*Behavioural Neurology (1995)*, **8**, 109–114

# Migraine with prolonged aura: correlation of clinical and EEG features

A.O. Ogunyemi

*Division of Neurology, Health Sciences Centre, Faculty of Medicine, Memorial University, St John's, Newfoundland, Canada A1B 3V6*

**Migraine with prolonged aura has rarely been examined with regard to the sequence of the neurological symptoms and the associated EEG changes. This report describes five patients who underwent clinical assessment and EEG recordings during attacks of migraine with prolonged aura. CT scan of the brain was obtained in four of them. Follow-up EEG was also obtained. The aura symptoms either preceded the headache or were coincident with it. The aura symptoms evolved in a manner consistent with posterior-to-anterior dysfunction of the cerebral cortex. The EEG abnormalities were non-epileptiform and consisted of focal delta slow waves or theta slow waves. The EEG abnormalities showed good correlation with the patients' aura symptoms and resolved when the patients became symptom free. The posterior-to-anterior sequence of the aura symptoms is in accord with the findings during cerebral blood flow studies in patients having migraine with aura. Also the symptoms and EEG changes in our patients indicate dysfunction of the cerebral cortex, consistent with the notion that spreading cortical depression may be the underlying pathophysiological event in migraine with aura.**

**Keywords: Aura – Cerebral cortex – Electroencephalogram (EEG) – Headache – Migraine – Neurogenic sterile inflammation – Spreading cortical depression – Trigeminovascular**

## INTRODUCTION

Migraine is an important clinical disorder on account of its high prevalence (Linet and Stewart, 1984; Ogunyemi, 1984; Pryse-Phillips *et al.*, 1992) and the discomfort to sufferers. Also, among women younger than 45 years of age there may be a significant association between migraine and cerebral infarction (Tzourio *et al.*, 1993). The Headache Classification Committee of the International Headache Society recognized several varieties of migraine, including "migraine with prolonged aura" (Headache Classification Committee, 1988). The premise for the subcategorization of migraine was the presence of a specific constellation of symptoms and their duration.

According to the Committee, migraine with prolonged aura is "migraine with one or more aura symptoms lasting more than 60 minutes and less than a week. Neuroimaging is normal." Without objective laboratory tests such as EEG, CT scan or MRI scan of the brain to confirm the diagnosis, it is probable that physicians would consider the diagnosis to be one of exclusion. Furthermore, without confirmatory tests, patients may not readily accept the diagnosis, especially since the symptoms are frequently quite dramatic.

In view of the extended duration of the aura symptoms and signs in migraine with prolonged aura, the condition lends itself to clinical verification. Patients can undergo neurological examination and suitable laboratory testing during on-going attacks. Since the aura symptoms are believed to represent dysfunction in parts of the cerebral cortex (Lashley, 1941; Fisher, 1971; Blau, 1992), the EEG may be considered as a candidate investigative tool. We here report clinical and EEG observations on five patients having migraine with prolonged aura.

## METHODS

Between 1 January 1991 and 30 June 1992 the author evaluated five successive patients with the clinical diagnosis of "migraine with prolonged aura" in the emergency room at the Health Sciences Centre, St John's, Newfoundland. All the patients had complete neurological examinations and EEG performed during on-going attacks. Emergency CT scan of the brain was obtained in four patients, the exception being the patient who was pregnant at the time of her attack (Patient 2).

Follow-up neurological assessment and EEG were performed for all the patients. The intensive evaluation was carried out because even though migraine with prolonged aura was strongly suspected as a

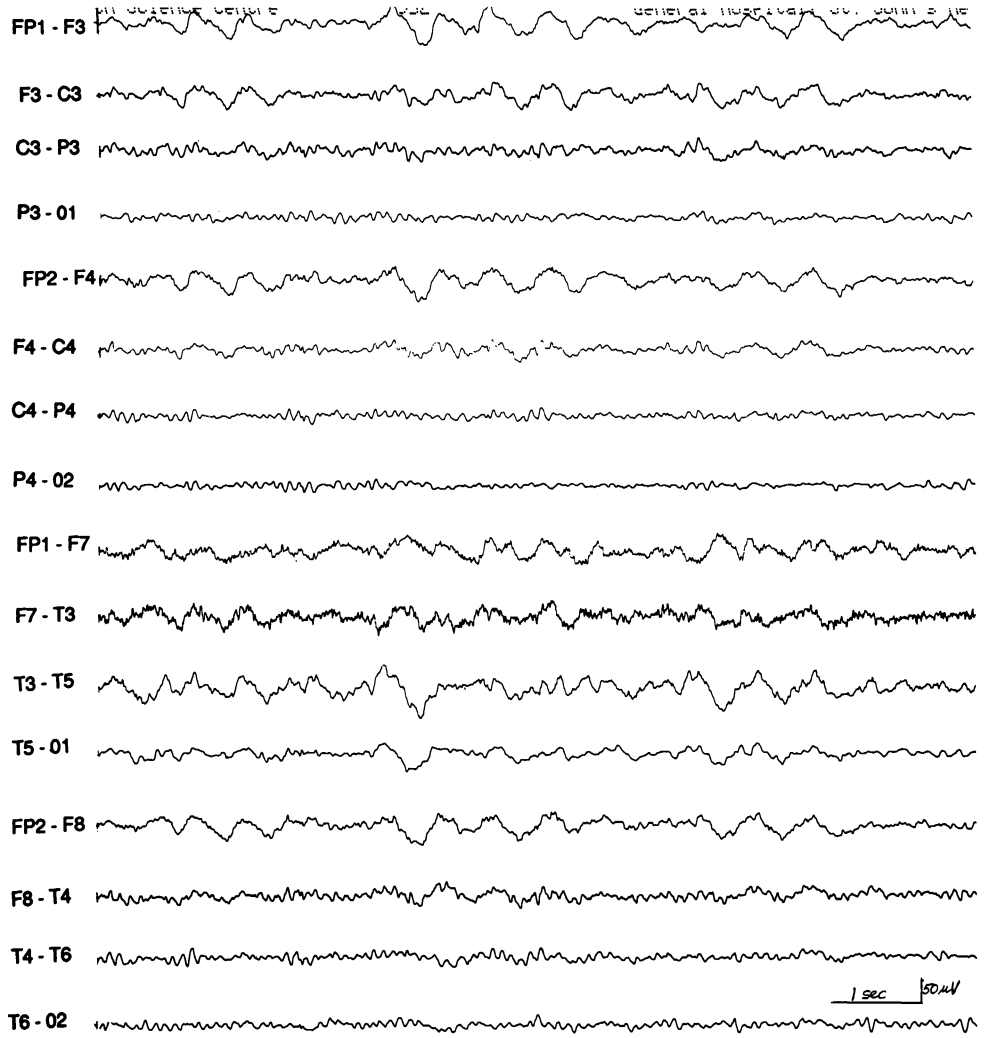


FIG. 1. EEG record of a 30 year old woman, obtained during migraine with prolonged aura. The tracing shows a long train of bilateral frontotemporal slow waves, maximum on the left.

result of the presenting symptomatology, the diagnosis was by no means conclusive or secure, especially during the attacks.

## CASE REPORTS

### Patient 1

This 30 year old woman had mild left frontal headache and nausea upon awakening in the morning. Her mother noted that she was "confused". The head pain rapidly became severe and was associated with vomiting. Upon arrival at the clinic of her family physician, it was observed that she had difficulty in describing her symptoms. Her speech was observed to be laboured and hesitant. In addition, she could not recall the name of her doctor nor that of her boyfriend. She had had migraine without aura for almost 6 years, suffering one or two attacks per year. She had been taking premarin (estrogen) for about 2 years, following hysterectomy and oophorectomy. She neither smoked cigarettes nor abused alcohol. The family history was negative for migraine.

In the emergency room she was alert with normal vital signs. The neurological examination revealed effortful, non-fluent speech. Repetition of sentences was disturbed but comprehension was intact. There was poor memory for the events of the morning. Also, she could not recall any one of three objects after 5 min. There was no motor or sensory impairment in the face or extremities. Emergency CT scan of the brain was normal. EEG obtained about 50 min from the onset of symptoms showed almost continuous train of medium-to-high amplitude 1.5–

2.5 Hz delta slow waves over the bifrontal and left temporal regions (Fig. 1). The slow waves were accentuated by hyperventilation. Follow-up EEG obtained 1 week later, when she was asymptomatic, was normal.

### Patient 2

This 26 year old primigravida was 7 months pregnant when she presented to the emergency room. She awoke in the morning unable to see the right half of the visual space. Within a few minutes she felt numbness, cold sensation and tingling in the right half of the tongue, the right side of the face and the right arm. Upon arrival in the emergency room she was observed to have difficulty in enunciating her words. Soon afterwards, she developed gradual-onset throbbing headache localized to the left frontotemporal region associated with nausea and photophobia.

Examination of the vital signs was unremarkable. She was alert and orientated to time, place and person. The positive neurological findings were neglect of the right visual space, astereognosis, speech hesitancy and poor repetition. There was no motor weakness. EEG recording which was secured about 70 min after the symptoms began revealed persistent, irregular 1–2 Hz low amplitude delta slow waves in the left central–parietal–temporal region. The slow waves were more marked in the central–parietal area. A follow-up EEG 3 days later, when she was free of symptoms, was normal.

### Patient 3

At age 19 years, this young man had his first attack of migraine without aura. About 8 months later, he experienced an episode of gradual obscuration of vision in the right visual field. Soon afterwards, he noted difficulty in pronouncing some words, even though he knew what he wanted to say. About 20 min later he developed bifrontal and left retro-orbital pounding pain associated with nausea, vomiting and photophobia. The aura symptoms persisted during the headache.

In the emergency room, the general medical examination was normal. The neurological examination revealed language dysfluency and disturbance of repetition. Comprehension of language was normal. The visual field was full to confrontation. The EEG recorded almost 6 h after the onset of symptoms showed intermittent trains of low-amplitude 4.5–6 Hz theta slow waves in the left anterior temporal region. There were isolated low amplitude delta slow waves in the same region. CT scan of the brain was normal. A follow-up EEG recording 5 days later was normal.

### Patient 4

This 30 year old man was driving when he noticed that he could not see the vehicles travelling on his right. He felt that his right "eye" was unclear and he became nauseated. Within 10 min the thumb and index and middle fingers of the right hand also felt numb. His speech became garbled on the way to the hospital emergency room. He claimed that he felt disorientated, as if he was outside of his body. Later, he developed pain over the forehead, worse on the left.

On examination, the vital signs were normal. There was speech dysfluency and poor recent memory. Consistently, he could not recall any one of three objects after a delay of 5 min. He was aware of his memory impairment. The remainder of the neurological examination was normal. CT scan of the brain was also normal. The EEG recorded almost 4 h from the beginning of his symptoms disclosed intermittent, asynchronous, focal theta and delta slow waves in the left and right anterior–mid-temporal regions. A repeat EEG 2 weeks afterwards was normal.

### Patient 5

This 28 year old woman was at work when she noted that her vision was "cloudy" on the right side. Within a few minutes there was numbness in her right arm and the right half of the face. Soon after her speech became "thick", with difficulty in enunciation. Upon arrival in the emergency room she developed nausea and left frontal throbbing headache.

Seven years earlier she had been diagnosed to have pleural-based small cell carcinoma. She was successfully treated with tumour resection, radiation and chemotherapy. She did not smoke cigarettes or drink alcohol. Her only medication was the oral contraceptive pill.

On examination, she was alert and apprehensive. The vital signs were normal. The positive neurological signs were hesitant, dysfluent speech and difficulty with repetition of phrases and sentences. CT scan of the brain was normal. The EEG, which was obtained about 8 h from the onset of her symptoms, showed runs of focal 4–6 Hz theta slow waves in the left anterior–mid-temporal region. A follow-up EEG recording 2 days later, when she was asymptomatic, was normal.

## DISCUSSION

The succession of neurological symptoms occurring in migraine with prolonged aura can be quite alarming. Four of the five patients in this report were experiencing attacks of this type of migraine for the

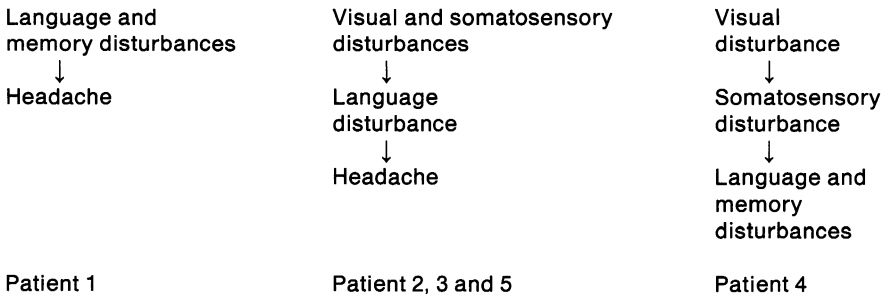


FIG. 2. The sequence of evolution of aura symptoms and headache during migraine with prolonged aura.

first time. They presented promptly to the emergency room of the hospital because they suspected that stroke was imminent. The apparent compromise of language may have accentuated the patients' concern. Therefore, our observation of migraine with prolonged aura in five consecutive patients with aura symptoms implicating primarily the left cerebral hemisphere, should not be construed as evidence that the dominant cerebral cortex is more commonly afflicted than the non-dominant cerebral hemisphere.

In view of the long duration of the aura, clinical neurological assessment and specific tests such as CT scan and EEG were obtained while the patients still had symptoms and signs related to the aura. Furthermore, by obtaining the historical details while the attacks were ongoing, it became possible to accurately determine the sequence in which the aura symptoms evolved as well as their relationship to the headache. It is of interest that in the vast majority of studies reporting EEG findings associated with migraine the recordings were obtained when the patients did not have aura symptoms or signs (Dow and Whitty, 1947; Smyth and Winter, 1964; Slatter, 1968; Hockaday and Whitty, 1969; Slevin *et al.*, 1981).

## Sequence of symptoms (Fig. 2)

In all the patients, the aura symptoms preceded the headache. Patient 1 woke up apparently with coincident language and memory impairment. Headache followed. Patient 2 also awoke with concurrent visual and somatosensory symptoms. Subsequently, she developed language deficits. Later, headache ensued. In Patients 3, 4 and 5 the aura symptoms began while they were fully alert. In these patients, the visual symptoms appeared first and somatosensory symptoms followed. The latter were succeeded by aphasia. In addition, Patient 4 suffered amnesia and depersonalization.

This sequential posterior-to-anterior dysfunction of the cerebral cortex resembles the findings described in cerebral blood flow studies (Olesen *et al.*, 1981, 1990; Lauritzen *et al.*, 1983; Lauritzen and Olesen, 1984; Olesen *et al.*, 1987; Andersen *et al.*, 1988). These investigators examined changes in cerebral blood flow during migraine with aura using xenon-133 administered by intracarotid or intravenous injections or inhalation. They consistently observed that during attacks of migraine the initial hypoperfusion began in the posterior part of one cerebral hemisphere, spreading anteriorly towards but not beyond the central (Rolandic) and lateral (Sylvian) fissures. The speed of the anterior propagation of the oligaemia was about 2–4 mm/min, consistent with the experimental observations of Leao (1944) and Leao and Morrison (1945) and the personal clinical experience of Lashley (1941).

The symptoms of our patients indicated involvement of the frontal lobe, specifically Broca's or motor speech area. Therefore, the disturbance of the cerebral cortex must have extended beyond the lateral fissure. The bifrontal slow waves in the EEG of Patient 1 (Fig. 1) supports this conclusion. Also, the occurrence of amnesia in two of our patients suggests bilateral frontal or temporal dysfunction. Therefore, the unilateral changes observed during cerebral blood flow studies do not explain all the events which transpire during attacks of migraine with prolonged aura.

## EEG changes

The changes in the EEG of patients with migraine have been well documented. Over the years, however, there have been advances in the classification of migraine as well as the analysis and interpretation of the EEG. Because of the changes in the criteria of EEG abnormalities, EEG patterns which were regarded by some earlier authors as abnormal or "borderline" are now recognized to be quite normal. Such patterns include posterior slow waves of "youth" (Slatter, 1968), rhythmic delta slow wave "build-up"

during hyperventilation (Weil, 1952; Slevin *et al.*, 1981) and prominent responses to photic stimulation (Hockaday and Whitty, 1969). It is understandable, therefore, that some authors expressed the opinion that the use of EEG "resulted in more confusion than clarification" (Pearce, 1987).

In three of our patients (2, 3 and 5) the EEG abnormalities were confined to the left cerebral hemisphere. Their symptoms were consistent with cortical dysfunction involving only that hemisphere. In the other two patients (1 and 4), the symptoms suggested bilateral cerebral cortical dysfunction. Similarly, the EEG changes were bilateral. The EEG abnormalities were most severe in the two patients (1 and 2) who presented to the hospital in the early stages of their attacks. Also, the anterior temporal region was most frequently involved in the EEG changes. The EEG became normal when the patients were free of aura symptoms. The good correlation between the aura symptoms and the EEG abnormalities is in accord with the notion that the aura symptoms of migraine result from electrophysiological disturbances of neurons of the cerebral cortex (Gowers, 1888; Lashley, 1941; Fisher, 1971; Lauritzen, 1994). It should be noted that the EEG abnormalities were non-epileptiform. They consisted of delta or theta slow waves.

### The migraine process

The pathophysiology of migraine remains elusive. Several theories have been proposed, but none has satisfactorily explained the relationship between the aura symptoms and the headache. The vascular theory, which was championed by Wolff (1963), proposed that cerebral vasoconstriction caused the aura symptoms, while extracranial vasodilatation with sterile inflammation was responsible for the headache. This notion has been challenged by the findings of cerebral blood flow studies (Lauritzen, 1994) showing that the spread of oligaemia transcends the territories of supply of any major cerebral artery. Also, the magnitude of the reduction in the cerebral blood flow does not reach the cerebral ischaemic threshold (Olesen *et al.*, 1990). In addition, the aura symptoms of our patients cannot be explained by ischaemia in the territory of single cerebral artery.

More recently, Moskowitz (1984, 1992) postulated that activation of the trigeminovascular fibres by unknown triggers forms the basis of headache in migraine. Orthodromic conduction of stimuli by the trigeminovascular axons would cause perception of pain in the head, while antidromic impulse conduction would result in the release of vasoactive neuropeptides, the latter being largely responsible for the vasodilatation and plasma extravasation, and hence the neurogenic sterile inflammation. This hypothesis, although helpful in understanding the mechanism of the headache of migraine, fails to account for the aura symptoms.

Currently, the phenomenon called "the spreading cortical depression of Leao" is the focus of investigations to explain the symptoms of the aura of migraine (Lauritzen, 1994). The phenomenon is a wave of slowly propagating disturbance of neuronal activity of the cerebral cortex. The cortical dysfunction spreads at a speed of 2–4 mm/min (Leao, 1944; Leao and Morrison, 1945). It may be elicited using direct electrical or chemical stimulation. Local trauma to the cortex may also initiate a similar event. The aura symptoms and the EEG abnormalities in our patients indicate that disturbances of cerebral cortical functions are present in patients who experience migraine with prolonged aura. The observations do not prove, however, that there is a cause and effect relationship between the neural abnormalities and the migraine process. It is noteworthy that Moskowitz *et al.* (1993) recently found that the neocortical spreading depression activated the trigeminal nucleus caudalis. The inference from this observation is that the spreading cortical depression could trigger the headache of migraine through trigeminovascular mechanisms. Clearly, further research is necessary to elucidate the underlying neural events which trigger several headache syndromes, including migraine with aura, migraine without aura and tension-type headaches.

## CONCLUSIONS

(1) Patients having "migraine with prolonged aura" experience symptoms suggesting sequential posterior-to-anterior disturbance of regions of the cerebral cortex.
(2) EEG abnormalities recorded during the attacks correlate well with the aura symptoms.
(3) The EEG abnormalities are non-epileptiform and gradually resolve as the patients become free of symptoms.
(4) The EEG changes, which may be quite severe, do not denote fixed or irreversible brain insults.
(5) Neurologists and electroencephalographers should be aware of these EEG changes and their clinical implications.
(6) The good correlation between the EEG abnormalities and the aura symptoms suggests that disturbance of cortical neuronal activity is a fundamental change in the migraine process. This notion is in accord with recent experimental observations.

## Acknowledgements

The author is grateful to the staff of the EEG Laboratory, Health Sciences Centre, St John's, Newfoundland, Canada for performing the Emergency EEG recordings. Mrs Cynthia Sweeney provided secretarial assistance.

## REFERENCES

Andersen AER, Friberg L, Olsen TS and Olesen J (1988) Delayed hyperaemia following hypoperfusion in classic migraine. *Archives of Neurology*, **45**, 154–159.

Blau JN (1992) Migraine: theories of pathogenesis. *Lancet*, **339**, 1202–1207.

Dow DJ and Whitty CW (1947) Electroencephalographic changes in migraine. *Lancet*, **2**, 52–54.

Fisher CM (1971) Cerebral ischemia –– less familiar types. *Clinical Neurosurgery*, **18**, 300–335.

Gowers WR (1888) *A Manual of Diseases of the Nervous System*. Churchill, London.

Headache Classification Committee (1988) Classification and Diagnostic Criteria for Headache Disorders. *Cephalalgia*, **8** (Suppl 7), 13–96.

Hockaday JM and Whitty WE (1969) Factors determining the electroencephalogram in migraine: a study of 560 patients according to clinical type of migraine. *Brain*, **92**, 769–788.

Lashley KS (1941) Patterns of cerebral integration indicated by the scotomas of migraine. *Archives of Neurology and Psychiatry*, **46**, 331–339.

Lauritzen M (1994) Pathophysiology of the migraine aura. The spreading depression theory. *Brain*, **117**, 199–201.

Lauritzen M and Olesen J (1984) Regional cerebral blood flow during migraine attacks by Xenon-133 inhalation and emission tomography. *Brain*, **107**, 447–461.

Lauritzen M, Skyhoj E, Olsen T, Lassen NA and Paulson OB (1983) Changes in regional cerebral blood flow during the course of classical migraine attacks. *Annals of Neurology*, **13**, 633–641.

Leao AAP (1944) Spreading depression of activity in cerebral cortex. *Journal of Neurophysiology*, **7**, 359–390.

Leao AAP and Morrison RS (1945) Propagation of spreading cortical depression. *Journal of Neurophysiology*, **8**, 33–45.

Linet MS and Stewart WF (1984) Migraine headache. *Epidemiologic Review*, **6**, 107–139.

Moskowitz MA (1984) The neurobiology of vascular head pain. *Annals of Neurology*, **16**, 157–168.

Moskowitz MA (1992) Neurogenic versus vascular mechanisms of sumatriptan and ergot alkaloids in migraine. *Trends in Pharmacological Science*, **13**, 307–311.

Moskowitz MA, Nozaki K and Kraig RP (1993) Neocortical spreading depression provokes the expression of C-fos protein-like immunoreactivity within trigeminal nucleus caudalis via trigeminovascular mechanisms. *Journal of Neuroscience*, **13**, 1167–1177.

Ogunyemi AO (1984) Prevalence of headache among Nigerian University students. *Headache*, **24**, 127–130.

Olesen J, Larsen B and Lauritzen M (1981) Focal hyperaemia followed by spreading oligemia and impaired activation of rCBF in classic migraine. *Annals of Neurology*, **9**, 344–352.

Olesen J. Friberg L, Olsen TS, Iversen HK, Lassen NA, Andersen AR and Karle A (1990) Timing and topography of cerebral blood flow, aura and headache during migraine attacks. *Annals of Neurology*, **28**, 791–798.

Olsen TS, Frieberg L and Lassen NA (1987) Ischemia may be the primary cause of the neurologic deficits in classic migraine. *Archives of Neurology*, **44**, 156–161.

Pearce JMS (1987) Neural aspects of migraine. In: *Migraine—Clinical and Research Aspects* (ED. JN Barr), pp. 247–263. Johns Hopkins Press, Baltimore.

Pryse-Phillips W, Findlay H, Tugwell P, Edmeads J, Murray TJ and Nelson RF (1992) A Canadian population survey on the clinical, epidemiologic and societal impact of migraine and tension-type headache. *Canadian Journal of Neurological Science*, **19**, 333–339.

Slatter KH (1968) Some clinical and EEG findings in patients with migraine. *Brain*, **91**, 85–98.

Slevin JT, Faught E, Hanna GR and Lee SI (1981) Temporal relationship of EEG abnormalities in migraine to headache and medication. *Headache*, **21**, 251–254.

Smyth VOG and Winter AL (1964) The EEG in migraine. *Electroencephalography and Clinical Neurophysiology*, **16**, 194–202.

Tzourio C, Iglesias S, Hubert J, Visy J, Alperovitch A, Tehindrazanarivelo A, Biousse V, Woimant F and Bousser M (1993) Migraine and risk of ischemic stroke: a case-control study. *British Medical Journal*, **307**, 289–292.

Weil AA (1952) The EEG findings in a certain type of psychosomatic headache: dysrhythmic migraine. *Electroencephalography and Clinical Neurophysiology*, **4**, 181–186.

Wolff HG (1963) *Headache and Other Head Pain*, Oxford University Press, New York.

*(Received 21 October 1994; accepted as revised 11 May 1994)*