Seizure 2003; **12:** 268–281
doi:10.1016/S1059–1311(02)00276-5

Complex partial seizures of frontal lobe onset statistical analysis of ictal semiology☆

P. KOTAGAL[†], G. ARUNKUMAR[†], J. HAMMEL[‡] & ED MASCHA[‡]

Departments of [†]Neurology, [‡]Biostatistics and Epidemiology, The Cleveland Clinic Foundation, Cleveland, OH, USA

Correspondence to: Dr Prakash Kotagal, M.D., Section of Epilepsy and Sleep Disorders, Cleveland Clinic Foundation, Desk S51, 9500 Euclid Avenue, Cleveland, OH 44195, USA. *E-mail*: kotagap@.ccf.org

***Objective*:** To identify the ictal semiology of complex partial seizures originating from the frontal lobe (FLCPS) and mesial temporal lobe (MTLE) in patients who became seizure free after surgery.
***Methods*:** We analysed 149 seizures from 42 patients, 28 with MTLE (75 seizures) and 14 with FLCPS (74 seizures) seizure free for at least 1 year after surgery. Fifty-eight symptoms and signs were looked for in every seizure and their time of onset and ending noted. Statistical analysis was then used to define the frequency, time of onset and cluster analysis of these symptoms/signs.
***Results*:** Epigastric aura was more frequent in MTLE while an aura of a general body sensation or indescribable feeling occurred only in FLCPS. Alimentary automatisms were more common and occurred earlier in MTLE ($P < 0.001$). Perseverative automatisms, retching and vomiting occurred exclusively in MTLE while bicycling movements occurred only in FLCPS. Abdominal, psychic or olfactory aura followed by behavioural arrest, alimentary automatisms, repetitive distal upper extremity movements, complete loss of consciousness, looking around and whole body movements were typical of MTLE. Repetitive coarse upper extremity movements, complete loss of consciousness, complex motor and hypermotor activity were typical of FLCPS.
***Conclusion*:** The earliest symptoms and signs as well as their order of appearance allow one to distinguish between complex partial seizures arising from the frontal lobe and mesial temporal lobe.

Key words: frontal lobe; complex partial seizures; statistical analysis.

INTRODUCTION

Frontal lobe epilepsy (FLE) occurs in approximately 30% of adults with partial epilepsy[1–3]. The differentiation of frontal lobe complex partial seizure (FLCPS) from mesial temporal lobe seizures is of importance in understanding the neuroanatomical basis of ictal semiology, and for the selection of patients for resective epilepsy surgery[4–9]. Several authors have tried to differentiate between seizures originating from various regions of the frontal and temporal lobes by analysing the sequential appearance of symptoms using statistical methods[10–13]. Wieser was the first to use cluster analysis techniques to differentiate psychomotor seizures arising from various locations[14]. Based primarily on the onset and patterns of spread of the ictal EEG discharge, he proposed five different subtypes of psychomotor seizures: (1) unilateral temporo-basal limbic, (2) temporal polar, (3) posterior temporal neocortical, (4) opercular and (5) fronto-basal cingulate. However, symptoms and signs which correlated these subtypes of psychomotor seizures did not form tight clusters and some characteristics were common to all subtypes. Only 10/23 patients in Wieser's series became seizure free, leaving open the possibility that ictal onset could have been from brain regions outside the margins of resection. Kotagal *et al*.[10] analysed the semiology of psychomotor seizures of temporal lobe onset in patients who became seizure free after temporal lobectomy. They also used statistical methods to define symptom/sign clusters and their order of appearance. The commonest sequence was behavioural arrest followed by alimentary and hand automatisms, looking around and whole body movements in that

☆This paper was presented at the 123rd Annual Meeting of the American Neurological Association, Montreal, October 1998.

order. Complex partial seizures arising from the frontal lobe remain less well defined compared to seizures of mesial temporal lobe epilepsy (MTLE). Manford *et al.*[13] analysed clinical seizure patterns and their localising value in frontal and temporal lobe epilepsy and concluded that relatively few seizures could be localised reliably on clinical grounds alone. Oral automatisms and experiential symptoms were significantly associated with temporal lobe lesions, whereas early focal tonic activity or head version were associated with frontal lobe lesions. Video-EEG telemetry was performed in only 30 out of 91 lesional cases and the seizure outcome after resection was not reported. Salanova *et al.*[49] analysed the frequency, time of onset and order of appearance of various symptoms and in frontal lobe. Their series included nine cases of supplementary motor, seven focal motor and eight complex partial seizures. Of 14 patients who underwent frontal resection, only 7 had >90% reduction in seizures. The patients with complex partial seizures frequently exhibited partial loss of consciousness, unilateral or bilateral tonic posturing and bicycling movements.

To date, no study has examined seizure semiology of FLCPS using only patients who became seizure free after resection of the seizure focus. Many of the patients in previous studies showed seizure semiology strongly suggesting frontal lobe onset. However, seizures originating outside of the boundaries of the frontal lobe may produce little by way of clinical manifestations until the ictal discharge spreads to symptomatogenic areas within the frontal lobe, such as the sensorimotor and supplementary motor areas[15–20]. These shortcomings could explain why previous studies were unable to clearly distinguish between FLCPS and MTLE using conventional methods of videotape analysis.

In our study, we have attempted to characterise more precisely with the help of statistical methods, the seizure semiology of FLCPS and distinguish it from MTLE. By selecting only those patients who became seizure free after frontal lobe resection, we can correctly assume that the ictal onset zone was within the margins of resection. We excluded patients with supplementary motor and perirolandic seizures because these have prominent motor symptoms that are readily differentiated from MTLE.

MATERIALS AND METHODS

Between 1980 and 1998, 92 patients with intractable localisation-related epilepsy underwent frontal lobectomy or frontal lesionectomy at our institution. We excluded patients with supplementary motor area (SMA) and perirolandic seizures, fronto-temporal and fronto-central lesions. Thirty-five patients in this subset had frontal lobe complex partial seizures and 14 patients (40%) became completely seizure free for longer than 1 year after focal resection—this group was chosen for our study. The patients' mean age at seizure onset was 10 years (range 6 months to 29 years). There were 10 males and 4 females. The mean interval between seizure onset and evaluation was 21 years (range 4–35 years). Five of the patients were seizure free of antiepileptic medications. For comparison, 28 MTLE patients who remained seizure free for at least 1 year after temporal lobectomy were taken from the series of Kotagal *et al.*[10].

All 14 patients with FLCPS underwent prolonged video-EEG monitoring, first with scalp electrodes and 7 of them subsequently had intra-cranial subdural recordings before resection. Two patients had intra-operative electrocorticography pre- and post-excision. MRI brain scan revealed a frontal lobe lesion in 11 patients, in whom subsequent pathological examination disclosed cortical dysplasia (6 pts), hamartoma (2 pts), dysembryoplastic neuroepithelial tumour (DNET, 1 pt), low-grade astrocytoma (1 pt), meningioangiomatosis (1 pt), cystic encephalomalacia (1 pt) and infarction (2 pts). The epileptogenic zone was determined to be in the frontal lobe by means of extra- and intra-cranial recording in 10 patients (7 patients had chronic subdural electrode recordings and 3 had intra-operative corticography and evoked potential recordings).

The responsiveness of patients during seizures was tested by the staff of the epilepsy monitoring units (technologists, nurses or physicians), and they were asked to remember test items (objects or words). The patients were judged to be unconscious during the seizure if they were not able to interact normally with the observer and were amnestic afterwards. Patients were judged to have partial loss of consciousness if they showed some interaction with their surroundings (e.g. turning around to look for an observer or reaching for an item being presented to them). Following the seizure, after patients had regained consciousness and could follow commands, they were interviewed to determine whether they (a) recalled having an aura prior to the seizure and describe it, (b) had any memory of what occurred during the seizure and (c) had dysnomia by asking them to name objects. A total of 74 FLCPS and 75 mesial temporal seizures saved on videotape were analysed by one of the authors (AK), and all ambiguous findings were reviewed with a senior investigator (PK). We also examined one best example of each patient's seizure to verify that results would not be skewed if a given patient had a disproportionately higher number of seizures relative to other patients. The seizures were analysed blindly without knowledge of EEG data. Each seizure was

viewed three to four times in its entirety to identify every symptom and sign. The ictal characteristics listed in Appendix A were looked for in every seizure, and their time of onset, end and duration were noted.

The clinical onset of the seizure was determined by the first visible change in the behaviour, or when the patient announced his/her aura or pressed the seizure alarm button. Auras were only counted if the patient announced it at the beginning of the seizure or was able to recall it during the postictal interview. The clinical seizure was judged to have ended when the patient's stereotyped behaviour ended or when the patient started to interact normally with the surroundings; when the clinical end of the seizure could not be easily judged, the time of EEG seizure termination was used as the cut-off point for analysis.

Statistical analysis

The time of onset, end and duration of each seizure as well as for each individual symptom and sign were noted. The data was entered into a VAX 8550 computer. SAS statistical software version 6.12 (Cary, NC) and S-Plus version 3.4 (Mathsoft, Inc.) was used to perform the statistical analysis. There were 28 patients with 75 seizures in MTLE group and 14 patients with 74 seizures in FLCPS group. The following analyses were carried out:

1. *Seizure duration and number of symptoms/signs per seizure*: Repeated measures analysis of variance in SAS PROC MIXED was used to compare the FLCPS and MTLE groups with respect to the mean seizure duration and mean number of symptoms/signs observed per seizure. This is analogous to standard analysis of variance (ANOVA), but accounts for the presence of multiple seizures per patient. The population means are estimated using the resulting 'least squares means' and the resulting *P*-values are based on ANOVA which accounts for multiple seizures per patient.

2. *Frequency of symptom/signs occurrence*: The frequency with which various symptoms/signs occurred in the FLCPS and MTLE group was determined. Ratio estimation methods were used to compare groups. These methods account for the possible association between seizures in the same patient, thus making them preferable to the standard methods of analysing proportions.

3. *Time of onset of symptoms/signs*: We compared the FLCPS and MTLE groups on the median onset time for a number of symptoms/signs using a procedure developed by Obuchowski[15] that is analogous to the Wilcoxon rank sum test, but adjusts for correlation within subjects. A significance level of 0.05 was used for each test. In case of infrequent symptom/sign occurrence in one of the groups, the medians were compared using the Wilcoxon rank sum test. In these cases, we could not adjust for correlation within subjects, but multiple occurrences per subject were minimal.

4. *Relative time of onset for symptoms/signs*: The time of onset in relation to the first one-sixth, and the first, middle and last third of the seizure was determined for each symptom/sign in the frontal and mesial temporal groups. This was done to minimise bias from seizures spreading very slowly or rapidly from the frontal and temporal lobes. We used the ratio estimation method with 95% confidence intervals to make the comparison[16] when analysing the frequency of occurrence of various symptoms/signs.

5. *Sequence of appearance of symptoms and signs*: We examined only the most common symptoms/signs for the frontal and temporal groups, i.e. those that occurred in at least 10% of the seizures studied. A symptom/sign pair then was given an ordering if the following rules held: (a) at least 15% of the seizures of the given type had both symptoms and (b) the ordering occurred in at least 70% of the seizures of the given type in which both symptoms/signs occurred. These rules indicate orderings that were 'typical' in the data, and we collectively called them the '10-15-70' rule. We also determined the frequencies of seizures that matched the patterns of symptom/sign onset identified for the frontal and temporal groups. This method is similar to that used in our previous analysis of MTLE[10].

6. *Cluster analysis*: For each cluster analysis, a symptom/sign was included if its onset occurred in the specified portion of the seizure in at least 10% of the seizures under study. The goal of cluster analysis was to identify symptom/sign pairs or groups of pairs that may have occurred more commonly for one type of seizure than another. Thus, 20 symptoms/signs were considered for frontal seizures, and 22 were considered for mesial temporal-onset seizures. Clustering of symptoms/signs requires a measurement of similarity for each pair of symptoms, and the number of seizures in which two symptoms both occur is the pairwise similarity measure. Complete linkage cluster analysis was performed: clusters were joined at a particular pairwise similarity threshold when each pair of symptoms/signs in

the new cluster occurred together at least as many times as the threshold value. Symptom/sign onsets were most often observed in the first third of the seizures; therefore, fewer were included in the analysis for the second third, and no cluster analysis was possible for the final third. Cluster analysis is summarised by Fig. 3a and b, which display the formation of clusters and the thresholds at which they occur. Clusters (horizontal lines), are continually being joined together (vertical lines) at the various pairwise similarity thresholds as we proceed from left to right. Every pair of symptoms/signs within a cluster occurred at least as many times as the pairwise similarity threshold at which it was joined. A scale appears below the Fig. 3a and b to indicate the percent of seizures, which a threshold represents.

The retrospective review of charts and videotapes of patients in this study was approved by the Cleveland Clinic Foundation's Institutional Review Board.

RESULTS

1. *Seizure duration and number of symptoms per seizure*: The seizure duration and number of symptoms/signs per seizure is shown in Table 1.

Table 1: Comparison of mesial and frontal seizures with respect to seizure duration and the number of observed symptoms per seizure.

Variable	Group	Range	Mean (SE)	Least squares mean (SE)[a]	*P*-value[a]
Seizure duration (seconds)	Mesial	5–175	59.7 (3.5)	60.2 (4.2)	0.07
	Frontal	10–145	44.7 (3.0)	48.2 (5.1)	
Number of observed symptoms per seizure	Mesial	4–14	7.93 (0.24)	7.92 (0.33)	<0.001
	Frontal	1–11	4.74 (0.19)	4.96 (0.45)	

[a] The least squares mean and the resulting *P*-value are based on an analysis of variance (ANOVA) which accounts for multiple seizures per patient. SAS PROC MIXED was used for the analysis. The least squares means are better estimates of the population means than the conventional means, and our analysis is superior to a standard ANOVA or *t*-test.

Table 2: Frequency of symptom occurrence.

No.	Symptom	All seizures (N = 149), N (%)	MTLE (N = 75), N (%)	FLCPS (N = 74), N (%)	*P*-value[a]
1	Somatosensory auras	2 (1%)	2 (3%)		0.50[b]
3	Auditory auras	2 (1%)	2 (3%)		0.50[b]
4	Vertiginous auras	2 (1%)	2 (3%)		0.50[b]
5	Olfactory auras	3 (2%)	3 (4%)		0.25[b]
7	General body sensations	8 (5%)	8 (11%)		0.003[b]
9	Epigastric sensations	17 (11%)	14 (19%)	3 (4%)	0.01
12	Behavioural arrest	52 (35%)	25 (33%)	27 (36%)	0.68
13	Staring	32 (21%)	9 (12%)	23 (31%)	0.006
14	Version	19 (13%)	15 (20%)	4 (5%)	0.012
22	Unilateral arm dystonic	28 (19%)	12 (16%)	16 (22%)	0.381
37	Generalised tonic–clonic seizure	23 (15%)	19 (25%)	4 (5%)	0.002
40	Perseverative automatisms	3 (2%)	3 (4%)		0.25[b]
41	Alimentary automatisms	73 (49%)	55 (73%)	18 (24%)	<0.001
43	Mimetic automatisms	21 (14%)	19 (25%)	2 (3%)	0.001
42	Repetitive upper extremity movements	85 (57%)	55 (73%)	30 (41%)	<0.001
44	Looking around	53 (36%)	43 (57%)	10 (14%)	<0.001
39	Complex motor seizure	67 (45%)	42 (56%)	25 (34%)	0.007
46	Complex gestures	12 (8%)	12 (16%)		<0.001[b]
47	Speech arrest	2 (1%)	2(3%)		0.50[b]
48	Positive speech	15 (10%)	13 (17%)	2 (3%)	0.009
49	Vocalisations	32 (21%)	14 (19%)	18 (24%)	0.402
52	Laughing/crying	13 (9%)	3 (4%)	10 (14%)	0.052
53	Complete loss of consciousness	117 (79%)	61 (81%)	56 (76%)	0.402
54	Partial loss of consciousness	79 (53%)	51 (68%)	28 (38%)	<0.001
56	Vomiting or retching	9 (6%)	9 (12%)		0.003[b]
38	Hypermotor seizure	28 (19%)		28 (38%)	only defined for frontal seizure
57	Dilated pupil	1 (1%)		1 (1%)	only defined for frontal seizure
58	Sniffing	1 (1%)		1 (1%)	only defined for frontal seizure

[a] Logistic regression/generalised estimating equations (GEE) used to account for within-subject correlation. [b] Fisher's exact test (does not account for within-subject correlation).

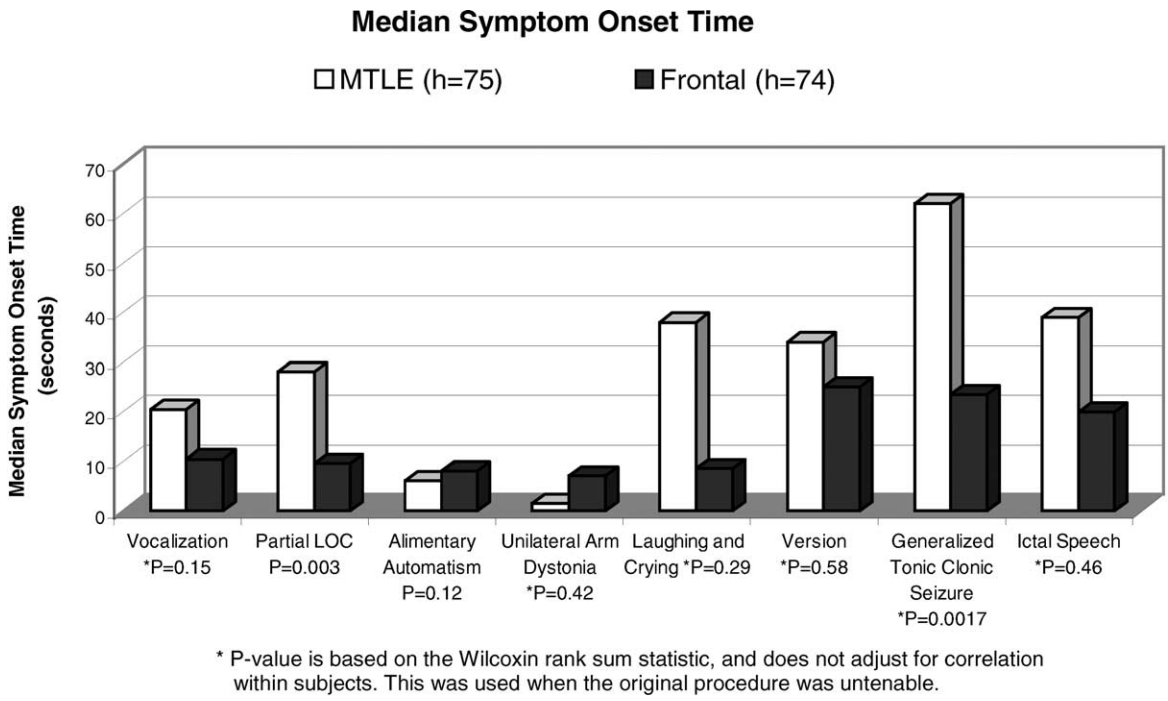

Fig. 1: Median symptom onset time in mesial temporal lobe seizures and frontal lobe complex partial seizures.

The mean seizure duration did not differ significantly between FLCPS (48.2 seconds, range 10–145 seconds) and MTLE (60.2 seconds, range 5–175 seconds; $P = 0.07$). The mean number of distinct symptoms/signs per seizure was significantly higher in MTLE (7.92, range 4–14) compared to FLCPS (4.96, range 1–11; $P < 0.001$).

2. *Frequency of symptom occurrence*: The frequency with which various symptoms/signs occurred in MTLE and FLCPS is shown in Table 2. An aura of epigastric sensation occurred more commonly with MTLE ($P = 0.01$) while the aura of a general body sensation was seen only in FLCPS ($P = 0.003$). Staring with eyelid retraction was more common with FLCPS ($P = 0.006$). Alimentary automatisms ($P < 0.001$), repetitive upper extremity automatisms ($P < 0.001$), looking around ($P < 0.001$) and complex gestures were much more common with MTLE ($P < 0.001$). Hypermotor seizures in which the predominant manifestation consisted of stereotyped complex movements involving the proximal segments of the limbs and trunk such 'pedalling' occurred exclusively in FLCPS. Generalised tonic–clonic seizures were commoner in MTLE ($P = 0.002$). Ictal vomiting and perseverative automatisms occurred exclusively with MTLE. Ictal speech was frequent in MTLE ($P = 0.009$), whereas laughing and crying was more frequent in FLCPS ($P = 0.052$). One patient with ictal laughter had a DNET in the left inferior frontal gyrus and the other had focal neuronal heterotopia in the left inferior orbital region. A third patient with ictal crying had meningio-angiomatosis in the left middle and inferior frontal gyrus.

3. *Median symptom/sign onset*: The median time of onset of symptoms/signs in relation to the first, middle or last third of seizure are shown in Fig. 1. Partial loss of consciousness (median, 9.5 seconds vs. 28 seconds; $P = 0.003$), looking around (median, 4.5 seconds vs. 18 seconds; $P \leq 0.001$), vocalisation (median, 10.5 seconds vs. 20.5 seconds; $P = 0.15$) and secondarily generalised tonic–clonic seizures (median, 18 seconds vs. 62 seconds; $P = 0.02$) appeared earlier in FLCPS compared to MTLE. Staring with eyelid retraction (91%) and complex motor activity (96%) occurred almost always at the start of the seizure in FLCPS, where as staring (with eyelid retraction) could be seen in the first or middle third in MTLE. Generalised tonic–clonic seizure always occurred in the last third of the seizure (100%) in MTLE, whereas it occurred during first (50%) or middle third (50%) in FLCPS. The following trends were also noted, though not statistically significant. Alimentary automatisms (median, 6 seconds vs. 8 seconds; $P = 0.12$), mimetic automatisms (median, 13 seconds vs. 22 seconds; $P = 0.63$) appeared earlier in MTLE compared with FLCPS. Version (median,

Table 3: Relative onset in relation to the first sixth, first, middle and last third of the seizure.

No.	Symptom	Origin	Onset in first sixth *N* (% of seizure)	*P*-value MTLE versus FCPS	*N* (% of total symptom occurrences)		
					First third	Middle third	Last third
9	Epigastric sensation	MTLE	14 (19%)		14(100%)	–	–
		FLCPS	3 (4%)	0.01	3 (100%)	–	–
13	Staring	MTLE	3 (4%)		4 (44%)	5 (56%)	0 (0%)
		FLCPS	18 (24%)	0.02	21 (91%)	2 (9%)	0 (0%)
33	Generalised tonic–clonic seizure	MTLE	0 (0%)		0 (0%)	0 (0%)	19 (100%)
		FLCPS	0 (0%)	–	2 (50%)	2 (50%)	0 (0%)
39	Complex motor seizure	MTLE	12 (16%)	0.04	21 (50%)	13 (31%)	8 (19%)
		FLCPS	22 (30%)		24 (96%)	1 (4%)	0 (0%)
41	Alimentary automatisms	MTLE	33 (44%)		44 (80%)	7 (13%)	4 (7%)
		FLCPS	6 (8%)	<0.001	11 (61%)	6 (33%)	1 (6%)
42	Repetitive upper extremity movement	MTLE	23 (31%)		36 (65%)	14 (25%)	5 (9%)
		FLCPS	12 (16%)	0.04	20 (67%)	10 (33%)	0 (0%)
43	Mimetic automatisms	MTLE	10 (13%)		14 (74%)	5 (26%)	0 (0%)
		FLCPS	0 (0%)	0.001	1 (50%)	1 (50%)	0 (0%)
44	Looking around	MTLE	15 (20%)		21 (49%)	17 (40%)	5 (12%)
		FLCP	7 (9%)	0.07	10 (100%)	0 (0%)	0 (0%)
46	Laughing/crying	MTLE	1 (1%)		1 (33%)	2 (67%)	0 (0%)
		FLCPS	4 (5%)	0.202	8 (80%)	2 (20%)	0 (0%)
47	Complete loss of consciousness	MTLE	38 (51%)		50 (82%)	6 (10%)	5 (8%)
		FLCPS	52 (70%)	0.015	53 (95%)	1 (2%)	2 (4%)
48	Partial loss of consciousness	MTLE	14 (19%)		20 (39%)	8 (16%)	23 (45%)
		FLCPS	11 (15%)	0.535	15 (54%)	6 (21%)	7 (25%)
49	Vocalisation	MTLE	2 (3%)		6 (43%)	2 (14%)	6 (43%)
		FLCP	9 (12%)	0.04	12 (67%)	4 (22%)	2 (11%)
55	Hypermotor activity	MTLE	0 (0%)		0 (0%)	0 (0%)	0 (0%)
		FLCPS	6 (8%)	–	13 (46%)	11 (39%)	4 (14%)

25 seconds vs. 34 seconds; $P = 0.58$) and ictal speech (median, 20 seconds vs. 39 seconds; $P = 0.46$) appeared earlier with FLCPS. Behavioural arrest and complete loss of consciousness occurred almost always at the start of the seizure in both groups.

4. *Relative symptom/sign onset*: The onset of symptoms/signs in relation to the first one-sixth and the first, middle and last third of the seizure are shown in Table 3. Only those symptoms/signs that occurred in at least 10% of the FLCPS and MTLE group were analysed. During the first sixth of the seizure, abdominal aura (4.8 times), alimentary automatisms (5.5 times), mimetic automatisms (10 times) and repetitive upper extremity movements (2 times) were the most frequent symptoms in MTLE, whereas staring (6 times), vocalisation (4.5 times) and complex motor seizure (2 times) were more common with FLCPS. Behavioural arrest occurred almost always at the start of seizures (96%) both in MTLE and FLCPS. Onset with staring (91%) was more common during the first third of the seizure in FLCPS, where as they were equally divided between the first (44%) and middle third (56%) with MTLE. Repetitive upper extremity movements were most common during the first third of the seizure in FLCPS (67%) and MTLE (65%). Responsiveness was maximally impaired in the first third of the seizure in FLCPS (95%) and MTLE (82%), with the patients becoming partially responsive in the middle or final third of the seizure. Laughing and crying was more common in the first third in FLCPS (80%), but occurred more often during the middle third of the seizure in MTLE (67%). Complex motor activity was most common during the first third (96%) in FLCPS, where as they occurred in the first (50%), middle (31%) and final third (19%) of the seizure in MTLE. Hypermotor activity occurred exclusively in FLCPS during first (46%), middle (39%) and final third (14%) of the seizure.

5. *Sequence of symptom/sign appearance*: Based on our '10-15-70' rule, sequences of symptom/sign appearance for the MTLE (Fig. 2a) and FLCPS (Fig. 2b) groups were constructed. Two or more of the most commonly occurring symptoms in a sequence consistent with the ordering diagram for MTLE occurred in 56% of mesial temporal-onset seizures and 50% of frontal-onset seizures. Two or more of the most commonly occurring symptoms in a sequence consistent with the ordering diagram for frontal seizures occurred in 59% of frontal-onset seizures, and in only 29% of mesial temporal-onset seizures.

6. *Cluster analysis*: Complete linkage yielded symptom clusters that were different for FLCPS and MTLE. The following symptom clusters occurred in more than 30% of the seizures—FLCPS:

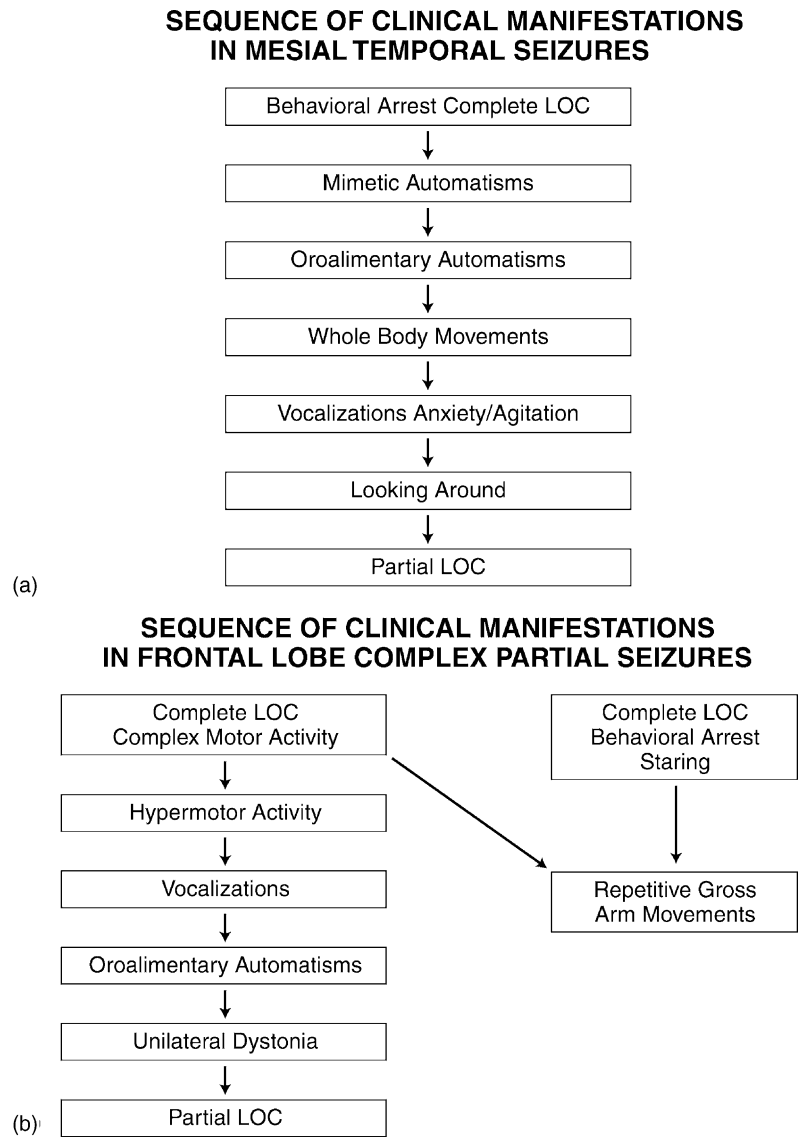

Fig. 2: (*a*) Two or more of these clinical manifestations occurred in 56% of evaluable seizures arising from the mesial temporal lobe origin (see 'MATERIALS AND METHODS' Section for more details). (*b*) Two or more of these clinical manifestations occurred in 59% of evaluable complex partial seizures arising from the frontal lobe (see 'MATERIALS AND METHODS' Section for more details).

repetitive upper movements and complete loss of consciousness (Fig. 3a); MTLE: alimentary automatisms, repetitive upper extremity movements, complete loss of consciousness, partial loss of consciousness, looking around and whole body movements (Fig. 3b). These symptom clusters also appeared earlier in MTLE compared to FLCPS.

DISCUSSION

FLCPS have been recognised for more than 30 years[21,22] and several investigators have described the semiology of seizures arising from various regions of the frontal lobe[2,3,5–7,13,14,26–28,33,34,36,37,39,46–48]. If seizure freedom is considered to be the 'gold standard' for documenting seizure origin within the margins of the resections, then the literature contains relatively few series of patients with FLCPS. In our study, we did not attempt to correlate seizure semiology with findings from invasive EEG recordings. Invasive recordings (depth or subdural electrodes) sample only limited portions of brain tissue; therefore, insufficient sampling can lead to difficulties with accurate localisation. This is especially problematic in the frontal lobe due to its large volume, rapidity of seizure propagation, varying spread patterns and predilection for spread to the opposite frontal lobe. To the best of our knowledge, this is the first study

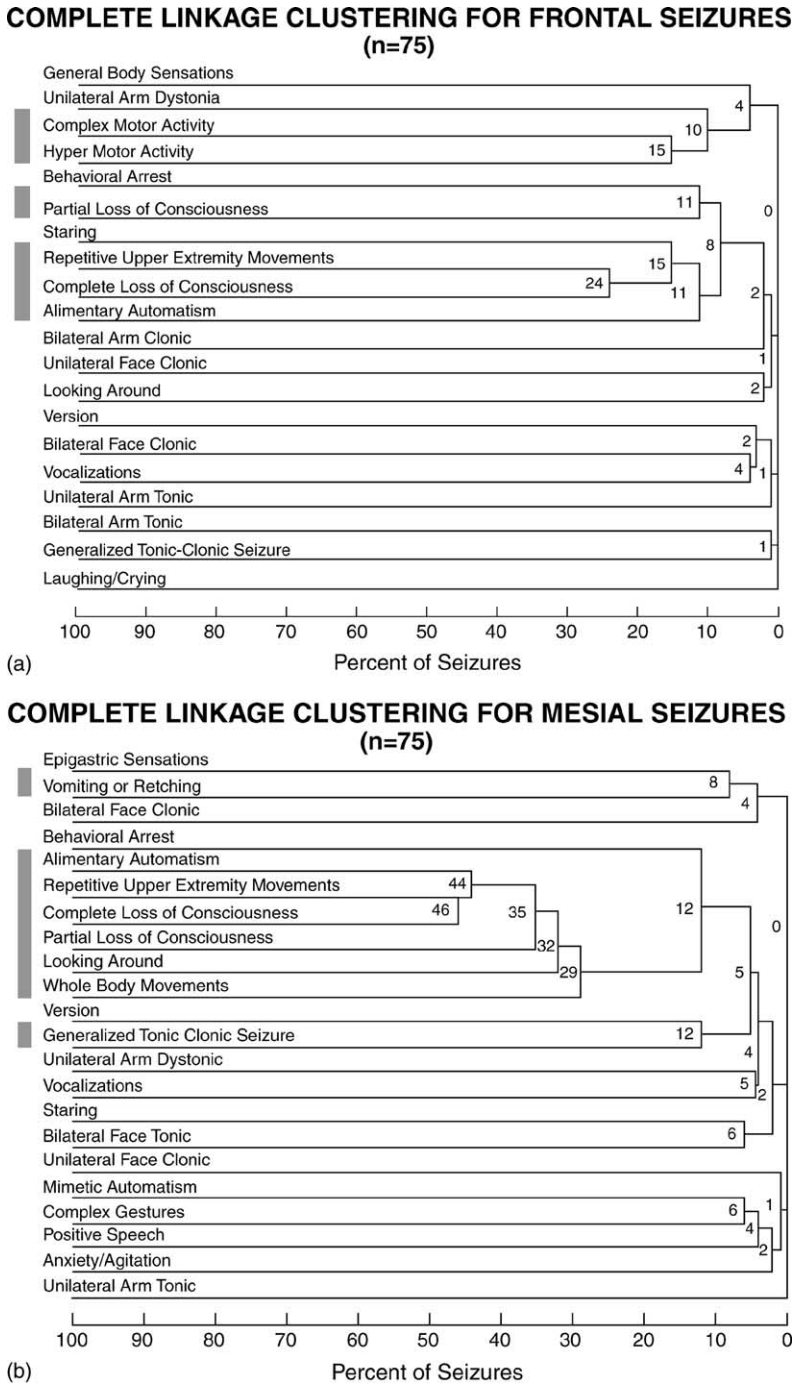

Fig. 3: (*a*) Cluster analysis results using complete linkage in FLCPS. The percentage of seizures in which these symptoms/signs clustered with one another is indicated by numbers next to the vertical lines (also shown on *X*-axis). The shaded vertical bars on the left highlight some of these clusters. (*b*) Cluster analysis results using complete linkage in seizures of mesial temporal lobe origin. The percentage of seizures in which these symptoms/signs clustered with one another is indicated by numbers next to the vertical lines (also shown on *X*-axis). The shaded vertical bars on the left highlight some of these clusters.

to apply statistical methods in identifying symptom clusters and sequences in a 'pure culture' of FLCPS, all of whom had class I seizure outcome following epilepsy surgery. This approach avoids the drawbacks of those studies that relied mainly on ictal EEG onset to determine the epileptogenic zone.

Rasmussen[23] described the clinical, EEG, radiological and pathological findings in 40 patients with non-tumoural epileptogenic lesions who underwent cortical excision of portions of the frontal lobe and remained seizure free for a minimum of 5 years. Seventeen (42%) of his patients reported no aura. Seven

(17%) had a somatosensory aura, and five patients (12%) each had epigastric, vague head and general body sensations as their auras. Absence or amnestic episodes were present in 14 (35%), automatisms in 12 (30%), focal sensorimotor attacks in 11 (27%), and generalised convulsions in 36 (90%) of their patients. Further details of seizure semiology could not be studied since this study antedated video-EEG technology.

Williamson *et al.*[24] reported 10 patients with FLE, 7 of who had surgical intervention and only 4/7 patients had good seizure control (not seizure freedom) after frontal lobectomy. They exhibited frequent, often nocturnal seizures with complex motor or sexual automatisms, vocalisation and high incidence of complex partial status epilepticus. Some seizures had bizarre symptomatology resembling psychogenic seizures. In our study, we did not find FLCPS to be much shorter than MTLE—this may have resulted from using clinical criteria rather than the ictal EEG to judge the end of the seizure. We noticed that 3/10 patients in Williamson's study had average seizure durations longer than 52 seconds[24]. Therefore, seizure duration does not appear to be an important distinction between FLCPS and MTLE.

Significant findings from our study are discussed under the following subsection.

Auras

In our group of FLCPS, auras occurred in only 15% of seizures, the commonest being vague general body sensation (11%). Although a higher proportion of frontal lobe patients (18–58%) have been reported to have auras in the literature[25–27], we included only those patients who verbally announced their aura, pressed the seizure alarm at seizure onset or recalled having an aura during the postictal interview (in other words, patients who did not experience an aura during their recorded seizures in the monitoring unit were excluded). We found that psychic, olfactory and auditory auras occurred only in MTLE, whereas an aura of a general body sensation occurred only in FLCPS. In Laskowitz *et al.*'s study[28], 5 out of 16 frontal lobe patients described an aura of fear or panic (psychic aura)—this could have resulted from spread of the ictal discharge to the temporal lobe.

Staring versus behavioural arrest

Delgado-Escueta *et al.*[29] drew attention to the lack of motionless stare at the onset of type II extra-temporal complex partial seizures. Saint-Hilaire *et al.*[30] studied 228 clinical manifestations of FLE during 63 seizures in 13 subjects subjected to surgery and found motionless staring in just 1.4% of frontal seizures. Laskowitz *et al.*[28] and Manford *et al.*[13] did not report staring in their frontal lobe cases. Many authors including Delgado-Escueta *et al.*[31] have used the term motionless stare and behavioural arrest interchangeably; we distinguished between these signs (see Appendix A). We noted that staring with eyelid retraction occurred in 31% of FLCPS, but only in 12% of mesial temporal seizures. Staring was most common in the first third of the seizure in frontal (91%), whereas they occurred during the first third (44%) and middle third (56%) in MTLE patients. Behavioural arrest occurred in one third of our FLCPS and MTLE patients and was seen during the first one third of the seizure in 96% of both groups.

Automatisms

More than 45 years ago, Penfield and Jasper[32] commented that frontal lobe automatisms differed from those associated with temporal lobe seizures. Several authors have emphasised the prominence of complex, semi-purposeful motor automatisms in FLCPS[33–37]. Williamson *et al.*[38–40] drew attention to the bilateral motor automatisms frequently involving both legs and arms with features of running, pelvic thrusts, frenetic, often bizarre behaviour and the appearance of oro-alimentary automatisms late in the seizure. In our series, perseverative automatisms and complex gestures occurred only in MTLE. Alimentary automatisms were more common and occurred earlier with MTLE. Repetitive upper extremity movements were also more common in MTLE, but there was a qualitative difference between our two groups. Upper extremity automatisms in MTLE involved the distal segments of the fingers and hands and were discrete, repetitive, co-ordinated and stereotyped. By contrast, upper extremity automatisms in FLCPS were coarse, irregular, complex, semi-purposive and involved the more proximal muscles of the shoulder, elbow as well as the hands. Complex motor automatisms such as laughing and crying were more frequent in our FLCPS group and occurred mainly during the first third of the seizure. Hypermotor activity characterised by complex movements involving the proximal segments of the limbs and trunk such as bicycling occurred only in FLCPS. This finding differs from that of Swartz[41] who noted that bipedal automatisms were not unique to frontal lobe seizures. This was probably the result of ictal spread from the temporal lobe to the dorso-lateral and mesial frontal regions. Kramer *et al.*[25] studied temporal and frontal complex partial seizures in 26 patients who had invasive EEG recordings. In seizures that did not spread or propagated

only to the homologous contralateral lobes, they noted that leg movements and hand posturing occurred only in frontal lobe seizures while oral automatisms occurred only in temporal lobe seizures. Ictal sexual automatisms were not observed in our study; this could be due to sample size.

Consciousness

Geier *et al*.[34] reported breaking off contact in all their 22 patients with FLE. The extent of loss of contact with the environment during a seizure varied widely, even in the same patient. Stores *et al*.[42] demonstrated impaired consciousness in all their cases, judged by the children's poor reactivity during their attacks and apparent difficulty in recalling them. In contrast, 8/10 patients in Williamson's study[39] claimed to be aware during FLCPS, but this was not verified by an examiner during the seizure. Both Wada[43] and Fusco *et al*.[44] have reported that FLCPS can occur without impairment of consciousness. Complete loss of consciousness occurred in 76% of FLCPS in the first third of the seizure in our series, but this was not statistically significant as compared to MTLE. Seizures arising from orbito-frontal, cingulate, anterior frontal and dorso-lateral frontal may produce loss of awareness. Ictal SPECT localisation to the non-motor fronto-polar or orbito-frontal region has been reported to be associated with impairment of consciousness, vocalisation and complex gestural automatisms[45]. Difficulty in detecting minor degrees of impairment and lack of a standardised method for assessing level of consciousness may account for differences in available studies.

Nocturnal occurrence and secondary generalisation

Although several investigators[5, 26] have described frontal lobe seizures as being primarily nocturnal, only 35% of our patients showed a nocturnal predominance of their seizures. One possible explanation is that patients with MTLE were usually taken off antiepileptic medications whereas FLCPS patients usually remained on their medications on account of their higher baseline seizure frequency. Several investigators[25, 28, 46] have reported that evolution to secondarily generalised tonic–clonic seizures is more common in FLCPS; however, only 5% of our patients with FLCPS had secondarily generalised seizures, in contrast to 25% of MTLE patients. Secondary generalisation was commoner ($P < 0.002$) and always occurred later during MTLE seizures. None of our FLCPS cases developed complex partial status epilepticus as was reported by other investigators[34, 38–40]. Bazil and Walczak[58] also found that secondary generalisation of temporal lobe complex partial seizures during sleep was more common compared with FLCPS which although activated by sleep, did not become secondarily generalised.

Relative time of onset of symptoms and signs

Analysing symptoms and signs that appear in the first one sixth of the seizure is likely to identify those which are most closely linked to the lobe of origin, whereas symptoms and signs beginning in the second or last third of the seizure probably represent spread of the ictal discharge to other brain regions. In our study, during the first one sixth of the seizure, abdominal aura, alimentary automatisms, repetitive upper extremity movements, looking around and mimetic automatisms were more common in MTLE, but staring with eyelid retraction, vocalisation and hypermotor seizure were more frequent in FLCPS. When the median symptom onset time was analysed, vocalisations, version, partial loss of consciousness, ictal speech and generalised tonic–clonic seizure occurred earlier with FLCPS, whereas alimentary automatisms and unilateral arm dystonia occurred later, perhaps due to spread of ictal discharge into the ipsilateral basal ganglia and/or temporal lobe.

The occurrence and sequencing of groups of symptoms/signs with an ordering diagram for FLCPS was seen in approximately 59% of FLCPS, but only in 29% of MTLE (Fig. 2a). On the other hand no significant differences between FLCPS and MTLE was observed when the symptom/sign pairs were compared with an ordering diagram for MTLE (Fig. 2b). Some of the FLCPS cases have complex motor and hypermotor activity, where as others are more bland with behavioural arrest and staring (Fig. 2b). Oro-alimentary automatisms and unilateral arm dystonia appeared later in the sequence in FLCPS cases.

Cluster analysis

Cluster analysis results (Fig. 3a and b) indicate those symptoms and signs which began during the first one third of the seizure in FLCPS and MTLE. In FLCPS, repetitive proximal upper extremity movements, complete loss of consciousness, complex motor and hypermotor activity clustered together, whereas in MTLE, oro-alimentary automatisms, repetitive distal upper extremity movements and complete loss of consciousness were clustered. These clusters also occurred earlier in MTLE which may partly be due to the fact that the mean number of symptoms/signs per seizure is greater for the mesial compared to the frontal group (7.93 vs. 4.74). We postulate that

these symptom clusters may indicate the ictal activation of functionally and/or anatomically related brain regions[10].

There are some limitations to the use of the cluster analysis. Within a cluster, we can make useful statements about the minimum frequency of occurrence of any symptom/sign pair, but there is little information available concerning the occurrence of three or more of the symptoms/signs. A second limitation is that the appearance of a dendogram is not unique. It is possible to rearrange the ordering of the symptoms in a dendogram to some degree without having an effect on the meaning of the diagram. Therefore, the displayed ordering of symptoms and perceived shapes in a dendogram do not always reflect systemic patterns or relationship among symptoms/signs.

The number of patients with MTLE and FLCPS in our study does not represent their relative proportions in the epileptic population, but are simply those patients who became seizure free after surgery and were collected over different but overlapping time periods. Future studies using larger number of patients may be able to adjust for the disparity in observed symptoms/signs per seizure in FLCPS and MTLE cases allowing for a meaningful statistical comparison of seizure types.

Although FLCPS and MTLE may sometimes overlap in their clinical manifestations, we have shown that statistical methods can identify symptom/sign clusters and sequences typical of FLCPS. If careful attention is given to the earliest symptoms/signs and the order of symptom/sign appearance, it should be possible to make this distinction clinically. Clinical semiology compares favourably with other methods of seizure localisation[50–57] and may be particularly helpful in patients without an obvious structural lesion on MRI scan. Prospective studies are needed to see whether these results can be validated in patients undergoing pre-surgical evaluation.

Appendix A

No.	Symptom and sign	Definition
Aura		
1	Somatosensory	Localised sensation of numbness, tingling, pain or cold.
2	Visual	Visual illusions or hallucinations
3	Auditory	Tinnitus, music and voices
4	Vertiginous	Dizziness and vertigo
5	Olfactory	Smell
6	Gustatory	Taste
7	General body sensations	Sensations referred to the entire body
8	Cephalic sensations	Sensation referred to the head
9	Epigastric sensations	
10	Fear	Scared sensation
11	Déjà vu	Altered perception of surroundings which seem strangely familiar
Motor signs		
12	Behavioural arrest	Immobile, fixed gaze without movement of the head or trunk, without eyelid retraction; oro-alimentary and hand automatisms may continue
13	Staring	Eyelid retraction not necessarily associated with an immobile gaze
14	Version	Forced, involuntary tonic or clonic movement of the head and eyes in a sustained and unnatural position.
15	Head or eyes turn left or right. Non-versive movement of the head and eyes	
16	Clonic movement of head	
17	Vertical head nodding	
18	Myoclonic jerking of head	
19	Unilateral face dystonic	
20	Unilateral face tonic	

Appendix A (*Continued*)

No.	Symptom and sign	Definition
21	Unilateral face clonic	
22	Unilateral arm dystonic	
23	Unilateral arm tonic	
24	Unilateral arm clonic	
25	Unilateral leg dystonic	
26	Unilateral leg tonic	
27	Unilateral leg clonic	
28	Bilateral face dystonic	
29	Bilateral face tonic	
30	Bilateral face clonic	
31	Bilateral arm dystonic	
32	Bilateral arm tonic	
33	Bilateral arm clonic	
34	Bilateral arm dystonic	
35	Bilateral leg tonic	
36	Bilateral leg clonic	
37	Generalised tonic–clonic seizure	
38	Hypermotor seizure	The main manifestation consists of complex movements involving the proximal segment of the limbs and trunk such as pedalling
39	Complex motor seizure	Complex elaborate body movements separate from No. 38 and 42
Automatisms		
40	Perseverative	Continuation of an action initiated prior to onset of the ictus
41	Alimentary	Chewing, lip smacking, swallowing
42	Repetitive upper extremity movements	Repetitive, distal fingering, fumbling, grasping, patting as well as proximal movements of the arms
43	Mimetic	Eye blinking, grimacing
44	Looking around	
45	Whole body movements	Turning over in bed, sitting up, walking
46	Complex gestures	
Speech		
47	Speech arrest	Inability to speak despite attempts to do so, with postictal recall
48	Positive speech	Identifiable spoken language
49	Vocalisations	Sustained or interrupted sound of no speech quality
Behaviour		
50	Anxiety/agitation	Anxious expression, with or without restlessness (subjective)
51	Aggression	Violence directed at a person
52	Laughing/crying	Laughter/weeping with appropriate effect
Consciousness		
53	Complete loss of consciousness	
54	Partial loss of consciousness	
55	EEG seizure	As recorded by subdural, scalp or special electrodes
Autonomic		
56	Vomiting or retching	Forced expulsion of gastric contents or attempts to do so
57	Dilated pupil	
Other		
58	Sniffing	

REFERENCES

1. Commission on Classification and Terminology of The International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989; **30**: 389.
2. Williamson, P. D. Frontal lobe epilepsy. Some clinical characteristics. *Advances in Neurology* 1992; **6**: 127.
3. Bancaud, J. and Talairach, J. Clinical semiology of frontal lobe seizures. *Advances in Neurology* 1992; **57**: 3.
4. Van Ness, P. C. Frontal and parietal lobe epilepsy. In: *The Treatment of Epilepsy: Principles and Practice* (Ed. E. Wyllie). Philadelphia, Lea and Febiger, 1993: pp. 525–532.
5. Williamson, P. D., Spencer, D. D., Spencer, S. S. *et al.* Complex partial seizures of frontal lobe origin. *Annals of Neurology* 1985; **18**: 497–504.
6. Quesney, L. F. Seizures of frontal lobe origin. In: *Recent Advances in Epilepsy*, Vol. 3. (Eds T. Pedley and B. Meldrum). London, Churchill Press, 1986: pp. 81–110.
7. Ludwig, B., Ajmone-Marson, C. and Van Buren, J. Cerebral seizures of probable frontal lobe origin. *Epilepsia* 1975; **16**: 141–156.
8. Bladin, P. F. and Woodward, J. Epilepsy and the frontal lobe. *Proceedings of the Australian Association of Neurology* 1974; **11**: 229–237.
9. Crandall, P. Developments in direct recordings from epileptogenic regions in the surgical treatment of partial epilepsies. In: *Epilepsy: Its Phenomenon in Man* (Ed. M. Brazier). New York, Academic Press, 1973: pp. 287–310.
10. Kotagal, P., Lüders, H. O., Williams, G., Nichols, T. R. and McPherson, J. Psychomotor seizures of temporal lobe onset: analysis of symptom clusters and sequences. *Epilepsy Research* 1995; **20**: 49–67.
11. Sayagi, S., Spencer, S. S., Scheyer, R., Katz, A., Mattson, R. and Spencer, D. D. Differentiation of temporal lobe ictal behavior associated with hippocampal sclerosis and tumors of temporal lobe. *Epilepsia* 1994; **35**: 737–742.
12. Mihara, T., Inoue, Y., Hiyoshi, T. *et al.* Localizing value of seizure manifestations of temporal lobe epilepsies and the consequences of analyzing their sequential appearance. *Japanese Journal of Psychiatry and Neurology* 1993; **47**: 175–182.
13. Manford, M., Fish, D. R. and Shorvon, S. D. An analysis of clinical seizure patterns and their localizing value in frontal and temporal lobe epilepsies. *Brain* 1996; **119**: 17–40.
14. Wieser, H. G. *Electroclinical Features of the Psychomotor Seizure*. Stuttgart/London, Fischer/Butterworths, 1983.
15. Obuchowski, N. A. Nonparametric analysis of clustered ROC curve data. *Biometrics* 1997; **53**: 170–180.
16. Cochran, W. G. *Sampling Techniques*, 3rd edn. New York, Wiley, 1977: pp. 64–66.
17. Williamson, P. D. Frontal lobe seizures: problems of diagnosis and classification. In: *Frontal Lobe Seizures and Epilepsies* (Eds P. Chauvel, A. V. Delgado-Escuetta, E. Halgren and J. Bancaud). New York, Raven Press, 1992: pp. 289–309. *Advances in Neurology* **57**.
18. Williamson, P. D., Thadani, V. M., Darcey, T. M., Spencer, D. D., Spencer, S. S. and Mattson, R. H. Occipital lobe epilepsy: clinical characteristics, seizure spread patterns and results of surgery. *Annals of Neurology* 1992; **31**: 3–13.
19. Williamson, P. D., Boon, P. A., Thadani, V. M. *et al.* Parietal lobe epilepsy: diagnostic considerations and results of surgery. *Annals of Neurology* 1992; **31**: 193–201.
20. Salanova, V., Andermann, F., Olivier, A., Rasmussen, T. and Quesney, L. F. Occipital lobe epilepsy: electro-clinical manifestations, electrocorticography, cortical stimulation and outcome in 42 patients treated between 1930 and 1991. *Brain* 1992; **115**: 1655–1680.
21. Penfield, W. and Jasper, H. *Epilepsy and the Functional Anatomy of the Human Brain*. Boston, Little Brown and Company, 1954.
22. Penfield, W. and Kristiansen, K. *Epileptic Seizure Patterns*. Springfield, IL, Thomas, 1951.
23. Rasmussen, T. Characteristics of a pure culture of frontal lobe epilepsy. *Epilepsia* 1983; **24**: 482–493.
24. Williamson, P. D., Spencer, D. D., Spencer, S. S., Novelly, R. A. and Mattson, R. H. Complex partial seizures of frontal lobe origin. *Annals of Neurology* 1985; **18**: 497–504.
25. Kramer, U., Riviello, J. R., Carmant, L., Black, M., Madsen, J. and Holmes, G. L. Clinical characteristics of complex partial seizures: a temporal versus a frontal lobe onset. *Seizure* 1997; **6**: 57–61.
26. Saygi, S., Katz, A., Marks, D. A. and Spencer, S. S. Frontal lobe partial seizures and psychogenic seizures: comparison of clinical and ictal characteristics. *Neurology* 1992; **42**: 1274–1277.
27. Salanova, V., Quesney, L. F., Rasmussen, T., Andermann, F. and Olivier, A. Reevaluation of surgical failures and the role of reoperation in 39 patients with frontal lobe epilepsy. *Epilepsia* 1994; **35** (1): 70–80.
28. Laskowitz, D. T., Sperling, M. R., French, J. A. and O'Connor, M. J. The syndrome of frontal lobe epilepsy: characteristics and surgical management. *Neurology* 1995; **45**: 780–787.
29. Delgado-Escueta, A. V., Bacsal, F. E. and Treiman, D. M. Complex partial seizures on closed circuit television and EEG: a study of 691 attacks in 79 patients. *Annals of Neurology* 1982; **11**: 292–300.
30. Saint-Hilaire, J. M., Giard, N., Veilleux, F. *et al.* Frontal compared to temporal lobe epileptic manifestations. Study with depth electrodes. *Epilepsia* 1988; **29** (2): 209.
31. Delgado-Escueta, A. V., Kunze, U., Waddel, G., Boxley, J. and Nadel, A. Lapses of consciousness and automatisms in temporal lobe epilepsy: a videotape analysis. *Neurology* 1977; **27**: 144–155.
32. Penfield, W. and Jasper, H. *Epilepsy and the Functional Anatomy of the Human Brain*. Boston, Little Brown and Company, 1954.
33. Geier, S., Bancaud, J., Talairach, J. *et al.* Automatism during frontal lobe epileptic seizures. *Brain* 1976; **99**: 447–458.
34. Geier, S., Bancaud, J. and Talairach, J. The seizures of frontal lobe epilepsy: a study of clinical manifestations. *Neurology (Minneapolis)* 1977; **27**: 951–958.
35. Tharp, B. R. Orbital frontal seizures. A unique electroencephalographic and clinical syndrome. *Epilepsia* 1972; **13**: 627–642.
36. Mihara, T., Tottori, T., Matsuda, K. *et al.* Analysis of seizure manifestation of pure frontal lobe origin. *Epilepsia* 1997; **38** (Suppl. 6): 42–47.
37. Waterman, K., Purves, S., Kosaka, B., Strauss, E. and Wada, J. An epileptic syndrome caused by mesial frontal lobe foci. *Neurology* 1987; **37**: 577–582.
38. Williamson, P. D., Spencer, D. D., Spencer, S. S., Novelly, R. A. and Mattson, R. H. Complex partial status of frontal lobe origin: a depth electrode study. *Epilepsia* 1983; **24**: 260.
39. Williamson, P. D., Spencer, D. D., Spencer, S. S., Novelly, R. A. and Matson, R. H. Complex partial seizure of frontal lobe origin. *Annals of Neurology* 1985; **18** (4): 497–504.
40. Williamson, P. D., Spencer, D. D., Spencer, S. S., Novelly, R. A. and Matson, R. H. Complex partial status epilepticus: a depth electrode study. *Annals of Neurology* 1985; **18** (6): 647–654.
41. Swartz, B. E. Electrophysiology of bimanual-bipedal automatisms. *Epilepsia* 1994; **35** (2): 264–274.
42. Stores, G., Zaiwalla, Z. and Bergel, N. Frontal lobe complex partial seizures in children: a form of epilepsy at particular risk of misdiagnosis. *Developmental Medicine and Child Neurology* 1991; **33**: 998–1009.

43. Wada, J. A. Predominantly nocturnal recurrence of intensely affective vocal and facial expression associated with powerful bimanual, bipedal, and axial activity as ictal manifestations of mesial frontal lobe epilepsy. In: *Advances in Epileptology. XVIIth Epilepsy International Symposium* (Eds J. Manelis, E. Bental, J. N. Loeber and F. E. Dreifuss). New York, Raven Press, 1989.
44. Fusco, L., Iani, C., Faedda, M. T. *et al.* Mesial frontal lobe epilepsy: a clinical entity not sufficiently described. *Journal of Epilepsy* 1990; **3**: 123–135.
45. Harvey, A. S., Hopkins, I. J., Bowe, J. M., Cook, D. J., Sheild, L. K. and Berkovic, S. F. Frontal lobe epilepsy: clinical seizure characteristics and localization with ictal 99m TcHMPAO SPECT. *Neurology* 1993; **43**: 1966–1980.
46. Delgado-Escueta, A. V., Swartz, B. E., Meldonado, H. M., Walsh, G., Rand, R. W. and Halgren, I. E. *Complex Partial Seizure of Frontal Lobe Origin—Presurgical Evaluation of Epilepsies* (Eds H. G. Wieser and C. E. Elger). 1987.
47. Bancaud, J. and Talairach, J. Clinical semiology of frontal lobe seizures. In: *Advances in Neurology*, Vol. 57 (Eds A. V. Chauvel, Delgado-Escuetta *et al*.). New York, Raven Press, 1992: pp. 3–58.
48. Williamson, P. D., Weiser, H. G. and Delgado-Escueta, A. V. Clinical characteristics of partial seizures. In: *Surgical Treatment of the Epilepsies* (Ed. J. Engel Jr). New York, Raven Press, 1987: pp. 101–120.
49. Salanova, V., Morris, H. H., Van Ness, P., Kotagal, P., Wyllie, E. and Lüders, H. Frontal lobe seizures: electroclinical syndromes. *Epilepsia* 1995; **36**: 16–24.
50. Bleasel, A., Kotagal, P., Kankirawatana, P. *et al.* Lateralizing value and semiology of ictal limb posturing and version in temporal lobe and extratemporal lobe epilepsy. *Epilepsia* 1997; **38**: 168–174.
51. Chee, M., Kotagal, P., Van Ness, P. *et al.* Lateralizing signs in intractable partial epilepsy: blinded multiple-observer analysis. *Neurology* 1993; **43**: 2519–2525.
52. Spencer, S. S., So, N. K., Engel, J. Jr, Williamson, P. D., Levesque, M. F. and Spencer, D. D. Depth electrodes. In: *Surgical Treatment of the Epilepsies* (Ed. J. Engel Jr). New York, Raven Press, 1993: pp. 359–376.
53. Bautista, R. E., Spencer, D. D. and Spencer, D. D. EEG findings in frontal lobe epilepsies. *Neurology* 1998; **50**: 1765–1771.
54. Savic, I., Thorell, J. O. and Roland, P. (11C)Flumazenil positron emission tomography visualizes frontal epileptogenic regions. *Epilepsia* 1995; **36**: 1225–1232.
55. Swartz, B. E., Khonsari, A., Brown, C., Mandelkern, M., Simpkins, F. and Kristakumptorn, T. Improved sensitivity of 18-FDG-positrin emission tomography scans in frontal and "frontal plus" epilepsy. *Epilepsia* 1995; **36**: 388–395.
56. Da Silva, E. A., Chugani, D. C., Muzik, O. and Chugani, H. T. Identification of frontal lobe epileptic foci in children using positron emission tomography. *Epilepsia* 1997; **38**: 1198–1208.
57. Ryvlin, P., Bouvard, S., Le Bars, D. *et al.* Clinical utility of flumazenil PET versus (18F) flurodeoxyglucose-PET and MRI in refractory partial epilepsy. A prospective study in 100 patients. *Brain* 1998; **121**: 2067–2081.
58. Bazil, C. W. and Walczak, T. S. Effects of sleep and sleep stage on epileptic and nonepileptic seizures. *Epilepsia* 1997; **38**: 56–62.