it was classed as version/posturing; in 16 cases seizures with focal tonic posturing went on to generalized hypertonia and these were characteristically
Implications for seizure classification and brain. From the clinical point of view, this severely limits the relationships identified between clinical seizure type and neuroimaging and EEG associations of the majority of cases in that group and yet were clinically indistinguishable. Of note was the finding that of three cases with identified lesions and seizures characterized by bilateral clonic activity with preserved awareness, two were frontal parasagittal menin giomas, the only such lesions in the study. We have subsequently seen the same seizure type in a patient with a parasagittal glioma. The mechanism for this may be either the simultaneous activation of bilateral motor centres without spread to other regions, or bilateral motor activation from a unilateral discharge, as higher motor centres have a degree of bilateral representation (Geier et al., 1977).

Complex behavioural automatisms occurred with various seizure groups, and tended to be associated with temporal lobe abnormalities on investigation. This association of automatisms with TLE is recognized (Quesney et al., 1984; Marchini et al., 1989), but may appear paradoxical in that motor planning is generally considered a frontal lobe function (Luria, 1973). It contrasted with simpler ictal motor activity, which was related to FLE. These data are consistent with the view that simple automatisms and repetitive activity, including motor agitation, are due to direct epileptic activation of the frontal lobes, whereas more complex behavioural activity is expressed as an ictal or postictal release phenomenon with seizures restricted to the temporal lobes, as first suggested by Hughlings Jackson (Penfield and Jasper, 1954; Taylor, 1958). A key feature suggesting they are not due to seizure activation is that these automatisms may persist into the postictal period after the discharge has ceased (Gloor, 1991). It is suggested that an important element is amnesia and confusion, allowing complex activity to be expressed for which there is no awareness, either at the time and/or postictally (Jasper, 1964). It is likely that if the motor cortices are directly involved in the seizure discharge, it is impossible for them to express more complex motor activity.

Implications for seizure classification and mechanisms of ictal symptom generation

In all clinically defined groups, except somatosensory and Jacksonian motor seizures, there were substantial minorities that did not conform to the statistically significant associations on neuroimaging and EEG associations of the majority of cases in that group and yet were clinically indistinguishable. Our data also show important overlap of seizure manifestations from pure frontal and pure temporal lesions. Though the relationships identified between clinical seizure type and imaging abnormalities were statistically significant, they were, therefore, not absolute and similar seizures may be associated with abnormalities in more than one part of the brain. From the clinical point of view, this severely limits their localizing value. Another important negative finding was that overall characteristics of seizure timing, duration, diurnal variation and frequency showed no difference between frontal and temporal lobe lesion groups. Very frequent, brief motor seizures were more likely to be frontal, but equally frequent, brief, subjective seizures occurred in the temporal group.

The most commonly cited explanation for the overlap of clinical manifestations of seizures arising from different regions is the spread of seizure discharges. There are several intracranial EEG studies that support the contention that certain clinical manifestations occur only when there has been seizure spread to a specific part of the cerebral cortex (Geier et al., 1976; Gloor et al., 1982; Lieb et al., 1991; Williamson et al., 1992; Palmini et al., 1993). There are also, however, other possible explanations. First, methodological factors: a statistical technique was used to overcome the problem of large lesions that involved several functional areas, which formed the majority of epileptogenic lesions within the frontal lobes. If the epilepsy arises from a small part of a large lesion, then a statistical analysis may miss some associations. The large number of lesional cases in this study makes this less likely to be important and this technique also maximizes the significance of any associations identified. Secondly, some lesions may be a marker of more widespread abnormalities and this may be particularly true of congenital dysplastic lesions whose scan appearance may be the macroscopic representation of diffuse abnormalities of connectivity and which are beyond the limit of resolution of current imaging techniques (Desbiens et al., 1993). In post-traumatic lesions, contre-coup and shearing injuries may be more widespread than is apparent from the scan appearances and these are a common cause of FLE (Rasmussen, 1963). Thirdly, it is not clear to what extent functional connectivity may differ in the epileptic brain and how this may be reflected in differences in seizure expression. It is recognized that early cerebral insults may result in changes in location of cortical function (Pfolkey, 1990), but this may also be a factor in adults (Hedström et al., 1992; Weiller et al., 1992). Fourthly, the functional heterogeneity of association cortex may possibly cause different seizure patterns to be generated from the same region according to which functional systems are involved. This contrasts with the primary sensory and motor cortices, which are more strictly dedicated to an individual function, with a specific relationship to peripheral organs and where seizures were clinically the most easily localized both in this study and historically (Penfield and Jasper, 1954; Taylor, 1958). A related phenomenon is that of parallel and distributed processing, in which different brain regions subserve similar functions or different aspects of the same function, such that seizure activity in either may produce a similar manifestation; for example, the widely separated regions involved in the control of eye movements (Robinson, 1968) and the number of regions from which forced eye movements are a seizure manifestation (Cotte-Rittaud and Courjon, 1962). Recent evidence from cortical electrical
stimulation supports the view that identical manifestations can be produced by stimulation of disparate cortical regions, without after-discharge, in the same individual and suggest that the epileptogenic cortex may be in a matrix or network rather than a discrete anatomical region (Fish et al., 1993). It may be possible, therefore, only to localize a small number of typical partial epilepsy syndromes on the basis of clinical features, with many clinical seizure types having very limited localizing value.

The ILAE classifies seizure types on the basis of electroclinical criteria (Anonymous, 1989) and this approach may be valuable for well-defined syndromes where no pathological substrate has yet been found, e.g. benign epilepsy of childhood with centrotemporal spikes. In adult localization-related epilepsies, however, this study demonstrates that there is significant overlap between the clinical manifestations associated with lesions in different cerebral regions. Even though we found 14 clinical seizure groupings, none allowed reliable differentiation between temporal and frontal lobe seizures. Furthermore, only two seizure types had some limited degree of localizing value within the frontal lobes, with significant numbers of exceptions, limiting their utility in clinical practice. In addition, few individual symptoms showed a marked statistical association with frontal or temporal lobe lesions and criteria of seizure timing or duration did not reliably distinguish different seizure types. Thus, we cannot agree with the view that seven different localizable seizure types exist within the frontal lobes, as suggested in the ILAE electrophysiological classification. Since imaging has increased our ability to identify these lesions, and with the weight of evidence suggesting that the site of the lesion is the best guide to localization (Engel et al., 1981; Sammaritano et al., 1987; Wyler et al., 1989; Palmini et al., 1991; Cascino et al., 1992; Salanova et al., 1993), we feel that in this area, an anatomical-pathological definition may be more appropriate. In common with previous authors (Delgado-Escueta and Walsh, 1985), we have also found a proportion of patients with absence episodes and no localizing ictal manifestations, due to focal discharges—a group currently not recognized in the localization-related epilepsy classification of the ILAE.

**Association of seizure types: pseudo-generalized epilepsy**

The association of different seizure types is not a subject generally considered in the investigation of localization-related epilepsy. In this study, the only statistically significant association of seizure types was between absences and generalized motor seizures—pseudo-generalized epilepsy. There were no obvious shared features on investigation of this group of 13 patients; in particular interictal EEGs, where abnormal, were not generalized, although bifrontal in four. No ictal EEGs were available.

Ictal EEG studies by other groups show that rapid electrographic generalization is often due to rapid propagation of discharges between hemispheres (Ralston, 1961; Purves et al., 1988; Spencer et al., 1988) and these may manifest clinically as generalized seizures. Mesial hemisphere lesions are especially associated with this pattern. In this study, two parasagittal meningiomas were associated with bilateral clonic motor activity and clear preservation of awareness; a dissociation in the presence of a lesion ideally situated to cause bilateral motor activity, without generalized disturbance. Direct intracerebral recordings have also suggested that in some patients generalized convulsions may arise from discharges restricted to the prefrontal regions (Goldring, 1972). The associations of these clinically generalized seizure types with each other poses questions regarding the nature of secondary generalization: the relationships of secondary generalized seizures to primary generalized epilepsy syndromes which share similar associations of seizure types and the mechanisms underlying generalized epileptic manifestations.

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**References**


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Localizing clinical seizure patterns


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Appendix 1a

Definition of clinical manifestations

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>Non-specific cephalic or whole body sensations</td>
</tr>
<tr>
<td>Abdominal</td>
<td>Nausea, rising epigastric or other abdominal</td>
</tr>
<tr>
<td>Experiential</td>
<td>Déjà vu, jamais vu, forced thought, flashback or other non-hallucinatory distortions of reality</td>
</tr>
<tr>
<td>Emotion</td>
<td>Fear, depression, elation, anger</td>
</tr>
<tr>
<td>Visual hallucination</td>
<td>Formed or unformed hallucination</td>
</tr>
<tr>
<td>Auditory hallucination</td>
<td>Auditory manifestation unrelated to background noise</td>
</tr>
<tr>
<td>Olfactory hallucination</td>
<td>Olfactory sensation</td>
</tr>
<tr>
<td>Gustatory hallucination</td>
<td>Gustatory sensation</td>
</tr>
<tr>
<td>Non-Jacksonian somatosensory</td>
<td>Focal sensations, e.g. tingling without clear anatomical progression</td>
</tr>
<tr>
<td>Jacksonian somatosensory</td>
<td>Focal sensations with clear anatomical progression</td>
</tr>
<tr>
<td>Focal clonic</td>
<td>Clonic activity without clear anatomical progression</td>
</tr>
<tr>
<td>Jacksonian clonic</td>
<td>Clonic activity with clear anatomical progression</td>
</tr>
<tr>
<td>Version/posturing</td>
<td>Forced, sustained head turning or maintained postures of the limbs, excluding generalized hypertonia.</td>
</tr>
<tr>
<td>Generalized hypertonia</td>
<td>Simultaneous, symmetric hypertonia of all four limbs</td>
</tr>
<tr>
<td>Motor agitation</td>
<td>Frenetic motor activity, e.g. vigorous kicking or flailing of limbs</td>
</tr>
<tr>
<td>Simple automatisms</td>
<td>Involuntary repetitive movements, e.g. tapping, plucking of clothes</td>
</tr>
<tr>
<td>Behavioural automatisms</td>
<td>Complex acts performed without apparent awareness, e.g. undressing or exploratory behaviour</td>
</tr>
<tr>
<td>Oroalimentary automatisms</td>
<td>Swallowing, chewing or other complex oral movements, excluding facial involvement in tonic or clonic movements</td>
</tr>
<tr>
<td>Verbal vocalizations</td>
<td>Apparently involuntary speech</td>
</tr>
<tr>
<td>Non-verbal vocalizations</td>
<td>Other involuntary noises, e.g. shouting, crying, laughing, singing. Non-specific moans and grunts were excluded</td>
</tr>
<tr>
<td>Vegetative manifestations</td>
<td>Changes in colour, pupils, respiration and pulse</td>
</tr>
</tbody>
</table>
Appendix 1b

Definitions of distributions of EEG abnormalities

<table>
<thead>
<tr>
<th>Distribution</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal</td>
<td>Maximal at a single electrode with minimal spread</td>
</tr>
<tr>
<td>Regional</td>
<td>Maximal at two to four neighbouring electrodes</td>
</tr>
<tr>
<td>Bilateral</td>
<td>Symmetric, maximal at one to four electrodes on both sides</td>
</tr>
<tr>
<td>Hemispheric</td>
<td>Maximal at more than four electrodes on one side of the head only</td>
</tr>
<tr>
<td>Widespread</td>
<td>Asymmetric, involving many electrodes on both sides</td>
</tr>
<tr>
<td>Generalized</td>
<td>Symmetric generalized discharge</td>
</tr>
</tbody>
</table>

Appendix 2

Variables entered into cluster analysis

<table>
<thead>
<tr>
<th>Presence of a prodrome</th>
<th>Bicycling of legs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal sensation</td>
<td>Kicking</td>
</tr>
<tr>
<td>Cephalic sensation</td>
<td>General motor agitation</td>
</tr>
<tr>
<td>Chest sensation</td>
<td>Simple automatism group</td>
</tr>
<tr>
<td>Other physical sensation</td>
<td>Exploratory behaviour</td>
</tr>
<tr>
<td>Psychic sensation</td>
<td>Bed making</td>
</tr>
<tr>
<td>Fear</td>
<td>Complex automatism group</td>
</tr>
<tr>
<td>Other emotion</td>
<td>Oroalimentary automatism</td>
</tr>
<tr>
<td>Visual hallucination</td>
<td>Speech arrest</td>
</tr>
<tr>
<td>Visual distortion</td>
<td>Speech distortion</td>
</tr>
<tr>
<td>Auditory hallucination</td>
<td>Shout</td>
</tr>
<tr>
<td>Olfactory hallucination</td>
<td>Bizarre vocalization, e.g. giggling</td>
</tr>
<tr>
<td>Gustatory hallucination</td>
<td>Non-verbal vocalization group</td>
</tr>
<tr>
<td>Somatosensory hallucination</td>
<td>Coherent verbal vocalization</td>
</tr>
<tr>
<td>General hypertonia</td>
<td>Incoherent verbal vocalization</td>
</tr>
<tr>
<td>General motor arrest</td>
<td></td>
</tr>
<tr>
<td>Generalized clonic activity</td>
<td></td>
</tr>
<tr>
<td>Generalized hypotonia</td>
<td></td>
</tr>
<tr>
<td>Eye version</td>
<td>Pupillary change</td>
</tr>
<tr>
<td>Head version</td>
<td>Colour change</td>
</tr>
<tr>
<td>Body turning</td>
<td>Respiratory change</td>
</tr>
<tr>
<td>Version group</td>
<td>Pulse change</td>
</tr>
<tr>
<td>Focal clonic activity</td>
<td>Autonomic group</td>
</tr>
<tr>
<td>Focal paresis</td>
<td>Incontinence</td>
</tr>
<tr>
<td>Asymmetric tonic posture, e.g.</td>
<td>Tongue biting</td>
</tr>
<tr>
<td>Shout</td>
<td>Postictal confusion</td>
</tr>
<tr>
<td>Simple repetitive activity, e.g.</td>
<td>Postictal dysphasia</td>
</tr>
<tr>
<td>Tapping</td>
<td>Postictal motor deficit</td>
</tr>
</tbody>
</table>

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Appendix 3

Flow charts of sequence of seizure manifestations for groups 1–9

Explanation of flow charts

Flow charts describe the evolution of manifestations of each seizure in the group. The number of cases following a particular path is represented by the number next to each arrow. The proportion of the original cohort following that path is related to the thickness of the arrow. Where there are two subgroups for the seizure type, each is represented by different coloured arrows throughout the flow chart. In some instances the total number of cases leaving a manifestation box is smaller than that entering it; the difference represents those cases in whom there was a gradual recovery after the manifestation in the box. The shapes of the boxes follow a standard pattern from first manifestation to recovery. Where the relative timing of manifestations is not clear, they are linked by a line without an arrow.

Flow chart 1 Sequence of seizure manifestations of subgroup 1a: fear and fear behaviour and subgroup 1b; olfactory and gustatory aura.

Flow chart 2 Sequence of seizure manifestations of group 2: absence without focal features.
Flow chart 3 Sequence of seizure manifestations of group 3: experiential.

Flow chart 4 Sequence of seizure manifestations of group 4: visual hallucination.
Flow chart 5 Sequence of seizure manifestations of group 5: version/posturing.

Flow chart 6 Sequence of seizure manifestations of group 6: somatosensory.

Flow chart 7 Sequence of seizure manifestations of group 7: Jacksonian motor.
**Flow chart 8** Sequence of seizure manifestations of group 8: motor agitation.

**Flow chart 9** Sequence of seizure manifestations of group 9: generalized tonic, generalized tonic–clonic and generalized clonic with preservation of awareness.