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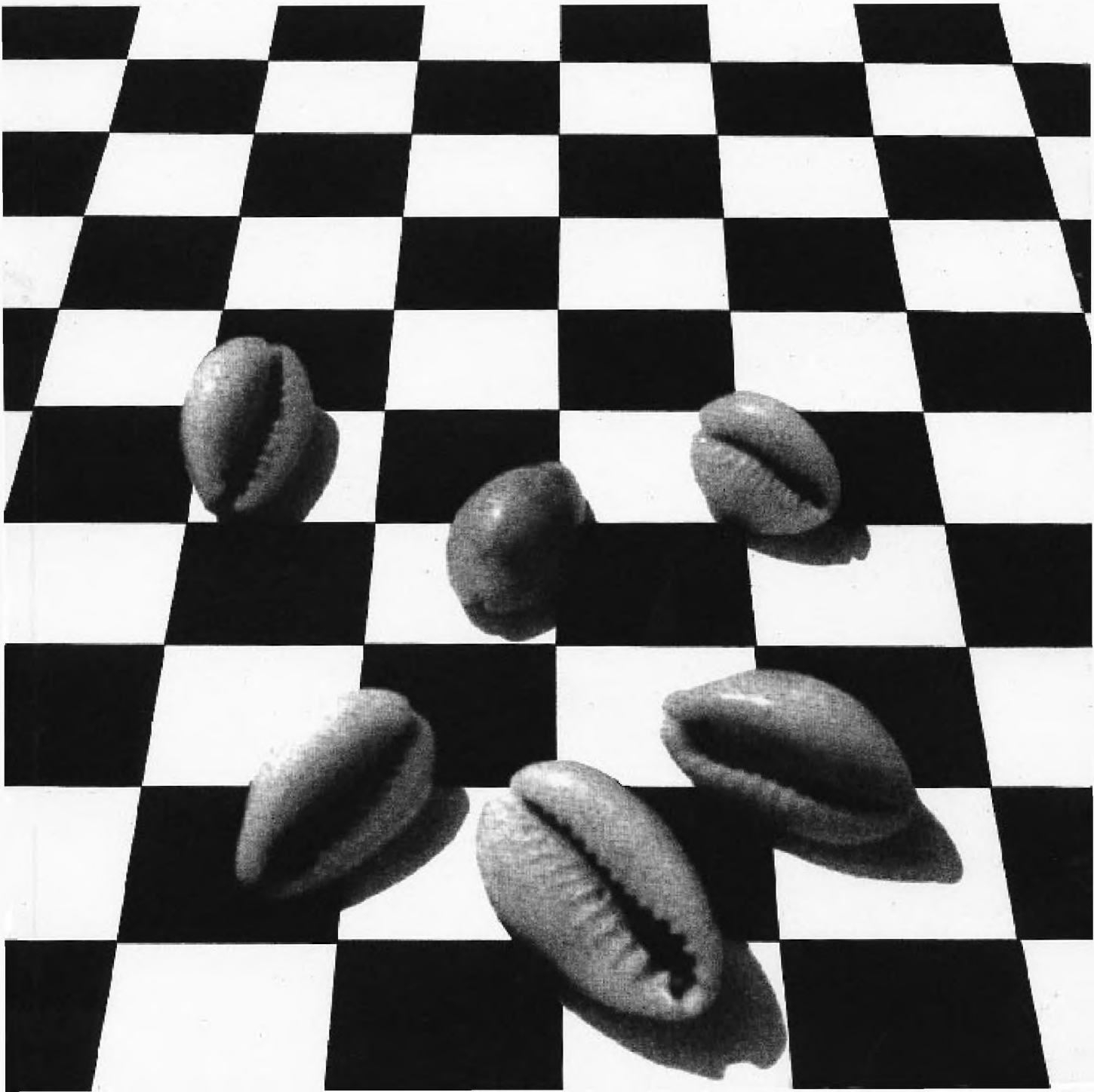
REFLEX EPILEPSY:

CLINICAL AND NEUROPHYSIOLOGICAL STUDIES IN A TROPICAL COUNTRY IN ASIA

Nimal Senanayake



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REFLEX EPILEPSY:

CLINICAL AND NEUROPHYSIOLOGICAL STUDIES IN A TROPICAL COUNTRY IN ASIA

Een wetenschappelijke proeve op het gebied van de Medische Wetenschappen

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TER VERKRIJGING VAN DE GRAAD VAN DOCTOR
AAN DE KATHOLIEKE UNIVERSITEIT NIJMEGEN,
VOLGENS BESLUIT VAN HET COLLEGE VAN DECANEN
IN HET OPENBAAR TE VERDEDIGEN OP
MAANDAG 29 JUNI 1998
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REFLEX EPILEPSY:

CLINICAL AND NEUROPHYSIOLOGICAL STUDIES IN A TROPICAL COUNTRY IN ASIA

Thesis submitted to
the Katholieke Universiteit Nijmegen
for the award of
the Ph. D. degree in Medical Sciences

by

Alagiyawanna Mohotti Appuhamillage
Nimal Kitsiri Senanayake

1998

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To My Parents

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Chapter 1: Senanayake, N. Epilepsies with seizures precipitated by specific modes of activation. In: P.J.Vinken and G.W.Bruyn (Eds.), *Handbook of Clinical Neurology, Epilepsy (New series)*. North Holland Publishing, Amsterdam *(in press)*

Chapter 2: Senanayake, N., Self-induction of seizures in photosensitive patients in a tropical country, *Epilepsy Res.*, 2 (1988) 61-64

Chapter 3: Senanayake, N., Epileptic seizures evoked by card games, draughts, and similar games, *Epilepsia,* 28 (1987) 356-361

Chapter 4: Senanayake, N., Epileptic seizures evoked by the Rubik's cube, *J. Neurol. Neurosurg. Psychiatry*, 50 (1987) 1553-1554

Chapter 5: Senanayake, N., Epilepsia arithmetices revisited, *Epilepsy Res.*, 3 (1989) 167-173

Chapter 6: Senanayake, N., 'Eating epilepsy' - a reappraisal, *Epilepsy Res.*, 5 (1990) 74-79

Chapter 7: Senanayake, N., Familial eating epilepsy, *J. Neurol*, 277 (1990) 388-391

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Abbreviations

AED	• antiepileptic drugs
CBZ	• carbamazepine
CLB	• clobazam (Frisium)
CLN	• clonazepam
CNS	• central nervous system
CPS	• complex partial seizures
EE	• eating epilepsy
EEG	• electroencephalogram
GTCS	• generalized tonic-clonic seizure
HWE	• hot water epilepsy
IPS	• intermittent photic stimulation
ICE	• International Classification of Epilepsies and Epileptic Syndromes
ICES	• International Classification of Epileptic Seizures
ILAE	• International League Against Epilepsy
JME	• juvenile myoclonic epilepsy
MGE	• musicogenic epilepsy
MIE	• movement-induced epilepsy
NPA	• neuropsychological activation
PB	• phenobarbitone
PCR	• photoconvulsive response
PHT	• phenytoin
PKC	• paroxysmal kinesigenic choreoathetosis
PMR	• photomyoclonic response
PPR	• photoparoxysmal response
PSE	• photosensitive epilepsy
PSGS	• partial seizures with secondary generalization

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PSW	• poly-spike and slow waves
RE	• reading epilepsy
SIE	• self-induced epilepsy
SPS	• simple partial seizures
STE	• startle epilepsy
SW	• spike and slow waves
TL	• temporal lobe
TV	• television
VPA	• valproic acid, sodium valproate

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Prologue

'A kind of sudden sickness 'tis, whose name has clung
Since of the votes a true count it prevents.
For often has this dread disease the people's council stopped,
When members down in fatal weakness fell. And God himself
Through changing phases of the unstable moon
Proclaims conception of a man oft thus to be outstretched'

wrote Quintus Serenus, the Roman poet-physician of the third century A.D., introducing epilepsy- or *morbus comitalis* as the illness was then known- for an attack of epilepsy used to spoil the day of the *comitia*, the assembly of the people[34].

Epilepsy through the Ages

During the Mesopotamian civilization, an Akkadian medical text (ca 2000 B.C.) describes a convulsive attack in terms which suggests epilepsy[18]. The text speaks of a person whose neck turns left, whose hands and feet are tense and eyes wide open, froth flowing from the mouth and consciousness being lost. This is diagnosed as *antasubbu* and related to *'the hand of Sin,'* the god of the moon, by the exorciser[34].

The ancient Greek identified convulsive seizures with religious, magical or divine causes, and called epilepsy the *'sacred illness'*. This tradition persisted until the 17th century, though the effort to counter it with rational explanations also began very early. One of the Hippocratic writers in the fourth century B.C. denied that epilepsy was sacred in any sense, asserted that its seat was in the brain, and, as a humoralist, diagnosed its cause as an excess of phlegm in the brain rushing into the blood vessels of the body. Another writer in the same tradition ascribed seizures to a mixture of blood and air[18].

The ancient Indian medical system, *Ayurveda*, meaning ' the science of life', defined epilepsy as *Apasmara*: *apa* meaning negation or loss of, and *smara* meaning recollection or consciousness. Aura was recognized, and was called *Apasmara poorva roopa*. A large number of symptoms indicative of aura included subjective sensation of sounds, sensation of darkness, feeling of delusion, and dream-like state. An actual attack of *Apasmara* consisted of falling down, shaking of the hands, legs and body, rolling up of the eyes, grinding of the teeth, and foaming at the mouth. Four major types of epilepsy, based on the disturbance of *doshas* (humors) that govern the physiological and physicochemical activities of the body, were mentioned. *Apasmara* was considered a dangerous disease that was chronic and difficult to treat. Among the causes mentioned were transgression of dietary rules, eating of contaminated food, abuse of rules of hygiene, weakness and extreme mental agitation by lust, fear, anxiety or anger. Treatment included correcting the aetiological factors and dietary regimen, and avoiding dangerous places that may result in injuries[17].

The 19th century produced a transformation in thinking about the brain and neural system in the West. Studies by physicians and neuroscientists of the calibre of W.R. Gowers, Sir Charles Locock, Charles Edward Brown-Séquard, John Hughlings Jackson, Jean Martin Charcot, Paul Broca, Carl Wernicke, Gustav Fritsch, Edward Hitzig and David Ferrier contributed to that revolution, and a better understanding of epilepsy followed. In the early part of the 20th century, the development of effective medication paralleled progress in surgical techniques, especially the improvement in diagnostic insight provided by the electro-encephalogram (EEG) which Johannes Berger developed between 1929 and 1938. Wilder Penfield and Hubert H. Jasper became the leading authorities on surgical treatment of epilepsy since World War II[18].

After a long circuit through ages of magic, black humours and blank disinterest, medical thought has returned to the affirmation of Hippocrates that epilepsy, like many other diseases, is rooted in natural causes. In terms of today, epilepsy is not cryptogenic- born of ignorance, but is merely a disturbance of the normal rhythm of the brain. In nature, rhythm is inherent; in man, dysrhythmia means disease; in brain, paroxysmal dysrhythmia spells epilepsy[19].

Definition of epilepsy

The Greek word *epilepsia* means 'a taking hold of, a something seizing the subject as though that "something" were outside himself'[20]. Since the time of Hughlings Jackson, epilepsy had been defined in physiological

Part 1
Overview

[1]
Epilepsies with seizures precipitated by specific modes of activation

Epilepsies with seizures precipitated by specific modes of activation, mediated by neural pathways, are designated *'reflex epilepsy'* (Merlis, 1974). Since the early descriptions by Hall (1833) and Brown-Séquard (1857), the term *'reflex'*, however, has been disputed by some on the grounds that no specific reflex arc is involved in such cases. The alternative term *'sensory precipitation epilepsy'* has its own limitations, because, for instance, in seizures precipitated by mental arithmetic, there is no discernible sensory stimulus. The designation *'reflex'* is therefore retained on the basis that a specific stimulus evokes a specific response, i.e., a seizure (Merlis 1974).

In Europe, an evoking factor had been found in 6.5% of 1,000 patients with epilepsy by Symonds (1959), and in 5% of 895 patients with epilepsy by Servit *et al.* (1962). Lower frequencies had been reported in India, 2.6% in Kerala (Devi and Iyer 1985) and 2.8% in Bombay (Chemburkar and Desai 1977) to 4.6% in Bangalore (Mani and Rangan 1990). Our Epilepsy Clinic at Peradeniya in Sri Lanka registers 150-200 new cases of epilepsy every year. Among 1,250 patients attending this clinic, 228 (18.2%) had the majority of their seizures evoked by a specific stimulus; 96 (7.7%) of them had reflex seizures exclusively.

Many different forms of external as well as internal stimuli are known to cause reflex seizures. Visual precipitation of seizures or photosensitive epilepsy (PSE) is by far the commonest, particularly in the West, accounting for more than half the number of cases (Forster 1977; Harding and Jeavons 1994). The pattern of reflex epilepsies is considerably different in the tropics (Senanayake 1994). In India, eating epilepsy (EE) is the commonest form of reflex epilepsy in Bombay (Chemburkar and Desai 1977), Kerala (Devi and Iyer 1985) and Srinagar (Koul *et al.* 1989), whereas hot water epilepsy (HWE) is the commonest in Bangalore (Mani and Rangan 1990) and Madras (Velumurugendran 1985). In Peradeniya, EE is by far the commonest type of reflex epilepsy.

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Photosensitive epilepsy (PSE)

The observation that epileptic seizures might be induced by changes in the light reaching the eyes is thought to date back to antiquity. Temkins (1945) mentions the test used in the slave market of Rome, *'the rotation of a potter's wheel before his eyes would make the epileptic feel giddy and might be the cause of a seizure'*. However, the interpretation that these seizures were light-induced has been challenged on the grounds that the potter's wheels used at the time had no spokes to produce a flicker (Harding and Jeavons 1994). The first reliable reference to PSE is by Gowers (1885). Radovici *et al.* (1932) and Goodkind (1936) drew attention to patients who induced fits using sunlight. Adrian and Matthews (1934) described the effects of intermittent photic stimulation (IPS) on the electroencephalogram (EEG), but its clinical significance was appreciated only when it was demonstrated that a paroxysm of wave-spike discharge as well as clinical seizures could be evoked by flickering light (Walter *et al.* 1946; Cobb 1947). This new form of epilepsy was initially called *'photogenic epilepsy'*, but now, the term *'photosensitive'* is used in preference to *'photogenic'*. Several monographs have been written on this subject (Jeavons and Harding 1975; Newmark and Penry 1979; Kasteleijn-Nolst Trenité 1989; Harding and Jeavons 1994).

EEG Criteria

IPS evokes a variety of anomalous EEG responses. Frequencies between 8-20 Hz evoke, in about 90% of normal children, clearly discernible rhythmic activity, confined to the occipital and parieto-occipital areas, at the stimulus frequency or its multiples (harmonics) or submultiples (subharmonics). This phenomenon, known as *'photic driving'*, has no pathological significance.

Another nonpathological, localized reaction to IPS, is 'occipital spiking', especially when a patterned stroboscope is used. *'Photomyoclonic response'* (PMR) consists of anterior spikes in the EEG at the same rate as the flash and rhythmic contractions of the orbital and other facial muscles synchronous with the photic stimuli occurring only or predominantly in the frontal areas. PMR is found only when the subjects' eyes are closed, and is more likely when the stroboscope is very close to the eyes and the intensity high (Jeavons and Harding 1975). PMR is age-dependent, seen mainly in older persons. IPS may also produce occipital slow waves and generalized spikes at the stimulus frequency which have no known significance (Kasteleijn-Nolst Trenité 1989).

Pathological *'photoconvulsive response'*(PCR) consists of generalized (poly) spike wave discharges. PCR is very strongly related to epilepsy,

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especially when associated with myoclonic jerks (Jeavons and Harding 1975). The association is even closer if the response outlasts the duration of the stimulus train. Because this response is not necessarily accompanied by convulsive movements, the term *'photoparoxysmal response'* (PPR), is preferred. The adjective *'classical'* indicates that the response outlasts the stimulus.

The flash rates used for IPS vary from 1 to 50 Hz, and the optimum rates to induce PPR are between 10 and 25 Hz, with a peak between 15 and 20 Hz. Duration of stimulation, intensity of light, distance of the light source from the subject's eyes, and background illumination are important factors which influence the results (Harding and Jeavons 1994).

Incidence

PSE occurs in approximately 1 in 4,000 of the population in England, with an incidence of about 1 per 100,000 per annum (Fish *et al.* 1993). This relative rarity is partly due to a steep age distribution in which 76% of patients have their initial attack between the ages of 8 and 20 years (Harding and Jeavons 1994). A much higher incidence (5.7 per 100,000) has been reported in a restricted population aged 7-19 years (Fish *et al.* 1993).

Among children with epilepsy, Jeavons and Harding (1975) found that 8% were photosensitive. A higher frequency of 17% was noted in the same clinic by Covanis *et al.* (1982). Harding and Jeavons (1994) found 3Hz spike-and-wave (SW) discharges on IPS in 2% of unselected patients referred for EEG. Binnie (1993), in London, found a figure of 5.4%.

Several studies have shown that black Africans are less photosensitive than Caucasians (Mundy-Castle, 1953; Bental 1979). In South Africa, in a comparative study of referrals for EEG, PPR was found in 2.5% of Whites, 1.3% of mixed race group, and 0.9% of Blacks (De Graaf *et al.* 1980), and a recent study has shown more pronounced differences, the respective figures being 5.2%, 4.2% and 0.4% (De Graaf 1992).

The frequency of PSE among patients with epilepsy in Saudi Arabia (7.3%) is similar to that in White populations (Obeid *et al.* 1991). In Pakistan, the frequency is 3.9% (Aziz *et al.* 1989), but 0.9% in South India (Devi and Iyer (1985), and 0.6% in North India (Saleem *et al.* 1994). In our series, none had PSE in that they did not experience seizures evoked by photic stimuli. However, IPS done on 874 unselected patients produced a PPR in 60 (6.9%) (Senanayake 1993a).

Visual stimuli precipitating seizures

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Sunlight, either reflected from water, snow, frost or waves of the sea, or broken up as one travels along an avenue of trees or past railings has precipitated seizures in photosensitive patients. The interruption of light by the blades of a helicopter has also caused fits. Flickering sunlight was an epileptogenic factor in 33 (7.3%) of 454 patients with PSE in Harding and Jeavons' series (1994).

Artificial light sources which had precipitated seizures include oscilloscopes, blades of a mechanical saw, cinema screen, and fluorescent lighting (Harding and Jeavons 1994). Of 94 patients with PSE reported by Kasteleijn-Nolst Trenité (1989), 13 (13.8%) had seizures in discotheques. Twenty-two (4.8%) of Harding and Jeavons' (1994) patients had seizures precipitated by artificial lights.

Viewing television (TV) is undoubtedly the commonest precipitant of seizures in photosensitive patients, in 65.9% of Harding and Jeavons' (1994) series. Livingston (1952), reporting the first case of *'TV epilepsy'* postulated that the seizures were provoked by TV sets which were defective and therefore flickered. A faulty set, adjusting the set, or watching very near to the set have subsequently been found to be important factors. Some patients who are *'TV sensitive'* show a compulsive attraction to the TV screen reminiscent of self-induction of seizures (Andermann 1971).

Patterns, especially black and white geometric ones, may induce clinical seizures and EEG abnormalities (Chatrian *et al.* 1970 a,b). About 30% of patients who are photosensitive are also pattern-sensitive, but only a few (2%) give a clinical history of pattern-sensitive epilepsy (Jeavons and Harding 1975). Steel steps of escalators, windscreen wipers, railway sleepers and posts viewed from the carriage window, bands formed by fluted glass in windows, roof tiles, striped material, the striped garage door of the up-and-over type, and the rotating turntable of a record player are some of the stimuli which had caused pattern-sensitive seizures (Harding and Jeavons 1994).

Since the initial reports by Rushton (1981) and Jeavons *et al.* (1981), video and computer games have been increasingly recognised to precipitate seizures. It is considered to be an extension of PSE (Cook and Hoskins 1992, Graf *et al.* 1994), or a form of pattern-sensitive epilepsy (Maeda 1990, Harding *et al.* 1994). Many of these patients, tested under rigorous conditions, were not sensitive to IPS (Harding and Jeavons 1994). Nonphotic factors such as excitement, fatigue, sleep deprivation, cognitive processing, and diurnal variation in susceptibility may play a role, particularly in nonphotosensitive patients (Ferrie *et al.* 1994).

Clinical features

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The onset of PSE is most common between the ages of 8 and 19 years, with a mean around 14 years, suggesting that puberty plays some part in the genesis. PSE shows a female preponderance (62.8%). A family history of PSE is present in about 8% of the patients (Jeavons and Harding 1975). The 3Hz SW activity characteristic of PSE is transmitted by an autosomal dominant gene (Metrakos and Metrakos 1969).

Generalized tonic-clonic seizure (GTCS) is the most frequent manifestation of PSE, the seizure types recorded by Harding and Jeavons (1994) being: GTCS (61.3%), myoclonic (12.3%), absences (11.4%), partial simple or complex (2.4%), and mixed 14.3%. Kasteleijn-Nolst Trenité (1989) found 15 categories of seizures in 94 patients, of whom 29% had a single type and 71% mixed seizures. GTCS occurred alone in 16%, but in combination with other seizures in 56%. Binnie (1993) reported idiopathic generalized seizures in 43%, symptomatic generalized seizures in 23%, and partial seizures in 29%.

Pathogenic mechanisms

Wilkins *et al.* (1980) concluded that the paroxysmal disturbance evoked by patterns was in the visual cortex; IPS probably evoked disturbance in a less specific and less consistent locus. The discharge appeared to occur when a critical level of excitation was reached, and the locus of excitation within the visual cortex was not critical. This abnormal reaction to massive excitation was thought to be the result of a failure of inhibitory mechanisms which was insufficient to disturb function under normal conditions of excitation.

Because the occipital spike appeared on the descending arm of the P_2 component of the visual evoked potential, it was previously thought that it would represent a failure of postsynaptic inhibition. However, more recent evidence indicates that the P_2 component is in fact enhanced in photosensitive patients and is slightly reduced when patients are receiving sodium valproate (VPA). The occipital spike is unaffected by treatment with VPA and this, and the evidence of at least normal, if not supranormal postinhibitory potentials, suggests that the occipital spike represents an excitatory phenomenon, rather than a failure of inhibition (Harding and Jeavons 1994).

PSE represents a secondarily generalized epilepsy, but one that is unusual in that the cortical focus is not consistently present but is responsive to particular visual stimuli. These visual stimuli may be defined in terms of temporal sequence, that is, the number of flashes of light per second, or the number of pattern image changes per second, and also in terms of spatial frequency, orientation, contrast,

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and the line width ratio (Harding and Jeavons 1994).

Treatment and prognosis

Prevention of critical visual stimulation, and VPA are the two effective therapies for PSE. Susceptible individuals should view TV only from a distance of >2 m in a well-lit environment. They should avoid approaching the TV set. If they need to, they should cover one eye (Harding and Jeavons 1994). Recommendations with regard to video games have been made in a consensus statement by Binnie *et al.* (1994). VPA is effective in abolishing or reducing photosensitivity in 80% of patients, and is equally effective in the control of seizures. Clonazepam (CLN), the other drug used in the treatment of PSE, is too sedating. One in 4 patients lose their photosensitivity, usually before the age of 30 years, but others retain the abnormality for the rest of their lives (Harding and Jeavons 1994).

The pharmacological property of abolishing PPR has also been utilised as a means of testing the efficacy of antiepileptic drugs (AED) (Binnie *et al.* 1986; Senanayake 1995b).

Self-induced epilepsy (SIE)

Since the report by Radovici *et al.* in 1932 of a case of *'reflex epilepsy provoked by optic excitation from rays of sun'*, the phenomenon of self-induction of seizures has been recognised as a clinical entity. Most of these patients are photosensitive, and they induce their seizures by gazing at the sun or a bright light and waving one hand in front of the eyes. Blinking movements (Andermann *et al.* 1962; Green 1966) and eye closure with forced upward deviation of the eyes (Binnie *et al.* 1980; Darby *et al.* 1980) have also been used as stimuli. Rare methods used by an occasional patient include hyperventilation (Fabisch and Darbyshire 1965), and compression of the carotid arteries (Lai and Ziegler 1983).

Incidence

SIE is considered rare, but in Kasteleijn-Nolst Trenité's (1989) study of 100 photosensitive patients, 35 had a history of self-induction. Although PSE itself is rare, SIE seems to be relatively common in the Indian Subcontinent (Maheshwari 1978; Iyer *et al.* 1979; Iyer *et al.* 1983; Devi and Iyer 1985; Senanayake 1988). Among 2,000 patients with epilepsy, Iyer *et al.* (1979) found 11 patients who were photosensitive, all but 1 having SIE. Six patients, in addition, exhibited heliotaxis- impulsive attraction to sunlight. At Peradeniya, we have seen 12 patients with SIE over a 5-year

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period (Senanayake 1993b). A clinical and neurophysiological study of two of the initial cases reported by me (Senanayake 1988) is presented in *Chapter 2*.

Clinical features

In a review of 99 cases of SIE, the average age was 14 years (range 1-52 years) (Kasteleijn-Nolst Trenité 1989). A female preponderance of 1.3:1 (Kasteleijn-Nolst Trenité (1989) or 2.3:1 (Harding and Jeavons 1994) had been noted, but in our series the sex ratio was 1:1. The average age at onset was 7 years, with a range from 3 months to 20 years (Kasteleijn-Nolst Trenité 1989). In our patients, the age range was 9-38 years, and the onset of epilepsy was between 5-16 years. Andermann *et al.* (1962), reviewing the literature, concluded that self-inducing patients were mentally retarded. Four of our patients (33.3%) were mentally subnormal. Harley *et al.* (1967), Darby *et al.* (1980), and Kasteleijn-Nolst Trenité (1989), however, had a majority of patients with normal or above normal intelligence. Nevertheless, in Kasteleijn-Nolst Trenité's series, 11 of the 16 mentally retarded photosensitive patients showed self-inducing behaviour. Thus, it seems probable that mentally retarded epileptic patients with photosensitivity are more likely to develop SIE than their counterparts with normal intelligence.

The seizure type, in 23 patients of Kasteleijn-Nolst Trenité's (1989) series, was GTCS in 14, absences in 12, myoclonus in 5, and complex partial in 4, 13 of them having had mixed seizures. In our patients, the seizures were GTCS in 6, secondarily generalised partial in 5, and myoclonic in 1. One had rotatory seizures. The resting EEG contained temporal sharp waves in 4, and generalized polyspike and wave (PSW) discharges in 1. Only 7 patients showed a positive PPR.

The common methods of self-induction, in Kasteleijn-Nolst Trenité's (1989) review of 99 patients were hand-waving in 53, blinking in 51, looking at TV in 11, and looking at patterns in 9, many patients employing more than one method. TV screen has also been used as a flickering light source (Harley *et al.* 1967; Andermann 1971; Jeavons and Harding 1975; Harding *et al.* 1994). All our patients induced seizures by rubbing the forehead or waving a hand in front of the eyes while looking at the sun. Some showed heliotaxis.

Darby *et al.* (1980) found, in a quarter of patients with PSE, paroxysmal EEG discharges induced by slow eye closure accompanied by sustained upward deviation of the eyes. Self-induction had not been suspected prior to EEG monitoring. This phenomenon has since been observed by others (Watanabe *et al.* 1985; Senanayake 1988). Looking at

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patterns has also been employed rarely to induce seizures (Matricardi *et al.* 1990).

Pathogenic mechanisms

Hand waving presumably produces a flicker between 1 and 15 flashes/sec (Troupin 1966), and 15 f/s is considered the frequency most effective in inducing abnormal discharges (Hutchison *et al.* 1958). The hand movement had been considered a part of the ictus rather that the stimulus by some (Livingston and Torres 1964; Ames 1974). But, (Binnie *et al.* 1980) have described patients who initiate the seizure discharge by eye closure and prolong it by hand waving, which result in the commencement of the hand waving after the onset of the EEG discharge, which could lead to misinterpretation of the hand waving as an ictal phenomenon.

Why some patients deliberately evoke seizures remains a puzzle. Most of them are compulsively attracted to light. No good explanation is offered by them for their abnormal behaviour, although some admit to deriving a pleasurable or relaxing feeling. Psychological factors and stressful situations have an influence. Behavioural abnormalities leading to social isolation and learning problems are seen in these patients. Punishment never stops the self-induction habit.

Treatment and prognosis

Self-induction is very difficulty to treat. Drugs, particularly VPA, benzodiazepines and succinimide which are effective in suppressing photosensitivity and visually-induced seizures have been tried. CLN has produced the best results (Kasteleijn-Nolst Trenité 1989). CLB produced encouraging results in some of our patients. Wearing dark glasses have been shown to diminish the self-induction rate. However, noncompliance is a major problem. Psychotherapy has been tried in some patients with varying success (Kasteleijn-Nolst Trenité 1989).

Epileptic seizures evoked by higher cerebral functions

The phenomenon of seizure precipitation by higher cerebral functions had been appreciated for many decades (Gordon 1928; Symonds 1959). Reading epilepsy (RE) was one of the earliest reported, initially by Bickford (1954), and subsequently by Bingel (1957). Later, Geschwind and Sherwin (1967) introduced the term *'language-induced epilepsy'* to include writing and other linguistic functions which triggered seizures. Meanwhile, Ingvar and Nyman (1962) described arithmetic problem

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solving as a seizure-evoking stimulus and designated the condition *'epilepsia arithmetices'*. Calculation (Wiebers *et al.* 1979; Striano *et al.* 1983; Senanayake 1989; Devi and Iyer 1985; Goossens *et al.* 1990; Yamamoto *et al.* 1991) as well as other functions, namely, decision making (Forster *et al.* 1975; Forster 1977; Mutani *et al.* 1980; Wilkins *et al.* 1982), playing cards and board games (Ch'en *et al.* 1965; Cirignotta *et al.* 1980; Kalina *et al.* 1984; Senanayake 1987a; Devi and Iyer 1985), and performing spatial tasks (Brenner and Seelinger 1979; Senanayake 1987b; Matsuoka 1989), have since been recognized to precipitate epileptic seizures.

Reading epilepsy

In RE, prolonged reading precipitates seizures, which usually consists of generalized convulsions preceded by an aura of 'clicking' or movement in the jaw. Bickford (1954) and Bickford *et al.* (1956) reported 2 types of RE, *'primary'* which was idiopathic and in which seizures occurred only in relation to reading, and *'secondary'* in which seizures also occurred under other conditions. Although the term *'primary reading epilepsy'* has been accepted universally, the definition of the secondary type has been considered ambiguous.

RE is considered a rare disorder. Vercelletto *et al.* (1985) collected 11 cases over a period of 20 years, and Wolf (1992) saw only 7 cases in 18 years. Recently, Radhakrishnan *et al.* (1995) have reviewed 20 patients with RE diagnosed at the Mayo Clinic between 1949 and 1989, and delineated the epileptic syndrome.

Clinical features

RE seems to predominantly affect males, the male:female ratio being 2:1 approximately (Wolf 1992; Radhakrishnan *et al.* 1995). It manifests itself, not in the early school years when reading skills are acquired, but in adolescence and early adulthood. The mean age at onset was 17.7 years for 88 patients reported in the literature, only 3 being younger than 12 years and 5 older than 25 years (Wolf 1992). RE has a strong genetic predisposition. In 69 patients with RE, Wolf (1992) found a positive family history of seizures in 28 (41%). Of the 20 epileptic family members for whom more information was available, 11 had RE.

The most constant symptoms are abnormal sensations or movements, described by patients as jerking, clicking, stiffness, numbness or tightness in the musculature involved in reading and talking, which develop after a certain amount of reading. The jaw is involved most frequently, followed by the tongue and lips. Radhakrishnan *et al.* (1995) reported myoclonic jerks of the upper

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extremities in many of their patients. Although individual manifestations occur without alteration of consciousness, many patients experience a feeling of unrest, discomfort, anxiety or confusion. They may also develop GTCS, which, in many cases, are the cause for seeking medical advice. The reading time preceding the first symptom may vary. The type of reading material or the logistics of the reading activity are not important contributory factors for the seizures. Fatigue, menstrual periods, and alcohol may have a provocative effect (Radhakrishnan *et al.* 1995).

Not only reading, but also related and, rarely, unrelated activities may precipitate seizures in RE. Of 91 patients reviewed by Wolf (1992), 27% described seizures triggered by talking, especially when engaged in vigorous argumentative conversation, and 11% recognized writing as a triggering factor. Nine of the patients reviewed by Radhakrishnan *et al.* (1995) had other triggers- linguistic or non-linguistic higher mental activities.

Electroencephalogram

One-fifth of the patients have interictal EEG abnormalities, one half of them showing bilateral SW discharges. Photosensitivity has been reported in 9% (Wolf 1992). The ictal abnormalities vary from well-formed spikes, multiple spikes and slow waves to typical 3-Hz SW discharges. Radhakrishnan *et al.* (1995) found generalized and symmetric ictal discharges in 75% of their patients. Three patients with asymmetric discharges had left hemisphere dominance. The localization of the discharges may vary in the same patient. Gastaut and Tassinari (1966), who recorded two prolonged partial seizures precipitated by reading, found electrographic onset from the left parietal region in the first episode and from the right parietal region during the second episode.

Pathogenic mechanisms

Clinical and electrographic features and heredity suggest that RE is a specific syndrome. Although generally considered to be a partial epilepsy, the pattern and distribution of EEG abnormalities and the absence of demonstrable structural lesions in most cases of RE favour idiopathic generalized epilepsy (Radhakrishnan *et al.* 1995). Many clinical features of RE resemble those of juvenile myoclonic epilepsy (JME), such as age at onset, strong influence of heredity, myoclonic jerks progressing to generalized tonic-clonic seizures, response to VPA, and persistence, although well controlled, throughout life (Radhakrishnan *et al.* 1995).

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The neurophysiological mechanism and neuroanatomical substrate of RE are largely unknown. In addition to the primary role of visual stimuli, sensory inputs from jaw muscles and eye muscles, interrupted visual input or their combinations were thought to play a role. More recent investigations have stressed the involvement of complex central language and cognitive mechanisms (Wolf 1978; Ritaccio *et al.* 1992). The specificity of reading as the stimulus implies that a related neuronal substrate, language area, or more specifically, the dominant premotor cortex (Ritaccio *et al.* 1992) is responsible for triggering seizure discharges (Radhakrishnan *et al.* 1995).

Treatment and prognosis

RE is a persistent, but non-progressive, disorder which does not impair the lifestyle of most patients. Patients learn to avoid an attack of major seizures by recognizing the early symptoms and stopping reading (Radhakrishnan *et al.* 1995). Anticonvulsant medication often can raise the threshold for precipitation of the seizures. Monotherapy with VPA is considered the therapy of choice whenever drug treatment becomes necessary (Vanderzant *et al.* 1982).

Epileptic seizures evoked by nonlinguistic cerebral functions

While conversing with a patient during routine EEG recording, Ingvar and Nyman (1962) first appreciated the possibility of seizure precipitation by arithmetic calculations. The patient underwent 14 cognitive tests with EEG monitoring, but only those which involved calculations produced epileptiform discharges. The condition is considered rare, and at the Mayo Clinic, mental arithmetic used as a standard activation procedure during EEG recording since 1951 had yielded only 1 positive case in more than 100,000 recordings (Wiebers *et al.* 1979).

At Peradeniya, we initially reported 3 patients who developed seizures evoked by card games, draughts (checkers) and a local game called '*punchi*' played with sea-shells (Senanayake 1987a) *(Chapter 3)*, and another patient when playing the Rubik's cube (Senanayake 1987b) *(Chapter 4)*. Subsequently, we reviewed 10 cases with epilepsia arithmetices, including 3 of our own patients (Senanayake 1989) *(Chapter 5)*. Goosens *et al.* (1990), adding 9 personal cases, reviewed 25 patients with reflex seizures induced by calculation, card or board games, and spatial tasks. Yamamoto *et al.* (1992) who performed neuropsychological EEG activation on 41 patients with JME found a positive response in 21 (51.2%). At our centre, cognitive tests done on 100 patients with JME produced positive results in 22.

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Clinical features

This disorder, like RE, is commoner among males, the male:female ratio being 3:1 (Goosens *et al.* 1990). The onset is usually in the second decade of life (Senanayake 1987a, 1989; Striano 1993), the mean age at onset being 15.4 years (Goosens *et al.* 1990). Almost all patients experience GTCS, which are often preceded by a series of myoclonic jerks. The seizure disorder is suggestive of JME (Senanayake 1987a, 1989; Striano 1993). The range of the stimuli is remarkably wide, but those are basically related to calculation, measuring, and spatial thought. Linguistic stimuli may also precipitate seizures in some patients. Illustrative case histories are given in *Chapters 3, 4* and *5*.

Electroencephalogram

Generalized spike, SW or PSW discharges at 2-4 Hz were the dominant interictal EEG feature in 68% of the cases reviewed by Goosens *et al.* (1990), but all the cases (100%) reviewed by us (Senanayake 1987a, 1987b, 1989) *(Chapters 3, 4 and 5)*. These abnormalities, generalized discharges in particular, are triggered principally by arithmetic or spatial tasks in some patients (Senanayake 1987a, 1989) *(Chapters 4 and 5)*. In many others, the frequency of discharges increases during specific activation (Cirignotta *et al.* 1980; Wilkins *et al.* 1982; Senanayake 1989; Yamamoto *et al.* 1992).

Pathogenic mechanisms

Forster (1977) recognised 3 factors, namely, complex decision making, sequential decision making, and stress which may vary in their threshold effect of evoking seizures. Some patients show a marked specificity to the type of stimulus. For instance, puzzles involving pictures or numbers may be a very potent stimulus in a given patient, whereas puzzles involving words are ineffective (Senanayake 1989). A new hypothesis postulated by us to explain the pathogenic mechanism of epileptic seizures evoked by nonlinguistic cerebral functions is given in *Chapter 5*.

Treatment and prognosis

Since it is not practical to avoid arithmetical or spatial thought in daily life, treatment with AED is required in most instances. VPA or CLN (Goossens *et al.* 1990), as well as CLB (Senanayake 1987a, 1989) has been used successfully *(Chapters 3 and 5)*.

Eating epilepsy (EE)

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Seizures, which occur during eating or soon after, constitute EE. Allen (1945), describing a 35-year-old man who had generalised and partial seizures, noted: *'He had a sinking feeling in the stomach for as long as a day at a time. If he took solid food when that sensation was present, he at once had an attack.'* Boudouresques and Gastaut (1953) reported four patients with temporal lobe (TL) EEG foci who had postprandial seizures attributed to gastric distension. Symonds (1959), cited two patients with epilepsy whose attacks occurred only towards the end of a heavy meal. Vizioli (1962) referred to 9 patients in whom the onset of seizures was related to a rich meal. Subsequently, more cases were reported from different parts of the world (Scollo-Lavizzari and Hess 1967; Abenson 1969; Kerschensteiner and Dorstelmann 1970; Forster 1971; Cirignotta *et al.* 1977; Chemburkar and Desai 1977; Ahuja *et al.* 1980; Aguglia and Tinuper 1983; Senanayake 1983, 1990a, 1993c), and the condition came to be known as *'prandic epilepsy'* or *'eating epilepsy'*.

Incidence

EE had been considered a rare condition. In Rome, amongst 20,000 EEG examinations, only 9 cases had seizures related to eating (Vizioli 1962). In Wisconsin- USA, Forster (1977), over a 16-year period, saw only 2 cases of EE. In Bangalore in India, on the other hand, Nagaraja and Chand (1984) found 13 cases of EE amongst 11,783 patients with epilepsy (1.1/1000), and Mani and Rangan (1990) reported a much higher frequency of 12/1000. In Sri Nagar EE is the commonest form of reflex epilepsy (50/1000) (Koul *et al.* 1989). At Peradeniya, 196 (156.8/1000) had the majority of their seizures in relation to eating. Of them 76 (60.8/1000) had exclusively eating seizures. A description of 120 of these patients is presented in *Chapter 6*.

Clinical features

EE shows a male preponderance, 6:1 at our centre, and 8:5 (Nagaraja and Chand 1984) to 15:2 (Ahuja *et al.* 1988) in Indian studies. The onset is in the second decade of life in 60% of patients (Ahuja *et al.* 1988; Koul *et al.* 1989) to 80% in our series. Aetiological factors are not specific to EE. Mental retardation has been reported in 4% (Koul *et al.* 1989) to 15.4% (Nagaraja and Chand 1984). In our series, 7.9% had mental retardation. A deep forebrain astrocytoma causing EE had been reported by Robertson and Fariello (1979).

Familial occurrence of EE was observed by us in 9 different families, where 20 out of 59 siblings developed eating-related seizures. A remarkable degree of intra-family consistency was seen with regard to

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age at onset, symptomatology of seizures, and timing of eating seizures (Senanayake 1990b). The details of these families are given in *Chapter 7*.

Complex partial was the commonest seizure type reported in 70.6% (Ahuja *et al.* 1988) and 92.3% (Nagaraja and Chand 1984) to 100% (Koul *et al.* 1989). Our experience is that eating seizures are exclusively partial *(Chapter 6)*.

Electroencephalogram

Interictal EEG shows focal temporal epileptiform abnormalities. EEG monitoring at meals had produced variable results. We have noticed a substantial increase in the epileptiform discharges in some of our patients during eating.

Pathogenic mechanisms

Different stages in the process of eating had been proposed as the likely stimulus for eating seizures. Richness of the meal (Vizioli 1962), a chemical substance (Abenson 1969), a conditioned reflex (Scollo-Lavizzari and Hess 1967), 'satisfaction of a basic drive' (Cirignotta *et al.* 1977), and familiar atmosphere at home (Chemburkar and Desai 1977) had been thought to play a role. A new hypothesis postulated by us to explain the pathogenic mechanism of eating seizures is given in *Chapter 6*.

Treatment and prognosis

EE is considered difficult to treat (Forster 1977; Ahuja *et al.* 1980; Nagaraja and Chand 1984; Koul *et al.* 1989). However, most of our patients were satisfactorily controlled with the usual drug regimens for partial seizures. Some patients responded to clobazam (CLB) as monotherapy or adjuvant therapy *(Chapters 6)*.

Hot water epilepsy (HWE)

HWE, first described by Mani *et al.* (1968), is a peculiar type of reflex epilepsy precipitated by pouring hot water rapidly over the head while bathing (Mani and Rangan 1990). Although similar phenomena have been reported from different parts of the world (Keipert 1969, Stensman and Ursing 1971; Szymonowicz and Meloff 1978; Morimoto *et al.* 1985; Roos and van-Dijk 1988), the disorder shows geographical clustering in the Deccan plateau of Karnataka State in South India. In this part of India, HWE is the commonest form of reflex epilepsy accounting for as much as 57.7% (Velmurugendran 1985) or 73.2%

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(Mani and Rangan 1990). HWE constituted 4.4% (Satishchandra 1988) to 8.6% (Mani *et al.* 1972) of all cases of epilepsy seen in clinical practice, and 10-12% in an epidemiological survey (Gururaj and Satishchandra 1992).

Clinical features

HWE shows a male preponderance of 2.6:1 (Mani *et al.* 1975; Satishchandra 1988) or 3.6:1 (Gururaj and Satishchandra 1992). The onset is usually in the first 2 decades of life (Mani *et al.* 1975), but ranges from 2 months to 58 years (mean 13.4 years, SD 11.1) (Satishchandra *et al.* 1988). A family history of HWE is present in 7% (Satishchandra *et al.* 1988) to 15% of patients (Mani *et al.* 1975). Only 7% have a history of febrile convulsions, although temperature sensitivity is one of the causative factors for both (Satishchandra *et al.* 1988). Complex partial seizures constitute the most frequent manifestation in 67% (Satishchandra *et al.* 1988) to 80% of patients (Mani *et al.* 1975). Interictal EEG is mostly noncontributory, being either normal or showing diffuse changes (Mani *et al.* 1972).

Pathogenic mechanisms

The temperature of the bath which precipitates seizures is usually 40-50°C (Mani *et al.* 1975; Satishchandra *et al.* 1988). Data suggest that these seizures are precipitated by complex tactile and temperature-dependent stimuli (Stensman and Ursing 1971). A structural lesion in TL has been suggested (Szymonowicz and Meloff 1978), but it is not known whether deeper structures such as the hypothalamus are also involved. Animal experiments suggest that seizures could result from repeated exposure of the head to water heated to 45°C, and the phenomenon is known as '*hyperthermic kindling*' (Klauenberg and Spencer 1984). Experiments on patients and control subjects seem to indicate that the susceptible individuals may have an aberrant thermoregulatory mechanism, HWE being a '*hyperthermic seizure*' with a specificity of stimulus (Satishchandra *et al.* 1995).

Treatment and prognosis

The prognosis seems favourable, but 25% (Satishchandra *et al.* 1988) to 38% (Mani *et al.* 1972; Subramanyam 1972) have developed nonreflex epilepsy in 1-3 years. Therefore, AED are recommended, in addition to using lukewarm water for bathing. Carbamazepine and phenytoin are the most effective drugs (Satishchandra *et al.* 1988).

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Musicogenic epilepsy (MGE)

Critchley in 1937, describing 11 cases and referring to 9 others in the literature, coined the term *'musicogenic epilepsy'* to delineate seizures induced by listening to music. A total 76 cases had been described by 1980 (Newman and Saunders 1980).

The onset of seizures is during adult years, the predominant type of seizure being partial complex with frequent secondary generalization. Interictal or ictal EEG records usually point to TL involvement of either side (Tassinari *et al*. 1990).

Different types of music, from classical to popular-sentimental, may be effective. However, precipitating factors may be quite specific, such as listening to a particular composition or the actual playing of music on an instrument (Sutherling *et al*. 1980), the sound of church bells (Poskanzer 1963), a human voice (Forster *et al*. 1969), or a nursery rhyme (Herskowitz *et al*. 1984). Simple auditory stimuli have also been thought to provoke seizures, but the existence of such seizures is questionable (Gastaut and Tassinari 1966).

MGE probably involves the limbic brain at the level of emotional and waking integration of music (Vizioli 1989). Even though the effectiveness of the stimulus may be closely related to its emotional impact, the music presumably acts as a trigger activating a preexisting focus, perhaps through the establishment of a conditioned response (Tassinari *et al*. 1990). More recently, Wieser *et al* (1997), describing seven cases of MGE with an ictal single photon emission computed tomography (SPECT) study, concluded that MGE had a strong correlation to TL and a right-sided preponderance. A high musical standard was thought to predispose for MGE.

Startle epilepsy (STE)

Sensory stimuli with a startle effect, such as a sudden noise, touch or movement may cause seizures, the unexpectedness of the stimulus, rather than its character, being the important feature. STE begins during the first 2 decades of life, affecting patients with perinatal brain damage. Most patients show unilateral motor defect and mental retardation. The seizures consist of an abrupt startle response followed by a tonic phase involving the limbs of the hemiparetic side. The patient may fall and develop a few clonic jerks. Consciousness is usually blurred for 10-20 seconds. Bilateral seizures may also occur (Tassinari *et al*. 1990). STE should be distinguished from hyperekplexia, a nonepileptic startle disease (Saenz-Lope *et al*. 1984).

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Certain symptomatic epilepsies of metabolic origin also cause stimulus-provoked myoclonic seizures or seizure-like phenomena. In the late infantile form of neuronal ceroid-lipofuscinosis (Bielschowsky-Jansky disease), the myoclonus is initially segmental, asymmetric, and spontaneous, but becomes almost continuous and sensitive to any stimulus after a few months. In sialidosis type I (cherry-red spot-myoclonus syndrome), which begins in childhood, massive, bilaterally synchronous, symmetric, stimulus-sensitive myoclonic jerks as well as independent, sporadic, irregular, asymmetric, stimulus-sensitive facial myoclonus is a feature. Tay-Sachs disease presents at birth as an exaggerated startle reaction to sound, with bilateral myoclonic jerks of long duration rarely associated with EEG discharges. Myoclonia of degenerative diseases such as Creutzfeld-Jacob disease and subacute sclerosing panencephalitis may also be provoked by sensory stimuli, which should be differentiated from STE.

Both subcortical and cortical structures are thought to be involved in the pathophysiology of STE. External stimuli which trigger a startle reaction presumably activate, through a volley of proprioceptive influxes, an epileptogenic area located in or near the supplementary motor cortex (Tassinari *et al.* 1990).

Conventional anticonvulsants are often poorly effective. Carbamazepine in combination with benzodiazepines is the most effective therapy (Saenz-Lope *et al.* 1984; Tassinari *et al.* 1990).

Rare forms of reflex epilepsy

Movement-induced epilepsy (MIE)

Since the original record by Gowers (1885) of seizures induced by voluntary motion, the existence of MIE has been disputed. Many of such patients seem to have their seizures provoked by sudden and unexpected movements as in STE. A few have seizures induced by passive or active movements without a startle effect. Proprioceptive impulses set up by movement have been suggested as the effective stimulus (Tassinari *et al.* 1990).

Paroxysmal kinesigenic choreoathetosis (PKC) or dyskinesia, is a related disorder characterised by brief paroxysms of tonic, choreiform or athetoid movements which are unilateral or bilateral with no loss of consciousness, affecting children and young adults. The paroxysms are precipitated by a sudden movement such as getting up from a chair or running or rapid swimming. Some cases are familial, autosomal dominant or recessive (Iyer and Devi 1981). Because of the pattern of

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tonic and athetoid movements, retention of consciousness, and the frequently normal EEG, some consider PKC as a paroxysmal dysfunction of the basal ganglia rather than a form of reflex epilepsy (Lance 1977).

Somatosensory precipitation

Somatosensory stimuli devoid of a startle effect, such as touching (Scollo-Lavizzari and Hess 1967) or tapping skin (Forster *et al.* 1949), and tooth-brushing (Holmes *et al.* 1982; O'Brien *et al.* 1995), have also been known to induce seizures. The seizures are partial, usually occurring in patients with a cerebral lesion and unilateral motor defect (Tassinari *et al.* 1990).

Seizures induced by sexual activity

Coitus or orgasm may precipitate seizures rarely. A 20-year-old patient who had seizures due to a right TL astrocytoma, could trigger those by masturbation, sexual fantasies or suggestion (Bancaud 1971). A housewife developed her seizures immediately following completion of the sexual act. Under hypnotic suggestion that she was having intercourse with her husband, she developed a seizure. An EEG recording showed a slow wave discharge over the right frontotemporal area corresponding to the approach of the orgasm (Hoenig and Hamilton 1960).

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Part 2
Self-induced epilepsy

[2]

Self-induction of seizures in photosensitive patients in a tropical country

Summary

Two Sri Lankan girls who, in their childhood, developed self-induced epilepsy are reported. The seizures were tonic-clonic and induced by rubbing the forehead in one case and by waving one hand in front of the eyes in the other. These manoeuvres performed while gazing at a bright light evoked generalized polyspike-and-wave discharges. The patients had no explanation for their behaviour but the most likely basis for the act was attention-seeking. One patient whose seizures were not controlled with phenytoin received clobazam as adjuvant therapy and showed a marked improvement clinically and electronencephalographically.

Introduction

Since the report by Radovici *et al.*[14] in 1932 of a case of 'reflex epilepsy provoked by optic excitation from rays of sun,' the phenomenon of self-induction of seizures has been recognised as a clinical entity. The majority of patients are photosensitive and they induce their seizures by gazing at the sun or a bright light and waving one hand in front of the eyes[2]. Blinking movements[2,10,15] and eye closure with forced upward deviation of the eyes[4,7] have also been employed as stimuli.

Self-induction of seizures is considered rare[11,13]. It has been observed in 2 of 20,000 EEGs[17], 1 of 1000 patients with epilepsy[9] and 5 of 460 patients with photosensitivity[12]. On the other hand, Darby *et al.*[7], in 22 consecutive epileptic patients sensitive to intermittent photic stimulation, found 7 cases who self-induced paroxysmal activity and/or seizures by slow closure of the eyes. All these observations have been made with regard to patients in Western, temperate countries. This paper describes the clinical and EEG features of 2 village girls in Sri Lanka, a developing tropical country in South Asia, who presented with epileptic seizures self-induced by visual stimuli.

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Case reports

Case 1

Female, 22 years, had her first seizure at the age of 9. It happened one morning when she was in the schoolyard. She felt a 'funny sensation' in her forehead and began to rub the forehead, looking up. Then she had a generalized tonic-clonic seizure. Similar attacks occurred subsequently, mostly in school, when she was outdoors, on sunny days. While in the garden on a sunny day she would suddenly look up and begin to rub her forehead. Within 2-3 min she would get a convulsion and fall unconscious. She reported a sensation of a worm wriggling in the middle of her forehead, so she rubs it. She denied experiencing any pleasure during or after the act. All her self-induced attacks occurred only during daytime, outdoors, on sunny days. She had had a few spontaneous seizures in her sleep, usually around midnight, when the room was dark. When seen by us, she was taking phenytoin 200 mg/day with some improvement in the frequency of her seizures.

The physical examination was normal. She was right-handed and of dull-average intelligence (IQ 73 on Raven's scale). Psychological assessment showed that she was a shy, timid and over-protected person who lacked self-confidence.

Routine EEG showed a symmetrical dominant alpha rhythm of 10 Hz and a slight excess of generalized theta activity. Hyperventilation produced occasional sharp and/or slow wave complexes bilaterally. Photic stimulation at 6-22 flashes/sec (fps) frequently evoked generalized spikes or polyspikes with or without slow afterwaves.

The following tests were carried out using a Flectalux 1000 MLA, 1000 W lamp placed in front of the patient at a distance of 2m. Rubbing the forehead the usual way with her left hand with spreadout fingers crossing her open eyes horizontally, without the light for 5 min produced no abnormality. Looking at the light for 5 min without rubbing also produced no abnormality. However, rubbing with the light on constantly evoked generalized bisynchronous irregular polyspike-and-wave discharges immediately or within 2 min. While rubbing, when the lamp was switched on, similar discharges occurred immediately (Fig. 1a) or within 6 sec. These discharges disappeared when the light was switched off and reappeared when the light was switched on (Fig. 1b). A similar response was seen with regard to rubbing when the discharges disappeared when the rubbing was stopped and reappeared when the rubbing was restarted. Constant rubbing with the light on made the patient giddy and uncomfortable in 1-2 min and the test was never

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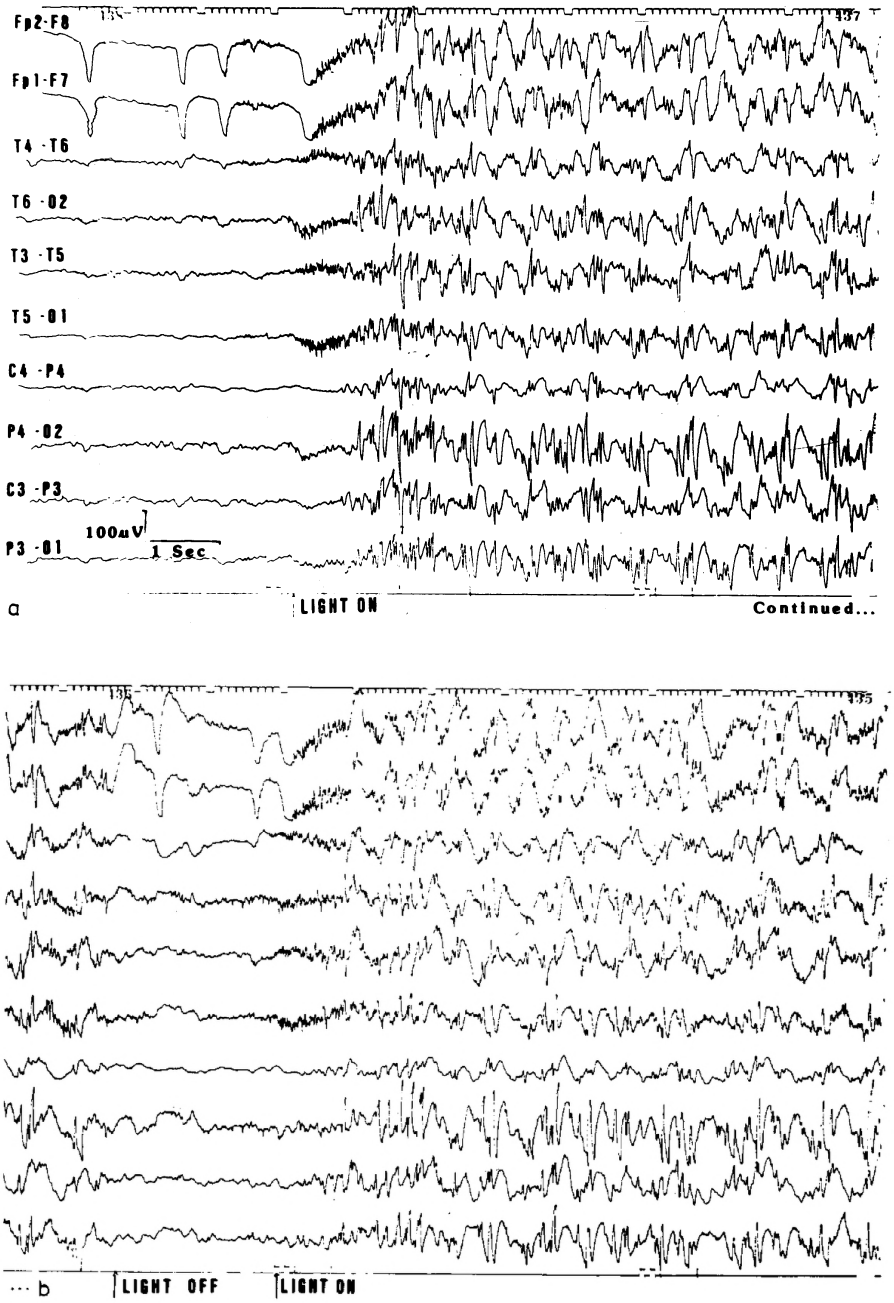

Fig 1. EEG of case 1 during test procedures. The patient was rubbing the forehead throughout this recording. Discharges appear when the light is switched on (a). Discharges disappear when the light is switched off and reappear when the light is switched on again (b).

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continued for more than 3 min because of the fear of a clinical seizure. The abnormal discharges often continued throughout the 3 min period but at times waxed and waned. These tests repeated 1 week later produced similar results.

Clobazam 10 mg twice daily was then added to the treatment regimen. At review 1 week later, the frequency and the duration of rubbing had markedly decreased. The patient volunteered that the compulsion to rub was also much less,even when she stayed in the hot sun, and the sensation of a worm wriggling in the forehead was no more. She still rubbed about thrice a day but the act did not produce seizures. The EEG tests were repeated but photic stimulation or rubbing up to 10 min, with the light on, failed to produce significant abnormalities. Two months later, the patient was still free of fits and the frequency of rubbing had decreased further.

Case 2

A 24-year-old housewife first experienced her seizure at the age of 8. She was crossing a stream when she saw a reflection of the sun in the water. She developed a grand mal convulsion and fell into the stream. Thereafter, she began to induce seizures by looking up at the sun and waving her hand in front of her eyes. This act, in 2-3 min, usually produced a grand mal convulsion and on many occasions she bit her tongue and injured her limbs. Attacks occurred commonly at sunrise or at sunset. She never had seizures indoors or at night. She denied experiencing any pleasurable sensation during or after the act, but said she was compelled to do it when she saw the sun. When her elders tried to stop her she became very angry, and often she performed her ritual in secret. In certain months she had 20-30 seizures. When she came to us she was 7 months pregnant.

The physical examination was normal. She was right-handed and of dull-average intelligence (IQ 79 on Raven's scale). The psychological assessment was similar to that of the previous patient.

Routine EEG showed a symmetrical dominant alpha rhythm of 11-12 Hz. Hyperventilation produced occasional sharp waves bilaterally. Photic stimulation at 6-18 fps evoked generalized spikes or polyspikes with or without slow afterwaves. The tests described in case 1 were then carried out. The results were very similar: waving her right hand in front of the eyes without the light and, looking at the light without waving, 5 min each, produced no abnormality. However, waving with the light on constantly evoked generalized bisynchronous irregular polyspike-and-

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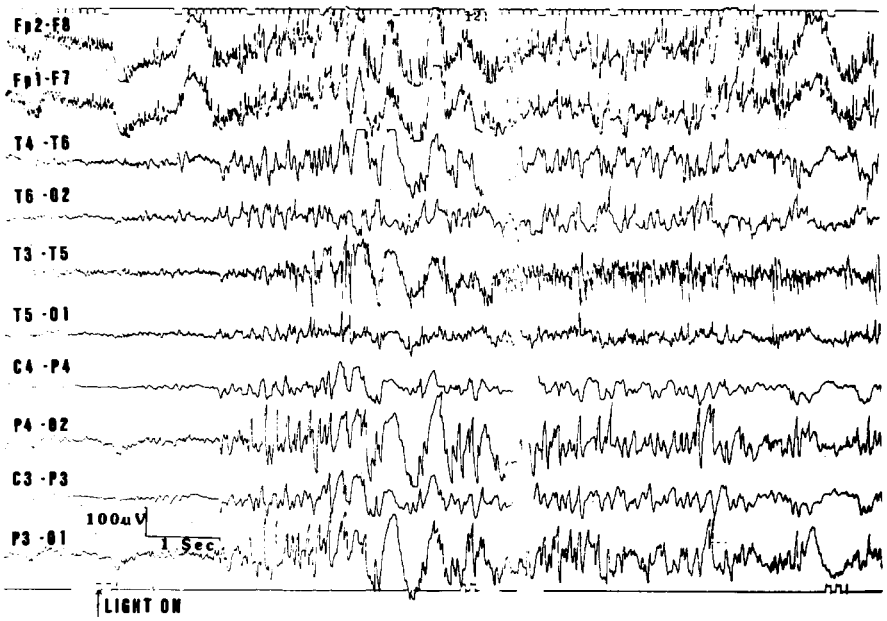

Fig 2. EEG of case 2. The patient was waving the hand throughout this recording. Discharges appear when the light is switched on.

wave discharges immediately or within 2 min. While waving, when the lamp was switched on, similar discharges occurred immediately (Fig. 2). The discharges disappeared when the light was switched off and reappeared when the light was switched on. Tests repeated 12 days later produced similar results.

In view of her pregnancy specific anticonvulsant medication was not started.

Discussion

Self-induced epilepsy in photosensitive patients occurs most frequently in children, especially females. There is often a history of retardation of development but only a few patients present definite signs of neurological damage[16]. Self induced seizures are commonly absence seizures and myoclonic attacks; occasionally periods of confusion, generalized convulsions or Jacksonian seizures occur[13]. In our patients the seizures were tonic-clonic.

Both our patients, as expected, were photosensitive. The EEG records (Figs. 1 and 2) clearly show an eye movement artefact before the epileptiform activity, suggesting that such activity begins with a slow closure of the eyes of the kind described by Darby *et al*[7]. Seizures induced

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by such a closure of the eyes are not rare[4,7]. They may occur in patients who have a history of seizures induced by techniques such as handwaving that more obviously provide an intermittent retinal stimulation[7]. Some authors have suggested that the hand movement, in some patients, is part of the ictus rather than the stimulus[1,12]. In our patients, the movement of the hand in the absence of a bright light failed to induce an electrographic response. But it does not necessarily follow that the hand movement was voluntary. The behaviour of hand-waving could still be ictal even though it was sustained only in the presence of bright light.

Photosensitivity, to a large extent, is genetically determined. Studies suggest that it is less common amongst an indigenous African population rather than in whites living in Africa[3,6]. There is also anecdotal evidence that photosensitivity is generally less common in countries with a large amount of sunshine (C.D. Binnie, personal communication). Our personal experience is also that clinical and EEG photosensitivity encountered in Sri Lanka is far less compared to that seen in a comparable practice in England. It is likely that these two patients used self-induction as an attention seeking manoeuvre following the chance discovery of the effect of sunlight on themselves after the first seizure.

The therapy of self-induction with clonazepam, nitrazepam or sodium valproate is the most likely to succeed[11]. One of our patients was given clobazam as adjuvant therapy in view of its effects on reflex epilepsies both in animals such as audiosensitive mice and photosensitive baboons[5] and in patients suffering from startle, reading and television epilepsies[8]. She, within a week, showed a marked improvement clinically, both in the frequency of seizures and also in her compulsive behaviour. There was striking improvement in the EEG as well; photic stimulation or the rubbing performed repeatedly failed to evoke any epileptiform abnormality.

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Part 3
Epileptic seizures evoked by higher cerebral functions

[3]

Epileptic seizures evoked by card games, draughts, and similar games

Summary

Three Asian patients, since adolescence, had myoclonic jerks and tonic-clonic seizures during card games, draughts, and a local game *'punchi'*. Interictal EEG showed generalized bisynchronous atypical 3-Hz spike and wave discharges. Test procedures evoked EEG dysrhythmia and clinical seizures in two patients. These patients and previously reported cases have the seizure disorder juvenile myoclonic epilepsy (impulsive petit mal), which seems particularly sensitive to provocation by cognitive functions, especially decision making. Myoclonic epilepsy is considered resistant to antiepileptic drugs other than clonazepam and valproate, but two of our patients responded well to clobazam.

Introduction

Charles Symonds (1959), in the Hughlings Jackson Lecture 'Excitation and inhibition in epilepsy,' mentioned that one of his patients was very likely to have an epileptic attack when playing chess. He also referred to a report by Bingel (1957) of a patient whose seizures occurred after playing cards for >2 hours. Since then, more reports have appeared of patients developing epileptic seizures during cards, chess, draughts, or similar games (Ch'en *et al.*, 1965; Forster *et al.*, 1975; Forster 1977; Cirignotta *et al.*, 1980; Striano *et al.*, 1983). This article documents the clinical and EEG features of three Asian Sri Lankan patients who presented with this rare phenomenon.

Case reports

Case 1

A 21-year old woman developed the first seizure, a generalized tonic-clonic attack, at age 12. During the next 3-4 years, several seizures occurred, mostly in sleep at about midnight. The timing of the seizures then changed, and fits began to occur while she ate or immediately

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afterwards, usually at supper. After 2-3 years, the pattern again changed with the seizures occurring when she played leisure games at home. First it happened with *'punchi'*, a local game for 2-4 players with six tiny sea shells used as a die. The scores of each player are indicated by markers on a chart. The patient, after playing *punchi* for 10-15 min, would develop left arm jerks. If she continued the game, she would have a generalized convulsion and fall unconscious. These attacks became so frequent and constant that her parents stopped her from playing *punchi*. She switched to card games, but these also soon began to cause seizures.

The seizures, including those induced by eating, were stereotyped. They begin with a blank expression of the face and rapid eyelid blinking, the left arm then begins to jerk, the mouth deviates to the left, and the head and the entire body turn to the left in writhing movement. A generalized convulsion follows with unconsciousness for 5-10 min. Often, the tongue is bitten and there is incontinence of urine. In addition to these 'major' attacks, she also has sudden jerks of her left arm during card games. The jerks are a warning to stop the game before a generalized seizure occurs.

The seizures were more frequent if money was at stake, but the likely outcome of the game, the number of players, or the time or the place of the game had no noticeable influence. Draughts (checkers), reading, writing, arithmetic, or watching television did not produce seizures. Of the 12 tonic-clonic attacks recorded during the year 1985, 10 were at card games, 1 at *punchi*, and the other at random.

She had been receiving phenytoin (PHT), up to 400 mg/day since 1983. Carbamazepine (CBZ) was added in 1984 and increased up to 800 mg/day. She had never been free of seizures for >2 months at any time.

Past and developmental history were normal. She studied up to grade 9, maintaining an above average work record, at which time she left school because of her illness. Thereafter, she stayed at home helping her mother in housework. She was the fourth child in a family of six children. There was no family history of epilepsy. Physical examination revealed no significant abnormality. She was right-handed and of normal intelligence.

EEG studies

A routine EEG in February 1983 showed a dominant rhythm of 10-11 Hz. No abnormalities occurred at rest or with hyperventilation. An EEG taken soon after a rice meal showed a burst of generalized, atypical 3-Hz spikes-and-wave discharges (Fig. 1). Another routine EEG including hyperventilation and photic stimulation in December 1985 showed no

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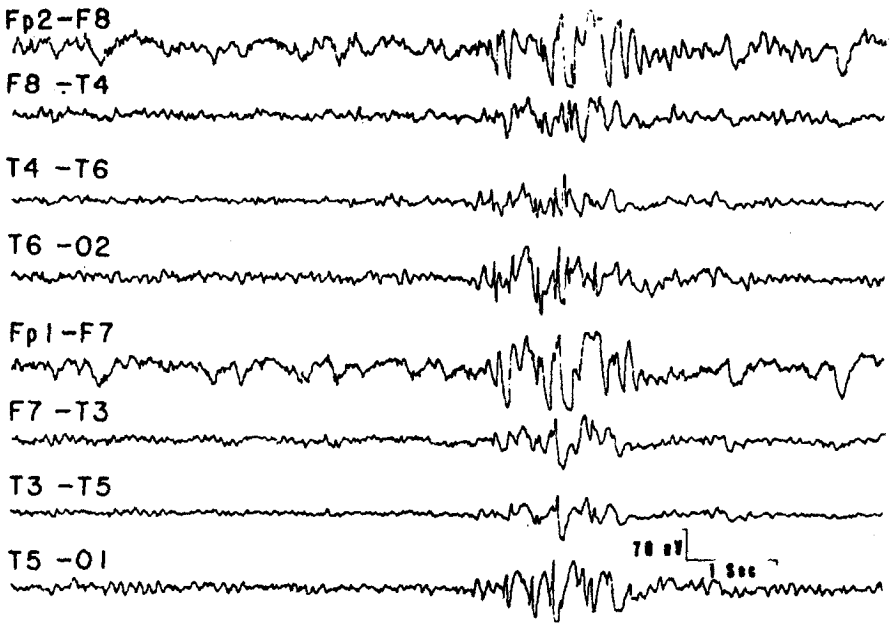

Fig 1. EEG of case 1 soon after a rice meal.

abnormality. Then the following tests were performed with continuous EEG recording. For each test, the number of epileptiform discharges and generalized spikes-and-waves is shown, recorded over a 10-min period. The number of minor spike/sharp or slow wave abnormalities is given within brackets: resting 0(4) (Fig. 2A), mental arithmetic 0(2), reading 2(2), and draughts 2 and card games 9(12) (Fig. 2B). The appearance of EEG discharges were not specifically related to a particular act or situation during the game. Discharges occurred usually when the patient was concentrating on her hand of cards but also when she was anticipating another player's move, throwing a card, or dealing cards, and also when relaxing after a game. Whether she was winning or losing did not seem to influence the EEG abnormalities. The game was continued for 10 min more, and the discharges became more frequent and prolonged. At the end of 20 min, the patient felt dazed and uneasy. The abnormal discharges continued to occur, and 7 min after the game the patient developed a tonic-clonic convulsion and was unconscious for ~5 min.

Clobazam (CLB, Frisium) 10 mg twice daily was added to her drug regimen. She remained well for 5 months and then had a tonic-clonic attack. The dose of CLB was increased to 10 mg t.i.d. Since then she has had occasional attacks, during games, while eating, or at random, but the frequency of attacks has decreased remarkably.

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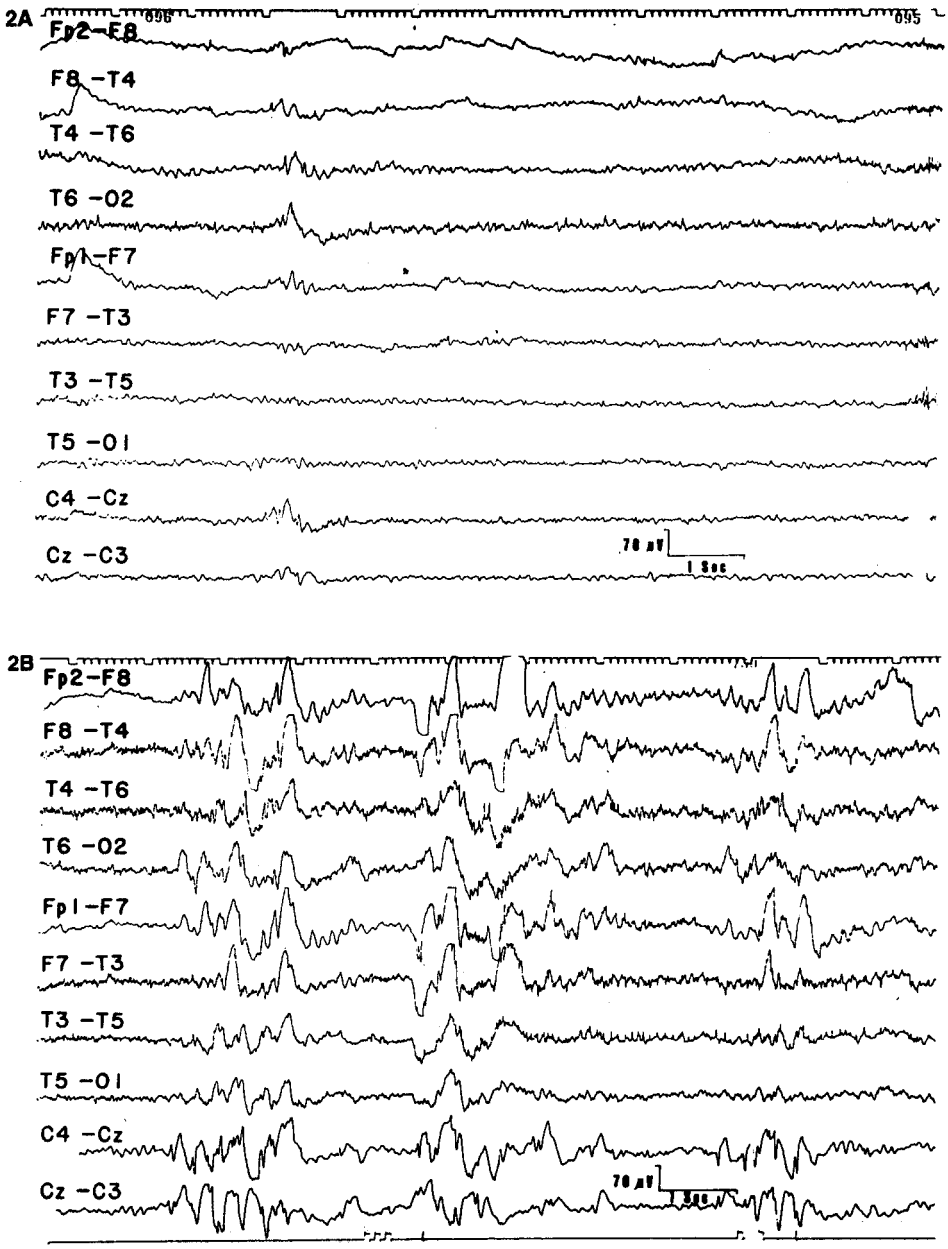

Fig 2. EEG of case 1 at rest showing an episode of minor dysrhythmia (A); EEG of case I during card games (B)

Case 2

A 20-year-old man developed the first generalized tonic-clonic seizure at

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the age of 14. It happened one morning while he was eating ice cream. The second attack, 1 year later, occurred ~30 min after he began playing cards. The attacks occurred without warning and consisted of head turning to a side, clonic movements of limbs, loss of consciousness lasting 10 min, postictal headache, and vomiting. He had 20-30 similar attacks, the majority when playing cards or *punchi*. Five attacks occurred during or within 5-10 min of a meal. Draughts, reading, writing, or arithmetic did not cause fits. There were no fits in sleep. During the past year, he had had several attacks of myoclonic jerks involving head and arms when playing cards.

Birth and development were normal. Past history was uneventful except for febrile convulsions. He studied up to grade 10 and left school because of epilepsy. There was no history of epilepsy among siblings, but the father had had four tonic-clonic fits.

The patient received phenobarbital (PB) 90 mg/day until March 1986, when medication was changed to phenytoin (PHT) 300 mg/day. After PHT, he had been free of both tonic-clonic and myoclonic seizures. Physical examination was normal. He was right-handed and of average intelligence.

EEG studies

A routine EEG in March 1986, before PHT was started, showed a dominant rhythm of 8-9 Hz, a slight excess of theta activity, occasional bursts of generalized, bilaterally synchronous sharp and slow complexes, and one atypical 3-Hz spike-and-wave discharge (Fig. 3). Three months later, while the patient was receiving PHT, a repeat EEG was normal except for an excess of generalized theta activity. Hyperventilation and photic stimulation did not produce significant abnormality.

A 30-min EEG recording carried out at rest, during and after a rice meal, during reading, and when doing arithmetic produced no epileptiform discharges. Draughts and *punchi* games produced one spike-and-wave discharge each, and card games produced two discharges.

Case 3

A 21-year-old man began to experience sudden, transient jerky movements of head, trunk, and upper limbs at the age of 17. The jerks occurred when he played card games or draughts for 10-15 min and occasionally when he played *punchi* or was doing arithmetic. If the jerks occurred while talking, his speech would become interrupted with an explosive 'ah'. Reading, writing, eating, sports, or watching television

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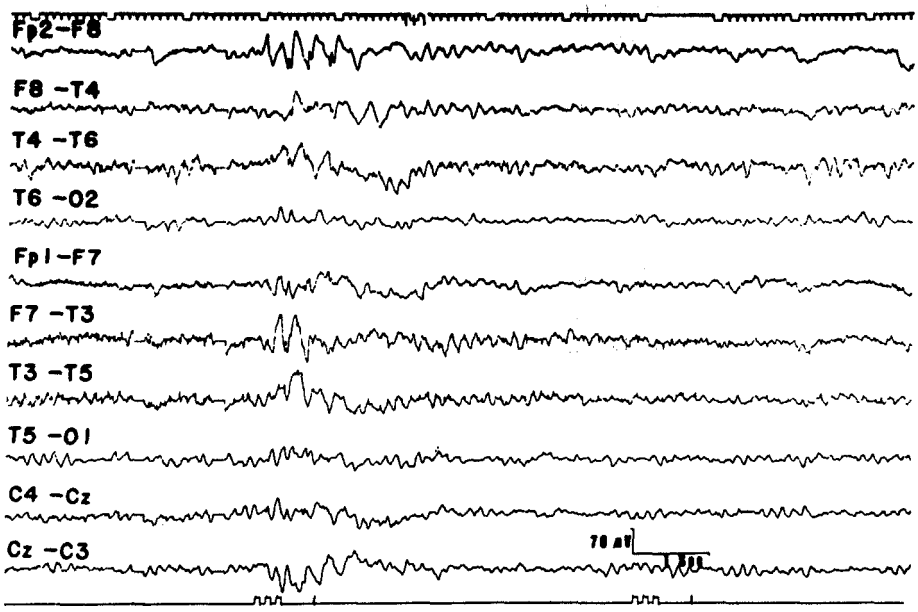

Fig 3. EEG of case 2 at rest before phenytoin was started.

did not cause jerks. He had also had two tonic-clonic seizures preceded by repeated jerks when playing draughts and he gave up these games because of fear of having a major seizure.

Birth and development were normal. Past history was uneventful except for febrile convulsions. He had studied up to grade 10 and passed the examination with credit. Since then he had been working as a sales assistant in a shop.

He had taken PB 60 mg b.i.d. in the past with some improvement, but was not receiving any treatment when he was first seen by us. The physical examination was normal. He was right-handed and of average intelligence.

EEG studies

A routine record showed a dominant rhythm of 10-11 Hz and minimal theta activity bilaterally. Generalized spike-and-wave discharges occurred once at rest and once at the end of hyperventilation. Photic stimulation produced no abnormality. The number of epileptiform discharges, generalized bilaterally synchronous irregular 3-Hz spike-and-waves, recorded during test procedures (30 min each) is as follows: resting 2, arithmetic (written) 1, arithmetic (mental) 3, draughts 4, and card games 9 (Fig. 4).

CLB 10 mg twice daily was prescribed for the patient, and since then he has been free of jerks even during card games and draughts. Two EEG

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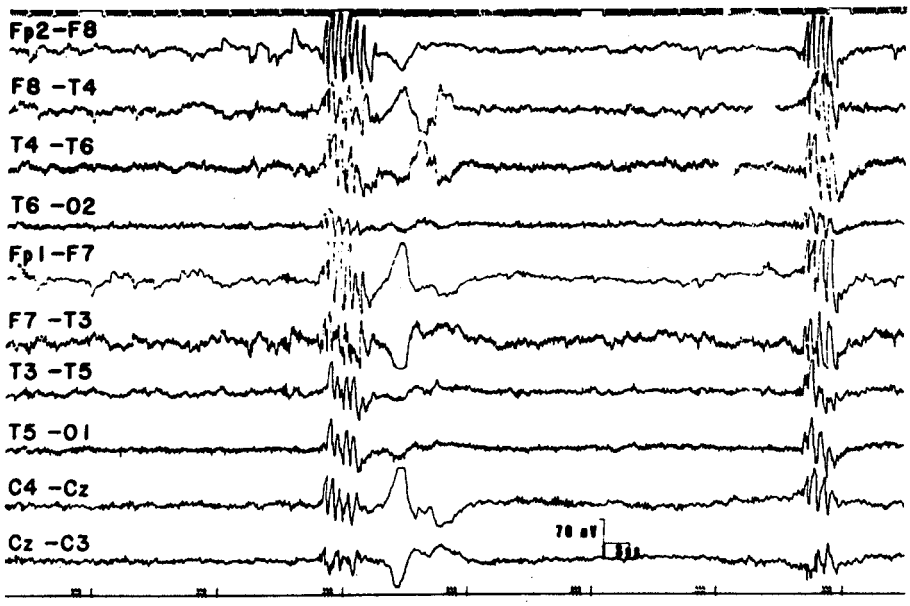

Fig 4. EEG of case 3 during card games.

studies, including the provocative tests listed above, carried out after 2 weeks and 1 month, respectively, showed no epileptiform abnormalities. He has now completed 10 months on CLB.

Discussion

The clinical and EEG features of our patients were those of primary generalized epilepsy. All three patients had myoclonic seizures. These were less prominent and noted only after several years of tonic-clonic seizures in cases 1 and 2. In case 3, however, the myoclonic seizures were the dominant feature; tonic-clonic attacks occurred only on two occasions when he continued playing draughts despite the warning of the jerks. The cardinal EEG abnormality in all three patients was the episodic, generalized, bilaterally synchronous, atypical 3-Hz single or polyspike-and-wave discharges. The history of myoclonic jerks, the onset in adolescence, and the EEG features fit Janz' description of juvenile myoclonic epilepsy: the 'impulsive petit mal syndrome'. The significant feature in our cases was the relationship of their seizures and the EEG dysrhythmia to card games, draughts, and similar games.

Precipitation of epileptic seizures by games and other activities that involve decision making is a rare but recognized phenomenon. Ch'en *et al.* (1965) reported four patients in Shanghai who developed epileptic attacks when watching or playing chess or card games. All had tonic-

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clonic seizures. Two had myoclonic jerks. The basic EEG features were 3- to 5-Hz single or multiple spike-and-wave complexes in two, and sporadic sharp waves or spikes in the others. The abnormalities worsened during card or chess games in two patients. Forster (1977) reported a United States airman who had myoclonic jerks and tonic-clonic attacks while playing cards or chess. He also had seizures when completing insurance forms and during military briefing. The EEG dysrhythmia was generalized atypical 3-Hz spike-and-wave discharges. In Italy, Cirignotta *et al.* (1980) documented a case of epileptic seizures, 'arrest of thoughts' associated with jerking of upper limbs and occasional tonic-clonic attacks during card games and draughts and also when solving mathematical problems. EEG showed bursts of 3-Hz spike-and-wave discharges. Striano *et al.* (1983) reported a patient who developed tonic-clonic seizures with sporadic absences and brief myoclonic jerks while solving arithmetical problems or playing cards or chess. The EEG showed bursts of 3-Hz generalized spike and wave complexes. Another patient who complained of generalized seizures when doing mathematics, produced clinical attacks and EEG abnormalities when playing card games and checkers during neurophysiologic testing (Mutani *et al.*, 1980). All these patients and the three cases reported by us have certain basic features in common: onset of epilepsy in the second decade of life, myoclonic jerks independent of or preceding tonic-clonic seizures, and, on EEG, generalized bilaterally synchronous, atypical single or polyspike-and-wave discharges at 3- to 5-Hz. In primary reading epilepsy, another form of evoked epilepsy related to a cognitive function, the basic features are similar, except that in reading epilepsy the myoclonia usually involves the jaw muscles and the palate (Forster, 1977; Merlis, 1974). Indeed, Forster (1977) reported a classical example of reading epilepsy: a patient who in addition had EEG dysrhythmia and seizures when playing cards. These observations suggest that all these epilepsies evoked by reading, writing, arithmetic, games, and other forms of decision making represent a spectrum of a basic seizure disorder that manifest clinically as myoclonic jerks with or without major seizures and have the EEG feature of generalized bisynchronous spike-and-wave discharges.

Juvenile myoclonic epilepsy is a relatively less recognized and neglected syndrome (Delgado-Escueta and Bacsal, 1984). However, visual stimuli commonly trigger seizures in these cases: Jeavons (1982) found that half his patients were photosensitive. Neither Jeavons (1982) nor Delgado-Escueta and Bacsal (1984- who reported 43 cases of juvenile myoclonic epilepsy) however, reported any patients whose seizures were triggered by cognitive functions.

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The pathophysiologic mechanisms underlying the phenomenon of seizure induction by cognitive functions is not yet established. This is a form of reflex epilepsy that has been suggested to be evoked by visual stimuli. For instance, in reading epilepsy, the passage of vision across the page may produce a pattern-evoked visual response (Marsden and Reynolds, 1982). The same authors also propose, as an alternative, that mental decoding of visual information may be responsible. However, these concepts do not adequately explain the seizure-evoking mechanism of all the cases in this category. Constant concentration on a certain visual pattern may be true of certain games such as chess, draughts, or even cards. But in the local game, *punchi*, the player's attention shifts between the sea shells used as the die and the scoreboard which is much less elaborate than a chess or draughts board. Moreover, one of our patients had a significant number of EEG discharges when doing mental arithmetic with eyes closed. Earlier reports cite similar situations in which mental concentration independent of visual stimulation produced clinical seizures and/or EEG dysrhythmia (Forster, 1977). These observations support Forster's view that the stimulus lies in the higher cognitive functions and acts under very specific conditions. The three factors suggested by Forster, complex decision making, sequential decision making, and stress, seem to be applicable to the situation under which our patients developed their seizures and EEG dysrhythmia.

As regards the seizure-evoking stimuli, case 1 is unique and of special importance because of the transition shown through several seizure-evoking factors, namely, sleep, eating and games. Case 2 also had a significant number of seizures during eating. In our center, we frequently encounter patients with 'eating epilepsy' (Senanayake, 1983), and to date we have recorded 153 cases. Most are cases of partial epilepsy with complex symptomatology with or without secondary generalization showing EEG epileptiform abnormalities in the temporal area. There is a high incidence of sleep attacks in these patients, but none of the patients has complained that seizures are evoked by cognitive functions. Further understanding of the pathophysiologic mechanisms and the psychological aspects underlying these phenomena— eating epilepsy and 'decision-making epilepsy' would be necessary before an explanation could be advanced as to the association between these seizure-evoking factors.

Although the tonic-clonic seizures respond to a variety of antiepileptic drugs, myoclonic jerks are difficult to control with drugs other than CLB or sodium valproate, (Delgado-Escueta and Bacsal, 1984; Jeavons, 1982). All our patients had initially been treated with PB and/or

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PHT. In case 2, both the tonic-clonic attacks and the jerks were satisfactorily controlled with PHT alone. This probably explains why the EEG did not show abnormalities during the testing procedures. The other two patients whose seizures were not controlled subsequently received CLB as adjuvant therapy (case 1) or monotherapy (case 3).

CLB was selected because it had been effective in reflex epilepsies both in animals, such as audiosensitive mice and photosensitive baboons (Chapman *et al.*, 1978), and in patients suffering from startle, reading, and television epilepsies (Gastaut, 1981). It had also been used successfully in the treatment of eating seizures (Aguglia and Tinuper, 1983). Both our patients responded well. Case 3 became completely free of seizures. Case 1 was also free of attacks, but at 5 months had a relapse, probably due to development of tolerance or exhaustion (Gastaut, 1981). However, she improved when the dose was increased to 30mg/day. In view of these encouraging results, we have now undertaken a study at our center to evaluate the efficacy of CLB in the treatment of juvenile myoclonic epilepsy and reflex epilepsies.

Acknowledgements

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Epileptic seizures evoked by the Rubik's cube

Summary

An Asian patient, with clinical features of juvenile myoclonic epilepsy, experienced myoclonic jerks- at times associated with loss of consciousness, when concentrating on a problem, doing arithmetic, and making decisions. Playing the Rubik's cube consistently produced seizures. The interictal EEG showed a few sharp and slow wave complexes, but EEG recorded while doing arithmetic (written and mental), and playing the cube, card games and board games produced an abundance of generalized bisynchronous atypical 3-Hz spike-and-wave discharges and also clinical seizures. These observations suggest that the neural substrate for triggering seizures in this patient lies in the parietal lobe, in an area responsible for spatial processing and calculation.

Introduction

The magic cube, invented by the Hungarian architect Ernö Rubik, is a three dimensional puzzle requiring the restoring of the scrambled coloured pieces of a 3 x 3 x 3 cube to their proper positions. We report on a patient whose seizures were precipitated predominantly and consistently when playing with the Rubik's cube.

Case report

A 30-year-old businessman had experienced sudden transient jerky movements of the body, the right arm in particular, since the age of 15 years. The jerks occurred when he concentrated on a problem; doing arithmetic, checking cash accounts, and making decisions on business matters, were some common situations. An activity which consistently produced the jerks was playing the Rubik's cube. Often the cube dropped out of his hands. The attacks were also associated with transient thought block. The jerks and the mental block made it difficult to proceed with a game. Following repeated jerks, on four occasions, he had become

unconscious for periods lasting 15-20 minutes. After these 'major' attacks he gave up playing the cube. Card games and draughts (checkers) which he played occasionally did not cause jerks as far as he could remember. Neither did other activities such as reading, writing or watching television.

He was taking phenytoin 300 mg/day regularly and diazepam 2-6 mg/day intermittently. With this treatment, he had been free of major attacks for 4 years. The diazepam prevented the jerks but he did not take the full dose regularly because it made him drowsy. Instead, he had trained himself to disengage his mind from a problem and 'let the mind go blank' when he developed a jerk. This avoided repeated jerks and possible major attacks. He was a right-handed man with normal intelligence. No abnormalities were found on physical examination.

The electroencephalogram (EEG) at rest (30 minutes) and on photic stimulation showed no abnormality. Hyperventilation (3 minutes) produced a few episodes of generalized bilaterally synchronous sharp and slow complexes. Playing the cube, within a minute, produced generalized bisynchronous symmetrical atypical spike-and-wave discharges of 3 Hz, each lasting 1-3 s (fig). Twenty such discharges and 11 minor spikes or sharp wave discharges occurred during the test period of 15 minutes. Myoclonic jerks corresponding with the EEG discharges were noted on six occasions. With each jerk, the play was interrupted and the patient appeared dazed. He later volunteered that he had mental block many times during the play. Looking at the cube while turning it around, but not manipulating the pieces, did not produce any abnormality. The following tests were then carried out. Against each test is the number of epileptiform discharges recorded over a 15-minute period: written arithmetic 7, mental arithmetic 23 (jerks +), draughts 17 (jerks +), card game 11, reading 3, verbal test on reading material 3.

Discussion

The basic seizure disorder in this patient is typical of 'impulsive petit mal' or 'juvenile myoclonic epilepsy'[1,2]. The remarkable feature was the precipitation of seizures and EEG abnormalities by specific activities. Visual stimuli are known to trigger seizures in juvenile myoclonic epilepsy, about half the number of patients being photosensitive[1]. However, our patient was not photosensitive. The experiment showed that playing the cube, not mere gazing at the colour pattern, was the important factor in producing dysrhythmia. Mental arithmetic which did not involve any visual or peripheral stimuli, was also a potent trigger. These observations suggest that in this patient, the seizure-providing

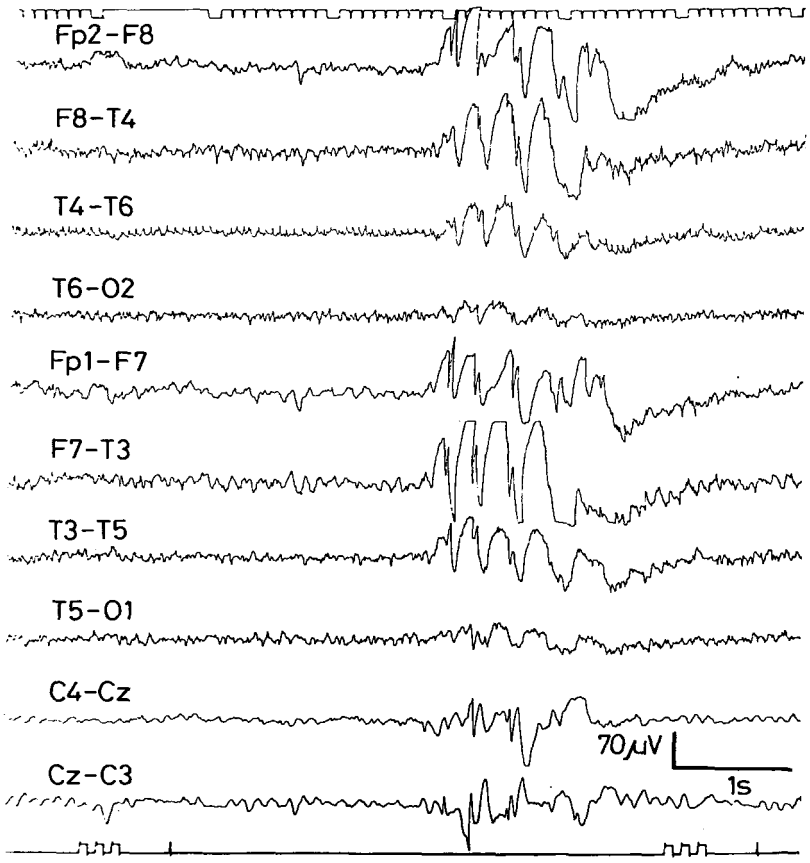

Fig. EEG epileptiform discharges induced by playing the cube.

stimulus lay in the higher cerebral functions, acting under very specific conditions. Epilepsy evoked by higher mental activities is a rare but recognized phenomenon. Reports are available of patients who develop epileptic seizures, including myoclonic jerks, during arithmetical calculations, decision making, and chess, draughts or card games.[3-7] The three factors suggested by Forster[4], complex decision making, sequential decision making, and stress, seem to be applicable to the situations under which our patient developed his seizures and EEG discharges.

The cube and draughts, two of the most potent seizure-evoking stimuli in our patient, involve processing of spatial information. It is noteworthy that in a previous case[6] also, many of the epileptogenic tasks (arranging blocks to form a design describing a letter outline, and drawing from memory) involved spatial processes. These observations could mean that the neural substrate for triggering seizures in these cases lies in the parietal lobe, in an area responsible for spatial processing and calculation.

In some centres, the standard EEG recording includes the performance of mental arithmetic[6]. In our EEG laboratory, we now employ the Rubik's cube as one of the provocative tests in the investigation of seizures related to higher mental functions.

Acknowledgements

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[5]
Epilepsia arithmetices revisited

Summary

Three patients whose epileptic seizures are precipitated by arithmetic calculations are reported and their clinical and EEG features analysed along with those of 7 previous cases. The seizure disorder, in general, was characterised by an onset in adolescence, of myoclonic jerks with or without tonic-clonic seizures and generalized bisynchronous 2-5 Hz spike-and-wave discharges in the EEG. Problems involving processing of spatial information were among the tasks which induced the dysrhythmia. The specificity and the consistency of the seizure-provoking stimuli suggest that in these patients the cortical areas responsible for calculations and related functions are abnormally hyperexcitable and the repeated stimulation during cognitive activities triggers seizure discharges. Two of our patients responded well to clobazam during a follow-up period of 6 months.

Introduction

'Epilepsia arithmetices' - epilepsy pertaining to the art of calculation - was the designation given by Ingvar and Nyman[12] in 1962 to the variety of epilepsy where arithmetic problem solving appeared to be a specific trigger mechanism in provoking seizures. The condition was recognized during routine electroencephalography on a 19-year-old girl with epilepsy. The authors accidentally observed that performance of an easy arithmetic task immediately gave rise to a typical high voltage bilaterally synchronous 3/sec spike-and-wave pattern. Subsequent examinations confirmed a very specific seizure-precipitating effect of solving arithmetic problems.

Previously, Charles Symonds[26] in his Hughlings Jackson Lecture entitled 'Excitation and inhibition in epilepsy' had mentioned that in one of his patients the addition of figures was very likely to result in an epileptic attack. Bickford *et al.*[2] had seen a patient who had right-sided myoclonic seizures and generalized spike-and-wave activity on the EEG

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that were triggered by numerous varied intellectual activities including calculation and recall. More recently, Forster *et al.*[9], in a report of reflex epilepsy evoked by decision making, described a case in which the performance of complex mathematical problems was one of the factors which triggered seizures. Wiebers *et al.*[27] in 1979 reported a 67-year-old woman with longstanding epilepsy in whom spike discharges in the EEG consistently appeared when she attempted to perform mental arithmetic. Four more examples of this disorder have appeared in the literature since then[5,21,25,29].

Cases of this sort are rare. For instance, since August 1951, the standard EEG recording at the Mayo Clinic has included the performance of mental arithmetic. In more than 100,000 recordings, the case reported in 1979 was the only one with EEG activation stimulated predominantly by mathematical calculation[27]. In our Epilepsy Clinic, we have seen 3 patients with this disorder during the past year. This paper documents the clinical and EEG features of these patients and takes a new look at the cases reported previously (Table I).

Report of cases

Case 1

A 16-year-old school girl had been experiencing sudden jerky movements of her right arm during the past year, accompanied by transient thought block when studying; in particular, when studying mathematics. During the term test, she began to develop jerks about 30 min after starting the mathematics paper. The pen dropped out of her hand and she found it difficult to concentrate. She completed the 1 h paper with difficulty but during paper 2 the jerks became more pronounced and in 45 min she had a grand mal convulsion and lost consciousness. She was taken to a doctor who prescribed phenobarbitone 45 mg/day. With this treatment there was some improvement but she continued to have occasional jerks during mathematics lessons. About 9 months after the first major seizure she had to sit the main examination. Again, during the mathematics paper, she started to jerk within 15 min. She forced herself to continue, but halfway through the paper she had a grand mal convulsion. Following this, her medication was changed to sodium valproate 400 mg twice daily. The frequency of jerks had decreased but she still had occasional attacks when doing calculations, especially if she had stayed up late the previous night. The attacks were also commoner during stress.

She had occasional headaches suggestive of migraine. In her early

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childhood she had had 3 attacks of febrile convulsions. Otherwise her past and developmental history was normal. She had 2 elder brothers. There was no family history of epilepsy.

The physical examination was normal. She was right-handed and of

Table I. Summary of clinical and EEG findings of cases of epilepsia arithmetices

Reference	*Age (years)/ sex*	*Age at onset (years)*	*Type of seizures*	*EEG dysrhythmia*	*Triggers*
Ingvar and Nyman[12]	19/F	13	1. Grand mal 2. Petit mal	1. Irregular bisychronous* SW 2.5-3 Hz 2. R frontal focal SW	Calculations
Forster *et al.*[9]	20/M	18	1. Grand mal 2. Myoclonic*	1. Generalised* SW 3 Hz 2. Low voltage spikes	Chess, cards, filling out forms calculations
Wiebers *et al.*[27]	67/F	39	1. Tonic-clonic 2. Minor (?TL) attacks	1. Generalised SW 2-3 Hz 2. R frontal spikes*	Calculations, spatial orientation
Cirignotta *et al.*[5]	26/M	14	1. Tonic-clonic* 2. Myoclonic*	Generalised* SW 3 Hz	Cards, draughts, Calculations
Mutani *et al.*[21]	17/F	17	Grand mal*	Bisynchronous* SW/PSW	Calculations, cards, checkers, puzzles
Wilkins *et al.*[29]	45/M	12	1. Tonic-clonic* 2. Myoclonic?	Generalised* bisychronous* SW 2.5 Hz	Calculations,cards, crossword puzzles, spatial orientation
Striano *et al.*[25]	26/M	14	1. Tonic-clonic 2. Myoclonic* 3. Absences*	Generalised* 4 Hz SW	Calculations, cards, chess
Present series					
Case 1	16/F	15	1. Grand mal* 2. Myoclonic*	1. Generalised * SW 2. Sharp ± slow waves	Calculations
Case 2	16/M	15	1. Grand mal* 2. Myoclonic*	Generalised bisychronous* SW/PSW 3 Hz	Calculations, cards
Case 3	27/M	21	Myoclonic*	Generalised bisychronous* SW/PSW	Calculations, cards, checkers, carrom, picture puzzles

* Provoked

SW = spike-and-slow waves; PSW = polyspike-and-slow waves; TL = temporal lobe.

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normal intelligence.

EEG studies

Routine EEG at the first visit showed a symmetrical dominant rhythm of 10 Hz, a slight excess of generalized theta activity and occasional bilateral sharp waves with or without slow after-waves, more on the right and at times focal in the mid-parasagittal area (C_4 electrode). Hyperventilation and photic stimulation produced no significant abnormality. A written test of arithmetic produced 2 brief episodes of generalized sharp and slow wave complexes, one at 23 min and the other at 35 min. The tests were repeated 1 month later when she was off anticonvulsant medication for 24 h. She was given a test of written arithmetic, multiplication and division. Within 1 min, the EEG began to show generalized irregular spike-and-wave discharges of 4-5 Hz, frontally predominant, more marked on the right and lasting 1-2 sec. There were 4 such major discharges and 10 minor sharp waves/spike discharges during a 30 min period. Then she was asked to do mental arithmetic: serial subtractions. This again, within 1 min, produced abnormalities and in 30 min there were 2 major discharges and 8 minor discharges. A rest period of 5 min produced no significant abnormality. She was asked to continue with the same dose of valproate regularly and the tests were repeated 2 weeks later. On this occasion the written arithmetic test produced only one minor discharge in 30 min.

The patient continues on valproate.

Case 2

A 16-year-old school boy presented with a 1-year history of epilepsy. The illness started with episodes of transient impairment of memory accompanied by jerking of the right arm during arithmetic lessons. Two months later, when doing calculations at school, he had a tonic-clonic seizure heralded by jerking of the arm and was unconscious for 15-20 min. Since then he had had 5 major seizures, 2 when doing arithmetic at home and 3 at random. He had many attacks of jerking and impairment of memory, 10-15/month, when doing arithmetic either at school or at home. These occurred about 15 min after starting a lesson. The attacks were most likely to occur when he was alone, bored or tired and when attempting to solve difficult problems. Other subjects such as languages, religion and natural sciences did not cause attacks. He played cards, 3-4 times/month. On 2 occasions when he was bored and tired after playing for about 0.5 h, his arm started to jerk. He did not play chess or draughts (checkers). Watching television did not produce jerks.

His birth and development and the past medical history were normal. He was the 4th in a family of 6 children. There was no family

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history of epilepsy. When seen by us he was on phenytoin 250 mg/day.

The physical examination was normal. He was right-handed and of normal intelligence.

EEG studies

Routine EEG including hyperventilation and photic stimulation produced no significant abnormality. The EEG was then recorded at rest (15 min) and during the tests (15 min each) listed below. The tests were interposed with resting periods of 5 min each.

Tests

(1) Reading (mental); (2) transcribing pages of a novel; (3) mathematics, learning a new type of sum; (4) mathematics (written); (5) arithmetic (mental) - serial subtractions; (6) arithmetic (written) - serial subtractions as in test 5; (7) mathematics (written) - as in test 4; (8) answering (in writing) a personality questionnaire. The resting periods and tests 1, 2 and 8 produced no specific abnormalities. Test 3 produced the first epileptiform abnormality, 9 min after commencement. This was a brief generalized bisynchronous spike-and-wave discharge. There were 3 such discharges during the test. Test 4 produced spike-and-wave discharges from the beginning. The frequency and the duration of the discharges steadily increased, so that by 10 min there were as many as 4 discharges/min, often lasting 2-3 sec. They were basically bisynchronous irregular spikes, or occasionally polyspikes and waves of 3 Hz (Fig. 1). Many were accompanied by visible jerks of the right arm. Often the patient appeared distressed by the jerks and stopped his task temporarily. As soon as the test was completed the jerks ceased and the EEG resumed the resting state. Test 5, mental arithmetic, produced only 3 minor spike-and-wave discharges. However, doing the same subtractions using pen and paper in test 6 produced EEG abnormalities and clinical jerks as in test 4. Test 7 also evoked a similar response.

Clobazam 10 mg twice daily was added to the treatment regimen. The testing procedures repeated the next day failed to produce any EEG abnormality or jerks. Clobazam was discontinued after 1 month, and 1 week later he began to experience jerks. EEG showed spike discharges when doing calculations. Two weeks later, at an arithmetic lesson, he developed a grand mal seizure preceded by myoclonic jerks. Clobazam was restarted, 10 mg twice/day. During the next 5 months he was free of jerks even when doing calculations, and the EEG with the test procedures carried out on 2 occasions was free of epileptiform

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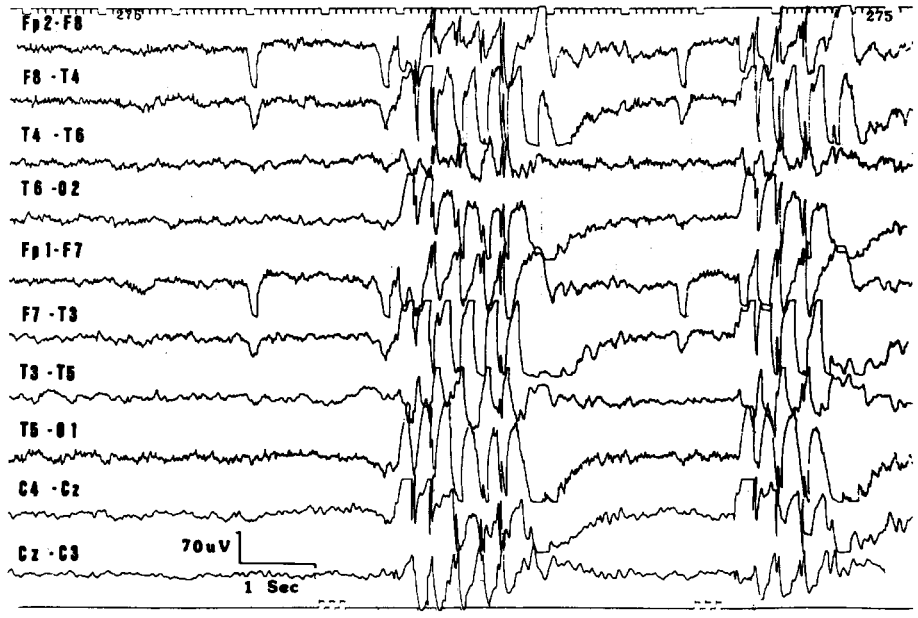

Fig. 1. EEG dysrhythmia evoked by calculations in case 2.

discharges.

Case 3

A 27-year-old male, school teacher, gave a history of sudden attacks of generalized jerky movements affecting the body, accompanied by transient thought block since the age of 21. These happened when concentrating on a problem, usually mathematical calculations. At the Chartered Examination he failed to complete the mathematics and the accounts papers because of frequent jerks. As a teacher he taught commerce subjects and the mathematics classes commonly produced jerks causing him much embarrassment. During the attacks, if he had been talking, his speech would become interrupted with an explosive 'ah'; if he had been writing on the blackboard, the chalk would drop out of his hand. He also had several falls. But he had never experienced tonic-clonic convulsions or lost consciousness. Other activities which occasionally evoked jerks were playing cards, draughts and carrom. He had been taking diazepam 2 mg thrice daily for the past 3 years with some improvement, but he was never completely free of seizures. When seen by us he was only taking propranolol 20 mg thrice daily for migraine.

His past history was normal. There was no family history of epilepsy.

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The physical examination was normal. He was right-handed and of normal intelligence.

EEG studies

Routine EEG including hyperventilation and photic stimulation and a resting record of 10 min showed no significant abnormality. However, a written arithmetic test produced generalized bisynchronous single or polyspike-and-wave discharges and minor spike discharges within 3 min. During 30 min, there were 2 major and 3 minor discharges. Response during Raven's (progressive matrices) IQ testing was most remarkable: the abnormalities began to appear within 5 min, and there were 45 major discharges, accompanied by visible jerks and mental block, and many minor discharges during 30 min.

More tests of intelligence were then carried out: (1) analogy tests - finding a comparative relationship existing between ideas and words, e.g., fur is to animals as clothes are to ... ; (2) series tests in an arithmetical series, indicating the next number in the order, e.g., 1,5,9,13,17... (3) figures test - similar to Raven's progressive matrices; (4) logic tests, e.g., A is older than B but younger than C. D is older than A. If D is not the eldest, who is the youngest?

These were written tests, administered in Sinhala - the mother tongue of the patient. The duration of each test was 6 min, and during this period the patient was asked to answer as many test items as possible. Test periods were interposed with rest periods of 3 min each.

The tests were performed well, and subsequent assessment showed that the patient had scored 50% or more in each category of tests: analogy test, 50%; series test, 67%; figures test, 60%; logic test, 80%. During 3 of the tests the EEG showed generalized bisynchronous spike or poly-spike wave discharges, some accompanied by clinical jerks and mental block, and also minor spike discharges. The number of major discharges during each test was: analogy test, 0; series test, 17 (jerks +); figures test, 8 (jerks +); logic test, 1. During the rest periods he showed no abnormality. These EEG studies repeated on the same day and 18 days later produced similar results.

The patient was then prescribed clobazam 10 mg twice daily. At review 2 weeks later, his condition had improved remarkably. He was free of symptoms except for a few instances of slight interruption of speech during mathematics lessons. The test procedures repeated on this occasion failed to produce any EEG abnormality. Subsequently, the palatal myoclonia also disappeared, and for the past 6 months, on regular clobazam therapy, he has been completely free of symptoms.

Discussion

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Clinically, the seizure disorder in our patients was dominated by myoclonic jerks, beginning at a relatively young age. The EEG was characterized by generalized atypical spike or poly-spike wave discharges of 3-5 Hz. The EEG abnormalities and the clinical seizures were triggered commonly, in 1 case exclusively, by mathematical calculations. Most of the previous cases also had similar features. In all except one[27], the onset was in the second decade of life. Four patients had myoclonic jerks in addition to tonic-clonic seizures or absences. The dominant EEG abnormality in 6 patients was generalized atypical spike- or polyspike-and- wave discharges of 2-4 Hz. There was no evidence of brain damage or an identifiable cause of the epilepsy. These features suggest primary generalized epilepsy, except in 1 case[27] who had right frontal spike discharges. In primary reading epilepsy, the basic features are similar except that the myoclonia involves the jaw muscles and the palate[8,19,22]. Other forms of language-induced epilepsy[1,11] and epilepsy evoked by card games, chess and similar games[4,23,24], also manifest as myoclonic seizures. Thus it appears that these reflex epilepsies related to cognitive functions share certain basic features, and myoclonia dominates the symptomatology.

The pathophysiological mechanism underlying the phenomenon of seizure induction by cognitive functions has not yet been established. In reading epilepsy, several factors such as pattern vision[18], proprioceptive input from the jaw and eye muscles, attention to reading, and conditioning to the circumstances of reading may be involved[6]. These concepts, however, do not adequately explain the seizure-evoking mechanism in all the cases. In some of our patients and in previous cases[9,25,27,29], mental arithmetic was equally or sometimes more effective than tasks involving visual stimuli, in provoking dysrhythmia. It has already been demonstrated that attention to task was not a sufficient condition for the occurrence of dysrhythmia[29] and conditioning of the patient during a long-lasting task was unlikely to play a major role in the pathogenesis of the seizures[12].

It is now well recognized[8,11,22] that complex cerebral activity can trigger seizures. The stimulus probably lies in the higher cognitive functions under very specific conditions, and 3 factors, namely complex decision making, sequential decision making and stress, may vary in their threshold effect[9]. The specificity of the task is a determinant as exemplified by 2 of our cases. In case 2, during test procedures, only calculations triggered dysrhythmia; reading, writing or filling in a questionnaire had no effect. In case 3, calculations and puzzles involving pictures or numbers were the seizure triggering stimuli, puzzles involving words being ineffective. Solving picture-puzzles

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requires spatial processing. In a previous case[29] also, many of the epileptogenic tasks involved spatial processes. Since calculation and spatial processing are functions delegated to the dominant parietal lobe, it could follow that an area in the parietal lobe provided the neural substrate for triggering seizures in these cases.

In the experimental animal, myoclonic jerks are probably mediated through brain-stem mechanisms[17]. The cortex does, however, facilitate the myoclonic mechanism[16,20]. In the development of generalized seizures repeated reflex bombardment may increase the responsiveness of both cortical and brain-stem centers[13]. In some patients, certain parts of the cortex are possibly more hyperexcitable than others[28]. Epilepsia arithmetices probably represents a situation where the areas responsible for calculation (and spatial processing) are abnormally hyperexcitable and possess a lower threshold for dysrhythmia. This concept is analogous to the hypothesis postulated by Wilkins *et al.*[28] that in pattern sensitivity the epileptiform disturbances originate in occipital regions. They suggest 2 stages in the generation of the photoconvulsive response. When normal physiological excitation exceeds a certain limit, a paroxysmal disturbance is triggered. When the disturbance exceeds a certain topographic limit, complete generalization occurs. Although in our patient no clear focal onset of the EEG dysrhythmia was noticed, in a previous patient[9], the 3 Hz wave-and-spike disturbances began at the F3 or F4 electrode. Another patient[27] showed spike discharges in the right frontal area during calculations and spatial orientation. These observations could mean that calculation functions are not confined to one specific area of the parietal lobe, but probably involve one or both frontal lobes as well. The view that the parietal lobe has no valid independence as an anatomical structure, and hence that the physiological functions of each parietal lobe are integrated with other activities of the brain as a whole, has also been expressed by other authors[15]. Epilepsia arithmetices and other language-induced epilepsies could thus provide an experimental model for the study of topographical aspects of higher cerebral functions.

Myoclonic jerks are difficult to control with any drugs other than clonazepam or sodium valproate[7,14]. Our case 1 responded well to valproate. The other 2 patients were given clobazam because their seizures were not controlled with phenytoin and diazepam. Clobazam had been shown to be effective in reflex epilepsies both in animals[3] and in man[10]. Both our patients responded well. In fact, after clobazam, the EEG failed to record any dysrhythmia even with repeated activation procedures.

Behavioural therapy has been used with some success in the mana-

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gement of certain types of reflex epilepsies[8]. Avoidance of evoking stimuli, repeated presentation of altered stimuli, repeated stimulations in postictal refractory state, vigilance inhibition and avoidance conditioning are the methods employed. Most of those methods are not applicable in epilepsia arithmetices for obvious reasons. Forster[8] attempted vigilance inhibition, signalling the subjective occurrence of the seizures while playing chess, but it was unsuccessful. As such, appropriate anticonvulsant medication is likely to continue as the mainstay of treatment in this form of epilepsy.

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Part 4
Eating epilepsy

[6]
Eating epilepsy - a reappraisal

Summary

One hundred and fifty patients with eating seizures were detected over a 9-year period in two hospital clinics in Sri Lanka. The clinical and EEG features of 120 of them are compared to a control group of 120 patients with epilepsy. Patients with eating seizures showed a male predominance of 3:1. In more than 50%, the onset of epilepsy was in the 2nd decade of life. A family history of epilepsy was obtained in 28.3% and 21 sibling themselves had eating seizures. The seizure type was simple or complex partial; secondarily generalized seizures were common. The EEG in 71.6% showed spikes, sharp/slow waves, focal in the temporal ares. The response to medication of eating seizures was similar to that of controls. Clobazam used in 17 patients as monotherapy or adjuvant therapy proved useful. The very high prevalence of eating epilepsy in the present series could pathogenically be related to genetic or ethnic factors and to the bulky meals rich in carbohydrates consumed by the patients.

Introduction

Charles Symonds[23] in his Hughlings Jackson Lecture, 'Excitation and inhibition in epilepsy' in 1959, suggested that precipitation of epileptic attacks by visceral stimuli was more common than generally appreciated. He cited the example of a man who suffered seizures during the day; these took the form of sudden confusion and a sense of familiarity which lasted 2 or 3 min while eating a heavy meal. A comparable case had been recorded by Allen[4] in 1945. In 1954, Boudouresques and Gastaut[5] reported on 4 patients with temporal lobe EEG foci who had postprandial seizures attributed to gastric distension. Subsequently, more case reports appeared from different parts of the world[1-3,7-10,12-21,24] and the condition came to be known as 'eating epilepsy'. Of a total of 76 cases, 33 were from India.

The Epilepsy Clinic and the Neurology Clinic at Peradeniya register

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150-200 new cases of epilepsy every year. During the past 9 years, we identified 150 patients from these 2 clinics whose seizures were related to a meal, either exclusively or in the majority of instances. In this paper we analyse the clinical and EEG features of these patients in comparison with a control group of epilepsy patients drawn from the same clinics. We also review the reported cases in the light of our experience.

Patients and methods

Patients who had more than 50% of the fits during or within 30 min of eating breakfast, lunch or dinner were considered to be suffering from eating epilepsy. The frequency of eating seizures was obtained from the history and, wherever possible, verified using fit-charts. The patients were interviewed personally using a standard questionnaire. A parent or an elderly relative and an eye-witness were also interviewed for information regarding birth, development, childhood illnesses and the seizures. Information was verified with clinic notes, especially with regard to medication and response to treatment. Previous EEGs were traced and reanalyzed. New recordings were made where necessary. EEGs were recorded on a 10-channel recorder according to the 10-20 system. Routine recording included hyperventilation for 2-3 min and photic stimulation.

Of the 150 cases of eating epilepsy on record, complete and reliable data and EEG tracings could be obtained for 120 patients. These 120 cases are referred to as the 'test group' in subsequent analyses. From the same clinics, 120 cases of epilepsy matched with the test group for age and sex were randomly selected to serve as controls.

Results

Forty of the 120 patients in the test group suffered only eating seizures. Twenty-three of them had experienced more than 10 seizures each. The other 80 patients also had random seizures. Seventy of them had experienced more than 10 seizures (eating or random) each and the remaining 10 patients a minimum of 6 seizures each. The age range of the patients was 13-43 years (mean 23.7 ± 6.1). The male:female ratio was 3:1. In the 40 patients who had exclusively eating seizures, the ratio was 6:1, 12 (10.0%) patients of the test group were married. The pattern of employment of the test and the control groups was similar. One hundred and seventeen (97.5%) patients of the test group were Sinhalese, 2 were Muslims and 1 was a Tamil.

The onset of epilepsy in 96 patients (80%) of the test group was in the 2nd decade of life. The age at onset of epilepsy for the control group was

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significantly different (P <0.002), the onset being in the 2nd decade in only 69 (57.5%). Factors of aetiological significance were similar in the two groups. However, there was a significantly higher incidence (P < 0.01) of left-hand dominance in the test group (18 patients - 15%) compared to the control group (6 patients - 5%). The prevalence of epilepsy among male siblings was significantly higher (P < 0.001) in the test group (20 patients - 16.7%) than in the control group (4 patients 3.3%). The prevalence among other family members was similar in the two groups and the figures for the test group were: parents - 4 (3.3%), sisters - 9 (7.5%), others - 9. Thirteen of the male siblings and 8 of the female siblings were themselves patients with eating epilepsy belonging to 9 different families.

The type of epilepsy and the predominant EEG features are presented in Table I. In these two respects, the differences between the test group and the control group were highly significant. The common symptomatology of the partial complex seizures experienced by the test group was: epigastric sensations - 12 (10.0%), gustatory/olfactory hallucinations - 10 (8.3%), fear - 39 (32.5%), dreamy states - 39, abnormal speech - 44 (36.7%), automatism of face and mouth - 46 (38.3%), and

Table I. Type of epilepsy/seizures and predominant EEG features

	Test group (n = 120)	Control group (n = 120)
*(Ia) Type of epilepsy/seizures**		
Partial epilepsy	120 (100.0)	76 (63.3)***
Partial complex	5 (4.2)	10 (8.3)
Secondarily generalised		
Partial simple	20 (16.7)	18 (15.0)
Partial complex	91 (75.8)	38 (31.7)***
Undetermined symptomatology	4 (3.3)	10 (8.3)§
Generalised epilepsy	0	39 (32.5)
Unclassified	0	5 (4.2)
*(Ib) Predominant EEG features***		
Spikes, sharp/slow waves focal in		
Right temporal area	64 (53.3)	26 (21.7)***
Left temporal area	10 (8.3)	11 (9.2)
Both temporal areas	12 (10.0)	12 (10.0)
Generalised spikes, sharp/slow waves	3 (2.5)	21 (17.5)
Focal and generalised abnormalities	8 (6.7)	0
Nonspecific abnormalities	19 (15.8)	16 (13.3)
Normal	4 (3.3)	34 (28.3)***

* Overall X^2 test of association, $X^2 = 53{,}878$, $P < 0.0001$.

** Overall X^2 test of association $X^2 = 61.533$, $P < 0.0001$.

*** Difference significant at $P < 0.001$.

§ Difference significant at $P < 0.05$.

Figures in parentheses are percentages.

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automatisms of limbs - 20 (16.7%). The symptomatology was similar in the two groups except for epigastric sensations which showed a significantly higher incidence ($P < 0.01$) in the control group (35, 29.2%).

The relationship of eating seizures to the 3 main meals is shown in Table II. One hundred and six (88.3%) patients had the seizures while eating, usually within 5 min of starting the meal. 47 (39.2%) had seizures immediately after the meal. Thirty-eight (31.7%) also, or only, had seizures during the postprandial period; these occurred within 30 min, but usually during the first 10 min. In 66 (55%) patients, the eating seizures occurred only in relation to rice meals, and in 3 (2.5%) only when eating meat or fish. The factors considered important by the patients in the causation of their seizures, together with the number of the patients who gave a positive response, were: eating late - 26 (21.7%), eating too much - 12 (19%), eating fast - 5 (4.2%), hot food - 4 (3.3%), cold food - 2 (1.7%). Sixteen (13.3%) patients had eating seizures only when eating alone, and 45 (37.5%) only when eating with others. Sixty-one (50.8%) patients had eating seizures only when eating at home and 1 (0.8%) only when eating out. Only 3 (2.5%) patients avoided a particular food item (meat or fish) because of the fear of fits.

Table II. Relation of the eating seizures to the main meals

	Lunch only	*Dinner only*	*B'fast only*	*Most at lunch*	*Most at dinner*	*Most at b'fast*	*Not specific*
Number of patients (n = 120)	14	14	3	29	45	10	5
(%)	(11.7)	(11.7)	(2.5)	(24.2)	(37.5)	(8.3)	(4.2)

The number of antiepileptic drugs taken by the test group at the time of the survey was: 1 drug by 72 (60%) patients, 2 by 38 (31.7%), 3 by 3 (2.5%), no drugs by 7 (5.8%). The antiepileptic drugs used were: phenytoin in 75 (62.5%) patients, carbamazepine in 43 (35.8%), clobazam in 17 (14.2%), phenobarbitone in 16 (13.3%), primidone in 4 (3.3%), valproate in 1 (0.7%). The result of medication as expressed by the patients and verified with the clinic records was: free of fits - 44 (36.7%) patients, improved - 59 (49.2%), same 9 (7.5%), worse - 3 (2.5%), unspecified - 5 (4.2%). The treatments received by the test group and the control group were significantly different but there was no significant difference in the response. Of the 17 patients treated with clobazam as monotherapy or adjuvant therapy, 2 were free of fits, 13 improved and 2 remained the same.

Of the 80 patients who suffered both random and eating seizures, the ratio between eating seizures and random seizures changed in 22 (27.5%) during the course of the illness. Some patients who initially had random seizures subsequently developed eating seizures and ended up

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with eating epilepsy. On the other hand, some who had mainly or sometimes exclusively eating seizures later began to develop mainly random seizures.

Discussion

Definition

Eating seizures, for the purpose of this study were defined as fits occurring during or within 0.5h of eating a meal. Postprandial seizures were included because of the observation that a proportion of the patients who had seizures during eating also had postprandial seizures. Some patients who initially had seizures during eating subsequently began to have fits only in the postprandial state and vice versa. The time limit of 0.5h for the postprandial period was arbitrary. In the majority, the seizures occurred soon after or within 10 min of a meal.

A patient takes about 15 min to eat an eastern meal. Even if one assumes that a meal lasts 30 min, together with the 30 min postprandial period, the total duration of meal-related behaviour in relation to the 3 meals is 3 h/day. The probability of a seizure occurring by chance during meal-related behaviour is therefore 3/24 = 0.125. The probability of a patient having 2 seizures, both related to meals, is then 0.125 x 0.125 = 0.0156, much less than the conventionally accepted criterion of 0.05 below which it is unreasonable to assume chance occurrence. Sixty of our patients had mixed seizures, but each patient had a minimum of 6 seizures out of which at least 3 were eating-seizures. Applying the binomial test[22], given that the chance probability of each seizure being meal-related is 0.125, the probability that 3 or more of the seizures will be meal-related is 0.042, again below the conventional criterion. Thus, in the present series, the relationship between seizures and eating could not have occurred by chance alone.

Prevalence

Eating epilepsy, judging by the previous reports, is a rare disorder. Vizioli[24] from 20,000 examinations in the Laboratory of Electroencephalography of the Rome University, found only 9 cases whose seizures were related to eating. Nagaraja and Chand[15] found 13 cases amongst a total of 11,783 patients with epilepsy who attended the National Institute of Mental Health and Neuroscience in Bangalore - a prevalence of 1.1/1000 epilepsy patients. The prevalence at our centre is about 100 times the Bangalore figure. Even if one only considers the 40 patients who had exclusively eating seizures, the prevalence would still

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be very high, about 25/1000 epilepsy patients. Our awareness and interest are insufficient in themselves to explain this high prevalence. Could it be that there are host characteristics, ethnic and/or genetic, which predispose our patients to develop seizures in relation to eating? Or is there any peculiarity in their diet, physical or chemical, which is epileptogenic? Eating epilepsy with its high prevalence in the Kandy District of Sri Lanka is reminiscent of 'hot water epilepsy' which shows a geographical predilection to the Deccan plateau of the Karnataka State in South India[14].

Patient characteristics

The male preponderance and the frequent onset in the 2nd decade as in our series had also been noted previously[15]. An aetiologically related factor was only evident in a small percentage of cases just as in the literature[19]. There was a high incidence of epilepsy among siblings of patients with eating epilepsy. Nagaraja and Chand[15] also found a high incidence (50%) of epilepsy among family members in their series. It is interesting that in our study 21 siblings themselves had eating epilepsy. This familial occurrence of eating epilepsy has not been reported before.

Among the previously reported cases, Aguglia and Tinuper[2] recognised 3 main types of seizure: (a) complex partial seizures: 1 of their cases, 4 cases described by Boudouresques and Gastaut[5], 7 by Vizioli[24], 1 by Forster[10] and 5 by Chemburkar and Desai[7]; (b) simple partial seizures: 1 case by Abenson[1], 1 by Robertson and Fariello[19] and 1 by Reder and Wright[17]; and (c) generalized myoclonic and/or atonic seizures: 2 of their cases and 1 by Cirignotta *et al.*[8]. Nagaraja and Chand[15] recorded temporal lobe epilepsy in 12 of their 13 cases. These reports confirm that partial epilepsy is the dominant type of epilepsy, and that partial complex seizures with or without secondary generalisation are the commonest seizure type. EEG in our series accordingly showed epileptiform abnormalities maximally in the temporal areas. The symptomatology of the partial complex seizures was not specific to eating epilepsy.

Relation to eating

In the majority of our patients, eating seizures accounted for more than 90% of all seizures. In the individual patient, eating seizures may be replaced by random seizures and vice versa as described earlier[3,8]. In the majority (88.3%) of the patients, the seizures occurred while eating. Some patients who initially had postprandial seizures subsequently had

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seizures while eating, and vice versa. 21 (17.5%) patients had occasional seizures while getting ready for a meal even before touching food as described earlier[20].

Food and eating habits

In Sri Lanka the staple diet is rice, and the two main meals, lunch and dinner, usually consist of rice served with several curries. Occasionally, bread or a preparation made of rice flour or wheat flour may replace rice. The breakfast is usually a light meal consisting of bread or any other preparation made of flour served with a curry. Some people may also have rice for breakfast. Most of the patients who had seizures at breakfast were those who ate rice for breakfast. The predilection of the eating seizures for a particular meal had already been noted, e.g., breakfast[8] or lunch[2]. Sixty-six (55%) of our patients thought that their eating seizures occurred only when they ate their staple diet, i.e., rice meals. Only 3 patients had noted that their seizures occurred only when they ate meat or fish. The relevance of the type of food is uncertain[2,8] considering an unusual case who developed fits only when eating an apple[1]. In the Bangalore series[15], 8 patients were strict vegetarians while the other 5 ate both vegetarian and non-vegetarian food. Factors such as eating late or eating too much were not considered important[23]. But Forster[10] in his experiments was able to eliminate the texture and temperature of food, time of eating, and the taste as specific or aggregate evoking factors. Nagaraja and Chand[15] thought that in 12 of their 13 cases, the seizures were brought on only by a specific pattern of eating a conventional Indian meal, which involved mixing and eating with the right hand a large bulk of rice with curries and vegetables.

Pathogenic mechanisms

Attempts to find a specific stimulus or a seizure-triggering mechanism have either been unsuccessful[10,15] or have produced variable results[2,8,20] including mastication and swallowing[20], passage of food along the oesophagus[12], gastric distension[5] richness of the meal[24] and a chemical substance[1], lifting food with the fork or cutting food[17]. The last case[17] subsequently lost the second, third and fourth digits of his right hand in an accident and ceased to have seizures. Our observations support the view that multiple stimuli may play a role in the pathogenesis or eating seizures. Several sites within the central nervous system have been suggested as the area responsible for initiating eating seizures. These include the diencephalon[19], hypothalamic areas[21] and the amygdala[3,9]. It is possible that during eating the amygdala becomes the site of additional stimulation, which may lower the seizure threshold and lead to rapid

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generalisation of seizures.

Treatment and prognosis

Eating epilepsy is considered difficult to treat[3,8,10,15]. Our experience was rather different; 85.9% or our patients were either free of fits or at least satisfactorily controlled. Many received clobazam[2,6,11] which shows promise in the treatment of eating-related seizures.

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[7]

Familial eating epilepsy

Summary

Eating-related seizures affecting 20 individuals among 59 siblings belonging to nine families are presented. The type of epilepsy was partial in all the affected individuals, and the seizures complex in 15 and simple in 5, secondarily generalized in the majority. The onset of epilepsy, in most cases, was in the second decade of life. A remarkable degree of intra-family consistency was observed with regard to age at onset, symptomatology of seizures and timing of eating seizures. The study demonstrates sibling clustering in a partial epilepsy, implicating for the first time, genetic susceptibility in the aetiology of eating epilepsy.

Introduction

The phenomenon of seizures related to eating was first appreciated by Allen in 1945 [5], and subsequently corroborated by the observations of Boudouresques and Gastaut [6] and of Symonds [21]. Further case reports appeared from different parts of the world [1-3, 7, 8, 10, 13, 16, 18, 22] and the condition came to be known as 'eating epilepsy'.

At Peradeniya, we have encountered a large number of patients with this disorder, 196 during the past 11 years. The clinical and electroencephalographic (EEG) features in 120 of these were analysed and the pathogenic aspects discussed in a previous paper [19]. A singular observation was the clustering of patients within certain families. This paper presents nine families where more than one member of a family had eating seizures. This is the first record, to our knowledge, of sibling clustering of eating epilepsy.

Patients and methods

Twenty patients having eating seizures were studied. Seizures which developed during, or within 30 min after a main meal (breakfast, lunch or dinner) were considered as eating related. The frequency of seizures

was verified with the fit charts wherever possible, and an eye-witness was interviewed. Information regarding birth, development and childhood illnesses was obtained from a parent or a family-elder. A complete physical examination was carried out. EEG was recorded with a ten-channel recorder on the 10-20 system.

Routine recording included hyperventilation for 2-3 min and photic stimulation. The parents and the asymptomatic siblings, wherever possible, were interviewed in person and examined, and their EEGs were recorded. The possibility of those not interviewed ever having manifested a seizure was excluded by cross-checking with several close relatives.

Results

Two families had 3 patients each, while the other seven families had 2 patients each, giving a total of 20 patients among 59 siblings. The age and

Table I. Age and sex structure of the sibships

Family	Age (years)/Sex of siblings							
1	34/F	25/F	**23/M**	22/F[a]	21/M	18/F	16/F[a]	15/M[a]
2	34/F[a]	32/F[a]	30/M[a]	**27/F**	25/F[a]	24/M	19/M	
3	40/M	37/F[a]	33/F[a]	28/M[a]	**26/M**	23/M		
4	36/F	34/F	**33/M**	29/M	23/M[b]	24/M	19/M	
5	30/F	26/F[a]	**19/M**					
6	47/M	44/M	42/M	40/F	38/F	36/F	33/M	32/M
	28/F	**23/F**						
7	31/F	28/M	26/F	**22/F**	15/M			
8	29/M	25/F	22/M	19/F	**16/F**			
9	38/F	36/M	34/F	32/M	30/M	**29/M**	25/M	20/M

M, male; F, female; underlining indicates epilepsy; bold print shows proband

[a] Asymptomatic siblings interviewed, examined, EEG recorded

[b] Died at age 23 years

sex structure of the sibships is given in Table I. The male:female ratio of the affected siblings was 13:7, whereas that of the unaffected was 18:21. Although the numbers were small, a chi-square test was done, which showed that the difference in the sex distribution between the affected and the unaffected siblings was not significant. The parents of sibship 1 were consanguineous. The siblings in each family had been brought up together in one household during childhood, and their diet and eating habits were similar. All the families were Sinhalese.

Birth and developmental milestones of all the patients were normal. Five (25%) patients were left-hand dominant. One of them (19/M of family 5) had hemiatrophy on the right, and another (16/F of family 8) had

atrophy of the right arm attributed to traction injury at birth. The only other finding of significance was a history of febrile convulsions in 3 patients (19/M of family 2, 29/M of family 4 and 22/F of family 7). None of the patients had evidence of mental subnormality. The minimum educational standard was grade 10, and 8 patients had passed the Advanced Level examination. Six patients were employed, 5 were students, 1 was a housewife and 8 were unemployed. With regard to these aspects, there was no appreciable difference between the patients and the unaffected siblings.

Table II summarises the features of the seizure disorder. The age at onset ranged from 12 to 28 years (median 17). Every patient had experienced at least 6 seizures. The majority had experienced more than 10 seizures, usually about 20, but some as many as 40-50. In 6 patients all the seizures were eating related. The others had random seizures in addition, but in all except 1 (33/M of family 6), eating seizures accounted for more than 50% of the total number of seizures. All the patients, including 33/M of family 6, had experienced at least 3 eating seizures. The majority of the patients had most of their eating seizures in relation to lunch. The sequence of meal-related behaviour, for descriptive purposes, was divided into three phases. Most patients had their eating seizures during the meal (phase 1). Some patients had the seizures immediately after the meal (phase II) or within 30 min (phase III). The others had their seizures during all three phases, but commonly during phase I.

The seizures were partial complex in the majority (15) and partial simple in 5, with secondary generalization in 17. The dominant focal manifestations of the seizures are listed in the Table II. The visual hallucinations took the form of a crowd of unknown people in patient 27/F of family 2, and snakes in patient 26/M of family 3. The auditory hallucinations in patient 24/M of family 2 were a voice of an unknown person. The automatisms of patient 23/M of family 3 consisted of spitting, chewing movements, lip smacking and hand movement. There was no difference between eating seizures and random seizures in the symptomatology. The interictal EEG in 18 of the 20 patients showed epileptiform abnormalities (sharp waves and/or spikes with or without slow after waves), focal in either or both temporal areas. These abnormalities were enhanced by hyperventilation. Photic response was negative. Among family members, there was a past history of fits, unrelated to eating, in the father of family 4. He was not available for examination or EEG. The EEGs of the siblings were normal except in two: 15/M of family 1 showed non-specific abnormalities and 34/F of family 2 showed frequent sharp and slow waves focal in both posterior

Table II. Features of the seizure disorder

Family/ patient	Age at onset (Years)	Total no. of seizures	% of E seizures	% Distribution of E seizures (B)	(L)	(D)	Timing of E seizures	Type of seizures	Focal symptoms of seizure	EEG abnormalities
Family 1										
25/F	12	>10	100	5	80	15	Phase I	CPS	Vertigo, fear	Sh focal R > LMT
23/M	15	>10	95	5	80	15	Phase I	CPS	Vertigo, fear, illusions abnormal talk	Sh focal R MT
Family 2										
27/F	17	>10	70		25	75	Phase I	CPS	Visual hallucination, fear	Sh focal R MT
24/M	15	>10	80	30	20	50	Phase I	CPS	Auditory, hallucination, fear abnormal talk	Sp+Sl focal R MT
19/M	15	6-10	60	10	40	50	Phase I	CPS	Illusions	Sp/Sh focal R PT
Family 3										
26/M	18	>10	90	30	60	10	Phase II, III	CPS	Visual and olfactory hallucination,fear	Sp + Sl focal R MT
23/M	17	>10	100	10	85	5	Phase II, III	CPS	Vertigo, fear, disorientation, automatisms	Sp + Sl focal R MT
Family 4										
33/M	28	>10	100		75	25	All Phases	CP	Abnormal talk, lip smacking	Sh focal R MT
29/M	18	6-10	>50		66	33	All Phases	CPS	Abnormal talk, lip smacking, hand movements	Non-specific
Family 5										
30/F	12	>10	100	10	30	60	Phase I, II	SPS	Head turns to L, movements L arm	Non-specific
19/M	13	6	80		50	50	Phase II	SPS	Vertigo, head turns to L	Sh + Sl R/L MT
Family 6										
33/M	18	>10	20		100		Phase I	CPS	Flashing lights, fear, abnormal talk	Sh focal R < L PT
28/F	17	>10	75		100		Phase I	CPS	'Fire flies' vertigo fear	Sh focal R > L PT
23/F	19	>10	75		40	60	Phase I	CPS	Visual blurring, fear	Sh focal R < L PT
Family 7										
28/M	17	>10	80	20	30	50	Phase I, II	SPS	Visual blurring, olfactory, hallucination	Sh focal R PT
22/F	17	>10	80	60	20	20	Phase I, III	CPS	Visual blurring, lip smacking	Sh focal R PT
Family 8										
29/M	26	>10	95	10	80	10	Phase I	SPS	'Blue vision'	Sh focal R > L PT
16/F	15	>10	85	20	50	30	Phase II	SPS	Visual blurring	Sp + Sl focal R PT
Family 9										
29/M	19	>10	100		80	20	Phase I	CP	Vertigo, disrientation	Sh focal R/.L MT
22/F	17	>10	100	20	60	20	Phase I	CP	Vertigo, disorientation, abnormal talk	Sh + Sl focal R/L MT

E seizures, Eating-seizures; (B), breakfast; (L), lunch; (D), dinner; SP, simple partial; CP, complex partial; CPS, CP secondarily generalized; R, right; L, left; Sh, sharp waves; Sp, spikes; Sl, slow waves; MT, mid-temporal; PT, posterior temporal

temporal areas.

Treatment received by the individual patients varied considerably; patients of the same family were not necessarily on the same medication. Eight patients were on two-drug regimens. The anticonvulsant used, in order of frequency, were: phenytoin, carbamazepine, clobazam and primidone. The response to treatment, in general, was good. Twelve patients were free of seizures for periods over 1 year. Two patients had intermittent minor seizures. Information was not available in the other 6 patients.

Discussion

Eating seizures, for our studies, have been defined as seizures which occur during or within 30 min following a meal. The question as to whether the relationship between seizures and eating could not have occurred by chance alone was addressed in our previous paper [19].

The time spent in eating an eastern meal is about 15 min. Having allowed 30 min for a meal and 30 min for the postprandial phase, we showed that the probability of a patient having two eating seizures was 0.0156. For patients with both eating and random seizures, applying the binomial test [20], the probability that three or more of the seizures would be meal related was 0.042. Both these values are less than the conventionally accepted criterion of 0.05 below which it is unreasonable to assume chance occurrence. Although 14 patients in the present series had both eating and random seizures, each had experienced a minimum of three eating seizures, satisfying the requirement to conclude that those could not have occurred by chance.

The proportion of eating seizures to random seizures in previous cases designated 'eating epilepsy' was variable.

The criterion used in our studies was that eating seizures accounted for more than 50% of the total number of seizures. Accordingly, all but 1 patient (33/M, family 6) in this series would qualify as having eating epilepsy. In fact, the percentage of eating seizures in most of the patients in this study is close to 100 (Table II).

Epilepsy with eating seizures is rare. Vizioli [22], from 20,000 examinations in the EEG Laboratory of the Rome University, found only 9 cases where seizures were related to eating. Nagaraja and Chand [13] found 13 cases amongst 11,783 patients with epilepsy who attended the National Institute of Mental Health and Neurosciences in Bangalore. Ahuja *et al.* [4] recently presented 17 cases seen over a 10-year period at the All India Institute of Medical Sciences in New Delhi. Together with the large number of cases seen at our centre, the relatively high

prevalence of eating epilepsy in the Indian subcontinent indicates that common dietary habits, feeding behaviour as well as ethnic origin may be significant in the aetiology of this disorder.

A family history of epilepsy had been recorded in 50% of the cases in the Bangalore series [13], and in 1 case (6%) in the New Delhi series [4]. However, the seizure disorder in those family members was not eating related. In our study of 120 cases [19], 20 (16.7%) patients had a brother with epilepsy, 9 (7.5%) had a sister with epilepsy, and 4(3.3%) had a parent with epilepsy. The remarkable observation was that, in some of the siblings, the seizures were eating related. Twenty siblings thus affected with eating seizures distributed among nine families together with 39 non-affected siblings are the subjects of the present study. None of the parents had eating seizures, although 1 had a history suggestive of epilepsy.

What significance may be ascribed to the sibling clustering of eating seizures? Common exposure to environmental factors and shared behaviour practices are known to cause clustering of disease within families. The siblings of each family in this study had been brought up together. They had shared the same food and followed similar eating patterns. Therefore, it may be argued that the sibling clustering was the result of external factors, food and eating habits in particular. Another proposition could be that timing the seizures to occur at eating was a form of learnt behaviour, one sibling learning from another affected sibling. This would not explain how the first affected sibling himself learnt to time his seizures.

A genetic susceptibility to epilepsy has long been recognized [12]. However, genetic factors have been assumed to be less important in the pathogenesis of partial than of generalized epilepsy [11]. Recent studies [9] have convincingly shown that genetic factors are as important in partial epilepsy as in generalized. Ottman [14] and Ottman *et al.* [15] have demonstrated that complex partial epilepsy in particular is only slightly less familial than other types of epilepsy. Further, in idiopathic cases, the difference in the genetic susceptibility between generalized and partial epilepsy becomes even less. Focal epileptiform EEG abnormalities are also known to be genetically influenced, albeit to a lesser extent than generalized abnormalities. In one study [17], a positive family history of epilepsy or isolated seizures was found in 35% of the patients with focal temporal sharp waves or spikes. In addition, abnormal EEGs were found in 31% of the siblings of patients with focal abnormalities. In the present study dealing with 20 affected among 59 individuals (34%), the type of epilepsy was partial, the seizures in the majority complex, and the epilepsy idiopathic in all except perhaps 1. With regard to EEG

abnormalities, all except 2 affected individuals had interictal spikes and/or sharp waves focal in one or both temporal areas, in keeping with the clinical seizure type.

This study provides evidence for a strong genetic susceptibility in yet another form of idiopathic, partial epilepsy with focal EEG abnormalities. It is postulated that the genetic susceptibility lies in a central mechanism as in all other epilepsies, whilst the triggering mechanism of the eating seizures is dependent on yet unidentified multiple stimuli which are more environmentally determined. The increased frequency of eating epilepsy in the Indian subcontinent may reflect a shared environmental effect on dietary and eating habits in these groups. By the same argument, even closer sharing of eating-related behavior in the family setting seems to be responsible for the sibling clustering observed in the present study.

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