Letters

Seasonal variation in the incidence of photoparoxysmal discharges among patients investigated after a single seizure

Sir: Among patients investigated after a single seizure, a recent study established that the incidence of photoparoxysmal discharges (PPD) was similar to that of clearly established epileptic patients suggesting that a single seizure was similarly associated with increased excitability of cortical neurons.¹ An earlier study observed a seasonal variation in the incidence of PPD among British epileptic patients.² Among known photosensitive patients, a seasonal variation has also been observed in the incidence of PPD.³

I report an observation of a seasonal variation in the incidence of PPD among patients investigated after a single seizure. The patients studied were the 408 consecutive patients investigated after a single seizure in the Department of Clinical Neurophysiology, The National Hospital for Nervous Diseases, Queen Square, London, between 1981 and 1985. The EEG of these patients was examined for evidence of photoparoxysmal response to photic stimulation (PPD). Details of methods of selecting these patients, photic stimulation during EEG and criteria for diagnosing PPD, have been described in a recent report on the same group of patients.¹

The patients were grouped into four in accordance with the season of EEG recording: patients investigated; in Winter (December, January and February); in spring (March, April and May); Summer (June, July and August) and autumn (September, October and November). Each group was separately analysed and incidence of PPD obtained. The various incidences were compared with one another. The significance of any differences found in the incidence was tested using Chi-square test (with Yates correction) of 2×2 contingency table and Fisher's exact test for samples less than 40 and expected cell frequency less than 5. The result showed a seasonal variation in the incidence of PPD among the patients, the

lowest occurring in summer and the highest occurring in winter. The result was consistent with the earlier observations in established epileptic patients.^{2,3} The relative rarity of PPD in summer has been related to increased environmental sunshine during that season.^{2,3} The inhibitory influence of sunshine on the incidence of PPD had been shown in experimental animals: Balzamo *et al* showed very low prevalence of PPD in Baboons (*Papio papio*) residing at the Eastern and Northeastern Savannah area of Senegal with abundant sunshine and a high prevalence of PPD in animals residing at the Southwest forest region with much rain and shaded environment.⁴ Relative rarity of PPD has been shown in African patients with grand mal epilepsy compared with Caucasian patients with similar diagnosis, due probably to the relatively larger amount of sunshine in Africa compared with Europe.⁵

It has been suggested that PPD is a significant pointer to increased excitability of the cortical neurons.^{6,7} The presence of PPD is therefore an expression of increased excitability of cortical neurons and the relative rarity of PPD among these patients in summer is a pointer to reduced excitability of their cortical neurons during that season, as a result of the increased environmental sunshine.

The mechanism for the inhibitory influence of sunshine on photoparoxysmal discharges, involves the influence of sunshine on the inhibitory neurotransmitters: adrenalin and dopamine. Details of the mechanism have been discussed in previous studies.^{2,3,5}

This report suggests that the phenomenon of seasonal variability in photoparoxysmal discharges is not limited to epileptic patients alone but also occur in patients investigated after a single seizure. This reinforces the suggestion that this phenomenon is a reflection of seasonal variation in excitability of cortical neurons and probably bears no relationship to clinical expression of photosensitive epilepsy.

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Optic neuritis, confirmed by visual evoked response, and the risk for multiple sclerosis: a prospective survey.

Sir: Studies concerning the development of multiple sclerosis after uncomplicated optic neuritis reveal a great variability in percentages of that risk (8-78%). These great discrepancies are probably due to differences in the periods of follow up in those studies, (1-25 years).¹ This despite the fact that 83% of the patients studied by Nikoskelainen *et al*,² who developed multiple sclerosis, did this within a period of no more than 5 years.

Another factor which may influence the risk of multiple sclerosis after an uncomplicated optic neuritis is that of an incorrect diagnosis of the latter.^{1,3} This indicates that previous studies on this matter, especially those before electrophysiology was introduced in neuro-ophthalmological diagnosis, may have involved other causes of visual loss than optic neuritis alone.

From the department of Electrophysiology (Eye Hospital, Rotterdam) 118 patients with sudden unilateral visual loss, seen from 1982-86, were reviewed. All patients underwent ophthalmological and

Table Seasonal variation in the incidence of photoparoxysmal discharges

Season	No of patients	No with PPD	Incidence (%)
Winter	89	10	11.2
Spring	99	6	6.1
Summer	108	2	1.85
Autumn	112	8	7.3

The lowest incidence (1.85%) occurred in summer and the highest incidence (11.2%) occurred in winter. The difference in the two incidences was statistically significant ($\chi^2 = 5.2$, $p < 0.05$).

neurological examination at the time of the decreased visual acuity. The following patients were excluded: (1) 21 (18%) because signs and symptoms indicative for multiple sclerosis were already present, (2) 14 (12%) without VER abnormalities (5/14 turned out to be hysteric) and (3) 19 (16%) with insufficient clinical data. The remaining 64 patients all had a history of rapidly progressive visual loss, in combination with painful eyemovements (72%), a central or paracentral scotoma (81%) and a delayed, decreased or absent P100 amplitude on pattern reversal, visual evoked response (VER) recording (100%).

During follow up period another 16 out of the 64 patients had to be excluded because the suspicion of intoxication (3), Leber's disease (2), vascular occlusion (3), Devic's disease (1), tumour compression of the optic nerve (4) or refractive disorder (3).

The remaining 48 patients all had a partly or complete recovery of the visual acuity within 4 weeks to 9 months. The follow up period of these patients varied from 6 months to 3.5 years. They all were re-examined neurologically in 1986-87.

During follow up four patients had a relapse of the optic neuritis (ipsilateral 1, contralateral 3). These four patients all had other neurological symptoms besides the decreased visual acuity at the time of this investigation. Another 25 developed signs and symptoms indicative for multiple sclerosis, such as paraesthesiae 14, sensory loss 8, impotence 2, bladder dysfunction 5, pyramidal syndromes 2, ataxia 3, diplopia 3. Mostly these signs and symptoms were found in mutual combination.

The total percentage of multiple sclerosis after optic neuritis within a period varying from 6 months to 3.5 years was 60% (29/48) which is rather high incidence compared with other studies, which were mostly concerned with longer periods of follow up.

The conclusion from this study is that VER recording in combination with case history and campimetry are able to select those optic neuritis patients who have a high risk for developing multiple sclerosis in the near future. The selection of the optic neuritis patients on the basis of VER and physical examination does give a higher certainty for the developing of multiple sclerosis than any other auxilliary diagnostic method, including lumbar puncture, and HLA typing or clinical examination alone.

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No viral antigens detected in brain tissue from a case of acute encephalitis lethargica and another case of post-encephalitic Parkinsonism

Sir: The cause of encephalitis lethargica is unknown. At the time of the 1915-1930 pandemic, it was suggested that a virus was responsible. In fact, in 1920 when Levaditi and Harvier¹ isolated herpes virus from the brain of a patient who died of the disease, they claimed that virus to be its cause. While a progressive Parkinsonism was a frequent sequela of encephalitis lethargica, sporadic and usually transitory Parkinsonian syndromes have continued to be reported in association with established viruses such as Japanese B encephalitis, Western equine encephalitis, central European tick-borne encephalitis, coxsackie group B and lymphocytic choriomeningitis viruses.²

The fact that the clinical and pathological features of encephalitis lethargica strongly suggested a viral aetiology, plus the unquestionable association of certain cases of postencephalitic Parkinsonism with conventional viruses, have sustained a continued interest in the possible connection

between encephalitis lethargica, including postencephalitic Parkinsonism, and a virus. Two relatively recent studies address the point: Rail *et al*³ described eight cases which conformed to the diagnosis of encephalitis lethargica, of which six presented between 1960 and 1980; serum and CSF from three of the patients were tested for antibodies against a number of viruses including influenza A and B, parainfluenza, adenovirus, measles, mumps, herpes and varicella-zoster, with negative results. Esiri and Swash⁴ tested midbrain sections from a patient who died of encephalitis lethargica in 1920 during the acute phase (day 7) of the illness with an antiherpes virus antibody by the immunoperoxidase technique; the reaction was negative for herpes antigen.

We report here the result of attempts to detect virus antigens in brain sections from the Esiri and Swash case (London Hospital case 15/20); and from one of the Rail *et al* cases (No 7 BW 34520) who presented with oculogyric crises in 1965, developed Parkinsonism shortly after, and died in 1981.

Coronal sections of frontal cortex, temporal cortex, substantia innominata, midbrain at the level of the superior colliculus (including the substantia nigra) and at the level of the rostral end of the 4th ventricle (at the location of the locus ceruleus), were examined after staining with haematoxylin-eosin, silver (Naoumenko-Feigin) and thioflavin S, in order to determine the nature, extent and intensity of the lesions. Haematoxylin-eosin sections of the 1920 acute case of encephalitis lethargica showed pronounced disruption and destruction of the few remaining melanin-containing neurons in the substantia nigra and locus ceruleus; very marked and widespread vascular cuffing with as many as six to eight layers of small mononuclear cells predominantly lymphocytic; large number of lymphocytic nodules and abundant astrocytes in both midbrain sections. The 1981 case showed much less generalised reaction but again, the remaining melanin-containing neurons in both substantia nigra and locus ceruleus were markedly reduced. No amyloid plaques or neurofibrillary tangles were detected in any of the sections stained with thioflavin S. The silver stain detected no plaques or tangles in the 1920 case and only occasional plaques or tangles in the later case. Confirmation of the astrocytic reaction in the substantia nigra sections in both cases was sought by means of the immunoperoxidase test using an antiserum against glial fibrillary acidic protein; the astrocytic reaction observed in the acute case was exceedingly intense particularly in the plexus