Acta Neurol Scand 1999: 99: 219–224
Printed in UK – all rights reserved

ACTA NEUROLOGICA
SCANDINAVICA
ISSN 0001-6314

Idiopathic generalized epilepsies with versive or circling seizures

Aguglia U, Gambardella A, Le Piane E, Messina D, Russo C, Oliveri RL, Zappia M, Quattrone A. Idiopathic generalized epilepsies with versive or circling seizures.
Acta Neurol Scand 1999: 99: 219–224. © Munksgaard 1999.

Objectives – To describe the electroclinical features of the idiopathic generalized epilepsies (IGEs) with versive or circling seizures. *Methods* – Sixteen patients with versive or circling seizures and interictal electroclinical features of IGE were studied. Patients with insufficient clinical or imaging data, with a follow-up period less than 1 year or with partial seizures in addition to the versive or circling ones were excluded from the study. All patients underwent full interictal clinical and neurophysiological studies. The EEG patterns of 13 versive or circling seizures from 4 patients were also analyzed. *Results* – A specific IGE syndrome was recognized in 9 out of the 16 patients (56%). More specific, 1 patient had childhood absence epilepsy (CAE), 4 had juvenile absence epilepsy (JAE), and 4 had juvenile myoclonic epilepsy (JME). No specific IGE syndrome was recognizable in the remaining 7 patients (44%). These 7 patients had a juvenile epileptic syndrome (mean age at onset of seizures was 15.7 years) characterized by versive or circling seizures followed or not by generalized tonic–clonic fits. Three main EEG patterns were identified during versive or circling seizures: 1) generalized spike-and-wave discharges at 3–4 cps; 2) generalized polyspike-and-wave discharges at 1 to 2.5 cps beginning with generalized fast activity at 12–14 cps, and 3) generalized spike-and-wave discharges at 3–4 cps intermingled with fast activity at 12–14 cps. Most patients had good response to treatment on a single drug regimen (mainly valproic acid). *Conclusions* – Versive or circling seizures may occur in the context of an IGE. Although many individuals share the features of different IGE syndromes including CAE, JAE and JME, a consistent number of patients, who show circling or versive seizures solely, remain without a specific syndromic diagnosis. When occurring in the context of IGE, circling or versive seizures do not worsen the prognosis.

U. Aguglia, A. Gambardella, E. Le Piane, D. Messina, C. Russo, R. L. Oliveri, M. Zappia, A. Quattrone

Institute of Neurology, School of Medicine, University of Catanzaro, Italy

Key words: absence seizures; circling seizures; idiopathic generalized epilepsy; versive seizures

Dr Umberto Aguglia, Università degli Studi, Clinica Neurologica, Policlinico Materdomini, Via T. Campanella, 88100 Catanzaro, Italy

Accepted for publication November 2, 1998

It has been suggested that the association of versive or circling seizures with generalized, interictal 3-cps spike-and-wave discharges represents a distinct and benign syndrome among the idiopathic generalized epilepsies (IGE) (1). Nonetheless, most of patients reported by Gastaut et al. (1) had associated non-versive seizures such as absences and myoclonic jerks, thus suggesting that versive or circling seizures could be observed in the context of specific IGE syndromes. Indeed, circling seizures have been found in association with well-recognized IGE, such as juvenile myoclonic epilepsy (2). Furthermore, according to the neurobiological approach (3), it may be questioned whether the occurrence of these "focal" manifestations in IGE have any prognostic significance, especially in terms of responsiveness to the medication.

In addition, although these seizures have been classically reported as strongly lateralized manifestations associated with generalized symmetrical and synchronous spike-and-wave discharges, their ictal EEG patterns have not been fully elucidated.

In order to answer these questions, we studied a group of 16 patients selected solely on the basis of IGE associated with versive or circling seizures.

Patients and methods

During the past 9 years, we found 26 patients who met the following criteria: 1) seizures characterized

Table 1. Clinical data of 16 patients with versive or circling seizures and rhythmic bilateral 3 cps spike-and-wave interictal discharges

Patient No.	Sex/Age	Type IGE	Fam. hist.	Pers. hist.	Versive seizures (age at onset)	Additional seizures (age at onset)	Additional interictal EEG abnormalities	Prognosis	Treatment
1	F/19 yrs	CAE	+		Left V (8 yrs)	A (8 yrs)		Recovered	None
2	F/26 yrs	JAE	+		Left C (13 yrs)	A (11 yrs), TC*(24yrs)		Good	VPA
3	F/29 yrs	JAE			Right V (18 yrs)	A (16 yrs), TC (10 yrs)	Spikes at Fp1, F3, F4	Resistant	VPA + PB + LMG
4	F/32 yrs	JAE	+	FC	Right C or V (15 yrs)	A (15 yrs)		Good	VPA
5	M/11 yrs	JAE	+		Right V (11 yrs)	A (11 yrs)	Spikes at Fp1, F3, Fp2, F4	Good	VPA
6	M/31 yrs	JME			Left C or V (12 yrs)	BMJ (12 yrs), TC (28 yrs)		Good	VPA
7	F/31 yrs	JME			Left C or V (7 yrs)	BMJ (19 yrs), TC*(19 yrs)		Good	PB
8	M/45 yrs	JME			Right C or V (14 yrs)	BMJ (14 yrs), A (14)	Spikes at Fp1, F3, Fp2, F4	Good	PB
9	F/25 yrs	JME			Left V (16 yrs)	BMJ (16 yrs)	Spikes at Fp1, F3, F4	Good	ACZ
10	M/18 yrs	UC			Right V (17 yrs)			Good	VPA
11	M/20 yrs	UC		FC	Right V (11 yrs)			Good	VPA
12	F/21 yrs	UC	+		Right V (11 yrs)	TC* (13 yrs)	ILS+	Good	VPA
13	F/57 yrs	UC			Right V (23 yrs)		ILS+	Good	VPA
14	M/39 yrs	UC	+		Right C (20 yrs)			Recovered	None
15	M/21 yrs	UC		FC	Right C (12 yrs)			Good	VPA
16	M/18 yrs	UC	+		Left V (16 yrs)			Good	VPA

ACZ = acetazolamide; A = absence seizures, BMJ = bilateral myoclonic jerks at awakening; C = circling; CAE = childhood absence epilepsy; CBZ = carbamazepine; F = woman; Fam. hist. = familial history for febrile convulsions or epilepsy; FC = *febrile convulsions*; IGE = *idiopathic generalized epilepsy*; ILS+ = photosensitivity; JAE = juvenile absence epilepsy; JME = juvenile myoclonic epilepsy; LMG = lamotrigine; M = man; PB = phenobarbital; Pers. hist. = personal history; TC = tonic–clonic seizures; UC = unclassified; V = version; VPA = *valproic acid*; *yrs = years*; * = seizures due to antiepileptic drug withdrawal.

by paroxysmal conjugate eye and head turning (versive seizures), or by adversion of one half of the body (circling seizures), associated with or without other generalized seizures; and 2) interictal electroclinical features consistent with the diagnosis of IGE (4). The criteria for exclusion were: 1) insufficient clinical or imaging data, 2) association with partial seizures in addition to the versive or circling ones, 3) follow-up period <1 year at our Institute, 4) poor compliance as assessed by periodic monitoring of the plasma concentrations of antiepileptic drugs (AED). Interictal focal epileptiform abnormalities were not considered as evidence of partial epilepsy. These patients were selected from 910 consecutive referrals to our Institute from January 1988 to December 1997.

A detailed history of the type and frequency of seizures was obtained from patients, parents and other relatives at the time of the investigation, and from a review of the patients' medical records. Special attention was paid to discovering a familial history of febrile convulsions (FC) or epilepsy, personal medical history, age at onset of epilepsy, classification and frequency of each type of seizure, and evolution and response to treatment. Neurological, neuropsychological (WAIS) and psychiatric examinations, as well as conventional brain MRI (0.5 T) were performed in all patients. In all patients, we scheduled at least 1 follow-up visit every 3–6 months after the AED treatment was initiated. Each visit included: neurological examination, survey of seizure frequency by means of a purpose-made calendar, routine blood chemistries, and monitoring of AED plasma concentrations. Regarding the prognosis, patients were considered to be recovered from epilepsy if they were seizure-free during at least 2 years after AED discontinuation, or to have a good or poor prognosis if they had or not ≥70% frequency reduction of seizures after appropriate AED treatment. The follow-up period averaged 3.3 years (range, 1 to 9 years). Awake and sleep EEG recordings were carried out in all patients (mean, 4 EEG recordings/patient; range, 2 to 9). Thirteen versive or circling seizures from 4 patients were also recorded.

Results

Clinical data

Ten of the 26 patients were excluded from the study because of insufficient clinical or imaging data (3 patients), association with partial seizures in addition to the versive or circling ones (5 patients), follow-up period less than 1 year at our Institute (3 patients) or poor compliance (2 patients). The remaining 16/26 patients constituted the study group. These 16 patients represented 1.75% of the 910 unselected patients, and 10.4% of the 154 patients with a diagnosis of IGE referred to our Institute during a 9-year period. The clinical and EEG findings of the patients are detailed in Table 1. Seven/16 (41%) patients had a history of febrile convulsions or epilepsy in their first-degree relatives. No patient had a history of a major disease. A personal history of simple FC was reported by 3 patients.

Versive or circling seizures occurred during the

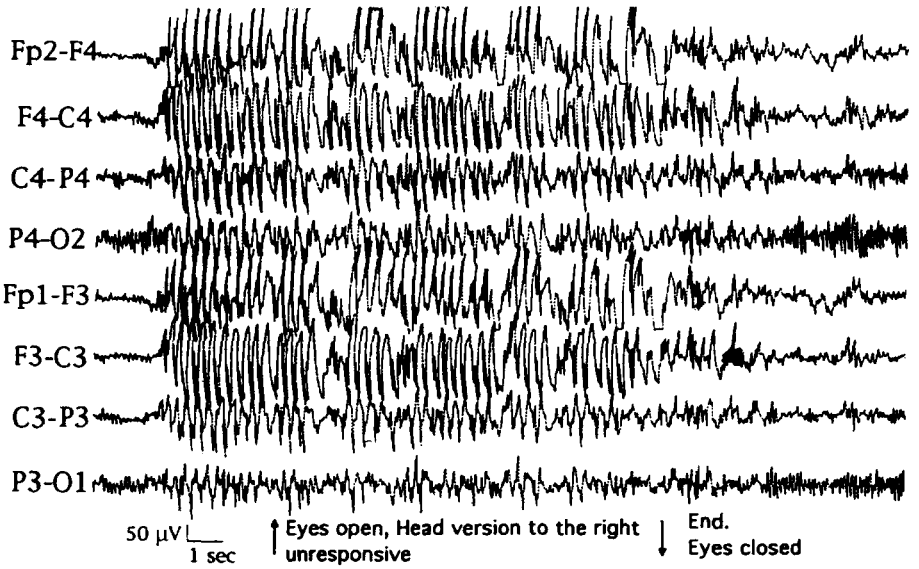

Fig. 1. Patient # 3. EEG pattern type 1. Generalized and rhythmic spike-and-wave discharges at 3 cps lasting 14 s, associated with unresponsiveness, eyes open, and head version to the right side.

evolution of their epilepsy in all patients. The mean age at onset of epilepsy was 14 years (range: 8 to 23 years). More specifically, 9/16 patients had versive seizures, 3 had circling seizures, and the remaining 4 patients showed both versive and circling seizures (Table 1). Paroxysmal adversion or gyration was always toward the same side in a given patient (Table 1). At onset of seizures, vocalization occurred in 6 patients (#4, 10, 12, 14, 15, and 16). Loss of consciousness always occurred during long-lasting (5 to 20 s) seizures. The degree of impairment of consciousness was difficult to ascertain during the shorter episodes. Circling seizures were usually linked to generalized tonic–clonic manifestations. Postictal paralysis never occurred. Seizure frequency before treatment ranged from 3 per week to 0.4 per year.

Nine/16 (51%) patients also displayed additional seizures, specifically absences (5 patients), bilateral myoclonic jerks at awakening (4 patients), and generalized tonic–clonic seizures (2 patients). At the time of this study, 13 patients were seizure free or had a 70% frequency-reduction of their seizures on a single drug regimen (valproic acid, 11 patients; phenobarbital, 1 patient; and acetazolamide, 1 patient); 1 patient had refractory tonic–clonic seizures despite a combination of 3 drugs (sodium valproate + phenobarbital + lamotrigine). More important, 2 patients had no antiepileptic treatment (Table 1): 1 (patient #1) had 3 versive seizures during her 6-year history of epilepsy, then she stopped treatment (valproic acid) and remained seizure free during the 4 years of the follow-up period; the other (patient #14) had 4 circling seizures during his 11-year history of epilepsy, and remained seizure free during the 8 years of the follow-up period without treatment, although his last sleep EEG recording (at the end of 7th year of the follow-up) continued to show generalized 3-cps spike-and-wave discharges.

Neurological and neuropsychological examinations were normal in all patients. Mild psychiatric disturbances (irritability and depression) were seen in 3 (patients #1, 3, and 14). Brain MRI study was normal in all patients.

Neurophysiological data

Interictal background activity was normal in all patients. Waking interictal generalized 3-cps spike-and-wave discharges were detected in all patients. Hyperventilation facilitated the spike-and-wave discharges in most patients (#1–5, 8, 16, 14). A photoparoxysmal response occurred in 2 patients (Table 1). Focal epileptiform discharges localized on the frontal leads were found in 4 patients (Table 1). There was, however, no relation between focal spikes and the side of the version (Table 1). These focal spikes never heralded the generalized discharges, and their location tended to change during the same or subsequent recordings. During non-REM sleep recordings, interictal epileptiform discharges were increased compared with wakefulness in all patients, and consisted of brief (0.5–2 s) discharges of generalized spike-and-waves (10 patients) or polyspike-and-waves (6 patients). Runs of subclinical, fast ($\geq$10 cps) discharges never occurred.

Thirteen versive or circling seizures were recorded from 4 patients (#3, 4, 12, and 14) and

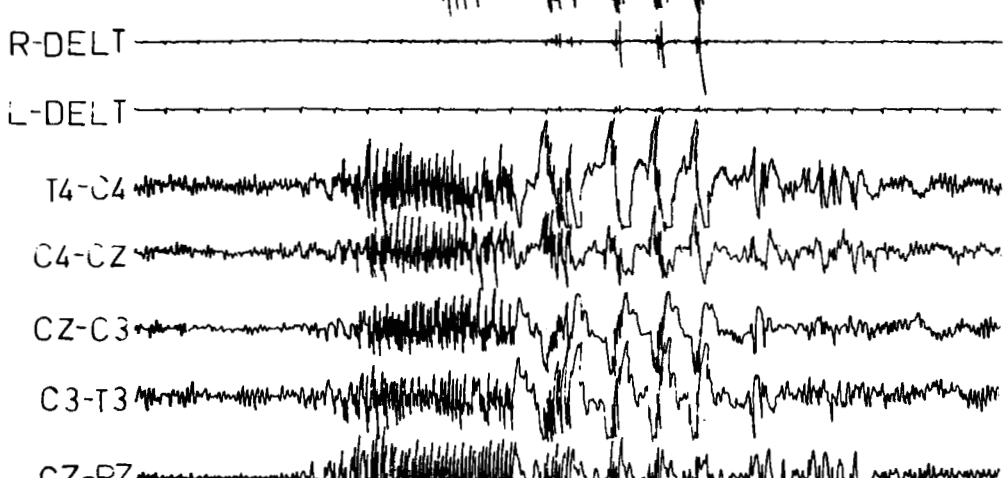

Fig. 2. Patient # 4. EEG pattern type 2. The beginning of the seizure is characterized by generalized polyspike discharges at 12 cps lasting 4 s associated with unresponsiveness and myoclonic jerks of the axial muscles (see EMG of the myloioideus muscle) leading to vocalizations and gyration toward the right side. This fast activity is followed by irregular, generalized, polyspike-and-wave discharges at 1 cps, lasting 7 s and corresponding to myoclonic jerks in both the myloioideus and right deltoid muscles.

three main ictal EEG patterns emerged: 1) generalized spike-and-wave discharges at 3 to 4 cps (Fig. 1) associated with unresponsiveness and slow version of the head and eyes lasting 7 to 15 s (2 seizures in patients #3 and 14); 2) generalized polyspike-and-wave discharges at 1 to 2.5 cps beginning with a generalized polyspike discharge (fast activity at 12–14 cps lasting 0.5–5 s) (Fig. 2), associated with unresponsiveness and asymmetrical myoclonic jerks leading to version or gyration of one half of the body, lasting 4 to 12 s (7 seizures in patients #3, 12, and 14); and 3) generalized spike-and-wave discharges, intermingled with fast activity at 12–14 cps (Fig. 3), associated with unresponsiveness and myoclonic jerks leading to version (4 seizures in patient #4).

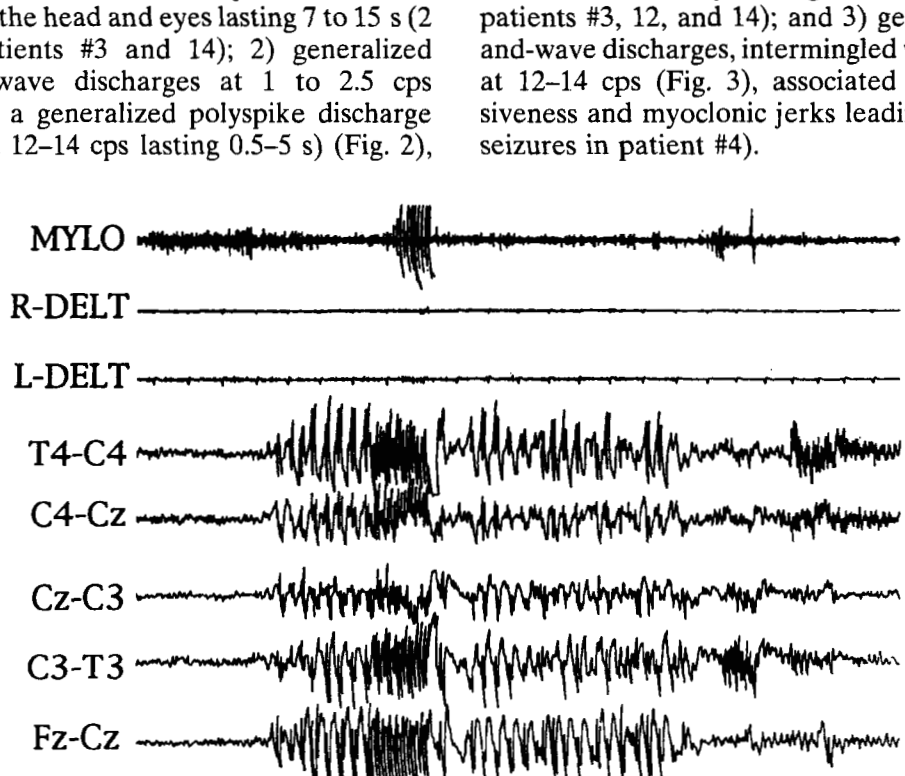

Fig. 3. Patient # 4. EEG pattern type 3. Generalized spike-and-wave discharges at 3–4 cps associated with unresponsiveness and intermingled with fast activity at 14 cps corresponding to myoclonic jerks of the myloioideus muscle, and leading to vocalizations with quick version toward the right side.

Nosological classification

A specific syndromic IGE category (4) associated with the versive or circling seizures was recognized in 9/16 (56%) patients (Table 1). Indeed, 1 patient (#1) had childhood absence epilepsy (CAE), 4 patients (#2, 3, 4, and 5) had juvenile absence epilepsy (JAE) and 4 patients (#6, 7, 8, and 9) had juvenile myoclonic epilepsy (JME).

The remaining 7/16 (44%) patients did not fit within a recognized syndromic category. They had a juvenile epileptic syndrome (mean onset of seizures was at 15.7 ± 4.7 years with a range from 11 to 23 years) characterized by versive or circling seizures alone (patients #10, 13, and 16) or associated with generalized tonic–clonic manifestations (patients #11, 12, 14, and 15). These seizures were usually few in number (0.4 to 10 per year), did not occur on awakening or in the evening period of relaxation, and were responsive to treatment. Sleep deprivation was not a common precipitant of seizures (Table 1).

Discussion

Both neurophysiological and clinical findings demonstrated that patients with versive or circling seizures may conform to the IGE syndromes of the ILAE Classification of Epilepsies (4). Nevertheless, a substantial group of patients without a specific syndromic IGE diagnosis under the current ILAE classification were also identified. Regardless of the type of IGE, a favorable response to treatment was usually seen, suggesting that circling or versive seizures do not worsen the prognosis of the underlying IGE.

On EEG recordings, we identified different ictal patterns accompanying versive or circling seizures. Of interest, the pattern of polyspike generalized activity preceding the generalized polyspike-and-waves or the more complex pattern with sequences of generalized 3–4 cps spike-and-waves intermingled with fast activity were previously recorded in IGE patients with persisting absences (5–7). Michelucci et al. (7) suggested that these ictal features indicate resistance to treatment, but this was not confirmed in the present series.

We also found that versive or circling seizures may represent the main clinical feature of a juvenile form of IGE that does not fit into any specific IGE syndrome (4). In this unclassified form of IGE, seizures were usually few in number and responsive to treatment; whereas sleep deprivation, awakening, or the evening period of relaxation were not precipitants of seizures. These characteristics, as well as onset during juvenile ages and the difficult syndromic classification, make these patients similar to those reported by Reutens & Berkovic (8) who showed only generalized tonic–clonic seizures that did not occur on awakening. All these EEG and clinical data provide further evidence for phenotypic overlap between the syndromes of adolescent generalized epilepsy (8).

The association of interictal generalized discharges with versive or circling seizures, however, always requires special consideration. It is well-known, in fact, that versive or circling seizures may occur in frontal lobe epilepsy (FLE) (9–12) and that FLE may mimic IGE (13–15). Nonetheless, patients with FLE frequently have additional seizures such as falling, motor automatisms, subjective sensations or other partial attacks (9, 10, 15–17). According to the selection criteria, none of our patients had additional partial seizures. Moreover, the generalized EEG discharges in FLE are usually preceded by focal epileptiform discharges, configuring the so-called "secondary bilateral synchrony" (18). In our 4 patients with focal epileptiform abnormalities, as already seen in patients with IGE (19, 20), these focal spikes never heralded the generalized discharges, and their location tended to change during the same or subsequent recordings.

Finally, the reason why some patients with IGE may display focal electroclinical manifestations still remains to be elucidated. Some authors (20) suggested that the focal features detected in IGE might originate from cerebral microdysgenetic foci, as described in post-mortem examinations of patients with different IGE syndromes (21, 22). On the other hand, a functional imbalance of generalized cerebral hyperexcitability was advocated to explain interhemispheric differences in photosensitive epilepsies (23, 24), or rare cases of absence status with unilateral predominance of spike-and-wave discharges (25). Our data, however, do not favor either hypothesis.

In conclusion, versive or circling seizures may occur in the context of an IGE. Although many individuals share the features of different IGE syndromes including CAE, JAE and JME, a consistent number of patients, who show circling or versive seizures solely, remain without a specific syndromic diagnosis. Furthermore, when occurring in the context of IGE, circling or versive seizures do not worsen the prognosis.

References

1. Gastaut H, Aguglia U, Tinuper P. Benign versive or circling epilepsy with bilateral 3-cps spike-and-wave discharges in late childhood. Ann Neurol 1986;**19**:301–3.
2. Lancman ME, Asconapé JJ, Golimstok A. Circling seizures in a case of juvenile myoclonic epilepsy. Epilepsia 1994;**35**:317–18.
3. Berkovic SF, Andermann F, Andermann E, Gloor P.

Concepts of absence epilepsies: discrete syndromes or biological continuum? Neurology 1987;**37**:993–1000.
4. Commission on classification and terminology of the International League Against Epilepsy. Proposal for classification of epilepsy and epileptic syndromes. Epilepsia 1989;**30**:389–99.
5. Gastaut H, Zifkin BG, Mariani E, Salas Puig J. The long-term course of primary generalized epilepsy with persisting absences. Neurology 1986;**36**:1021–8.
6. Panayiotopoulos CP, Chroni E, Dascalopoulos C, Baker A, Rowlinson S, Walsh P. Typical absence seizures in adults: clinical, EEG, video-EEG findings and diagnostic syndromic considerations. J Neurol Neurosurg Psychiatry 1992;**55**:1002.
7. Michelucci R, Rubboli G, Passarelli D et al. Electroclinical features of idiopathic generalized epilepsy with persisting absences in adult life. J Neurol Neurosurg Psychiatry 1996;**61**:471–7.
8. Reutens DC, Berkovic SF. Idiopathic generalized epilepsy of adolescence: are the syndromes clinically distinct? Neurology 1995;**45**:1469–76.
9. Geier S, Bancaud J, Talairach J, Bonis A, Skila G, Enjelvin M. The seizures of frontal lobe epilepsy. Neurology 1977;**27**:951–8.
10. Rasmussen T. Characteristics of a pure culture of frontal lobe epilepsy. Epilepsia 1983;**24**:482–93.
11. Ochs R, Gloor P, Quesney F, Ives J, Olivier A. Does head-turning during a seizure have a lateralizing or localizing significance? Neurology 1984;**34**:884–90.
12. Meshram CM, Prabhakar S, Sawhney IMS, Dhand UK, Chopra JS. Rotatory seizures. Epilepsia 1992;**33**:522–6.
13. Bancaud JJ, Talairach J, Morel P et al. Generalized epileptic seizures elicited by electrical stimulation of the frontal lobe. Electroencephalogr Clin Neurophysiol 1974;**37**:275–82.
14. Roger J, Bureau M. Distinctive characteristics of frontal lobe epilepsy versus idiopathic generalized epilepsy. In: Chauvel P, Delgado-Esqueta AV, Halgren E, Bancaud J, eds. Frontal lobe seizures and epilepsies, Adv Neurol 57. New York: Raven Press, 1992:399–410.
15. Dalla Bernardina B, Cantele P, Fontana E et al. Epilessia parziale frontale con quadro elettroclinico evocante una forma generalizzata primitiva. Boll Lega It Epil 1988;**62/63**:267–8.
16. Laskowitz DT, Sperling MR, French JA, O'Connor MJ. The syndrome of frontal lobe epilepsy: characteristics and surgical management. Neurology 1995;**45**:780–7.
17. Quesney LF, Constain M, Fish DR, Rasmussen T. The clinical differentiation of seizures arising in the parasagittal and anterolaterodorsal frontal convexities. Arch Neurol 1990;**47**:677–9.
18. Gastaut H, Zifkin B, Magaudda A, Mariani E. Symptomatic partial epilepsies with secondary bilateral synchrony: differentiation from symptomatic generalized epilepsies of the Lennox–Gastaut type. In: Wieser HG, Elger CE, eds. Presurgical evaluation of epilepsies. Berlin: Springer Verlag, 1987:308–16.
19. Aliverti V, Grunewald R, Panayiotopoulos C, Chroni E. Focal electroencephalographic abnormalities in juvenile myoclonic epilepsy. Epilepsia 1994;**35**:297–301.
20. Lombroso CT. Consistent EEG focalities detected in subjects with primary generalized epilepsies monitored for two decades. Epilepsia 1997;**38**:797–812.
21. Meencke HJ, Janz D. The significance of microdysgenesia in primary generalized epilepsy: an answer to the considerations of Lyon and Gastaut. Epilepsia 1985;**26**:368–71.
22. Meencke HJ. Pathological findings in childhood absence epilepsy. In: Duncan JS, Panayiotopoulos CP, eds. Typical absences and related epileptic syndromes. New York: Churchill Livingstone, 1995:122–32.
23. Wilkins AJ, Binnie CD, Darby CE. Interhemispheric differences in photosensitive epilepsy I. Pattern sensitivity threshold. Electroencephalogr Clin Neurophysiol 1981;**52**:461–8.
24. Binnie CD, Wilkins AJ, Dekorte RA. Interhemispheric differences in photosensitive epilepsy II. Intermittent photic stimulation. Electroencephalogr Clin Neurophysiol 1981;**52**:469–72.
25. Aguglia U, Tinuper P, Farnarier G, Gastaut H. Etat d'absence à prédominance EEG unilatérale (à propos d'une observation privilegiée). Rev EEG Neurophysiol 1984;**14**:241–6.