CHAPTER 11

On the EEG in Enuresis

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Introduction

The contribution made by electroencephalography (EEG) to the understanding of enuresis is slight. Two principal and manifold subsidiary reasons for this become apparent on reviewing the literature. The two principal reasons are, firstly, that the mechanisms governing the acquisition of urinary continence are not known, and, secondly, the significance of statistically unusual features in the electroencephalogram of children is not fully understood.

A parallel has frequently been drawn between enuresis and epilepsy, the earliest writings being those of Trousseau (1870) and Bradbury (1871). If a similarity exists, it exists at the level of the conceptual incoherence surrounding both phenomena. Gunnarson and Melin (1951), in an intelligent study of 90 children, used electroencephalography 'to rule out epilepsy as a cause of the disease'. They succeeded in this. One child 'had a great many spikes in the record', and another had a short 'petit-mal' during the EEG, with appropriate wave and spike changes. But 'slow dysrhythmical' EEGs were over twice as common (52 per cent) in the 62 children who had never been dry as in the 26 who had been dry for any period over three months. Indeed, only 23 per cent of the 'never dry' group were regarded as having entirely normal EEGs. No ages were stated; children with 'good reasons' to be wet such as diabetes mellitus or pyelonephritis had been excluded. The authors concluded that 'immaturity in the nervous system' was the cause of enuresis in children who had always been wet. However, since enuresis is often regarded as the persistence of an infantile trait, it could equally well have been attributed to immaturity without the interpolation of EEG data. Immaturity of the EEG record, if it means anything, must mean the persistence of forms at a given age which would be considered entirely appropriate in the records of children of a lesser age. The report cannot justify such a conclusion.

The study by Turton and Spear (1953) largely replicates that of Gunnarson and Melin (1951), but the electroencephalographic technique and the age composition of the sample are better described. They refer to 'severe enuretics', and acknowledge that their 100 patients do not represent a fair cross section. They excluded the mentally defective and the markedly backward, together with children with a history of fits or unconsciousness. Only 26 per cent of the EEGs were unequivocally normal, and 50 per cent were markedly abnormal, 14 per cent to the extent that would be 'pathognomonic of epilepsy'. Their results suggest a 'physical basis' for the disorder in a considerable proportion of severe enuretics who do not respond to simple measures. They regarded the concept of immaturity as an attractive explanation of this 'physical

basis', and, in keeping with the 'too slow' EEGs described by Gottlieb *et al.* (1945) in children with behaviours disorders, slowing was the principal anomaly in their series of enuretics.

In a more detailed report, Takayasu *et al.* (1963) showed that out of 140 patients studied, all the 20 with 'epileptic records' wet the bed every night, but so did 76·5 per cent of the 34 with 'borderline EEGs' and 67·4 per cent of those with normal records. Although these authors excluded 'epileptic' patients, 20 gave a past history of convulsions, of whom five appeared in the group of 20 patients with 'epileptic' records. In each case an EEG record was taken during hyperventilation, as is usual. However, photic stimulation and metrazole activation were used 'if necessary', and it is hard to judge the over-all significance of the change which activation used 'as necessary' produces in the age group under study. Nevertheless, Takayasu *et al.* wholeheartedly espouse the electroencephalograph, asserting 'it is needless to say that the problem of enuresis cannot be discussed without EEG investigation'. More dangerous still, they regard 'such patients' as 'subclinical epileptics without typical epileptic fits', and they discuss all the previous literature in that light. Their modest success in 'treating' enuresis with anti-convulsants reinforces their opinion. Where 'epilepsy' fails as an explanatory concept, 'immaturity' serves. If shifting between epilepsy and immaturity increased the explanatory power of the hypothesis, it might be permissible. As it is, we may as well grope in one dark room as another.

Campbell and Young (1966), whose 133 cases included 127 aged between three and fourteen years, found the predominant dysrhythmia to be 6 and 14 per second positive spikes, which occurred in 33 cases. In nine further cases these 6 and 14 per second positive spikes were accompanied by other paroxysmal disorders and a further thirteen manifested paroxysmal disorders only. The authors cite the view of Gibbs and Gibbs (1963) that the 6/14 phenomenon is definitely a sign of disease. In accordance with the non-convulsive epilepsy story, supported by responses to phenytoin therapy, they 'favour the consideration of an organic cerebral lesion as an aetiologic factor in enuresis and perhaps other forms of bladder dysfunction'.

Where does this style of reasoning lead to? The purpose of Fermaglich's (1969) study was 'to investigate enuretics electroencephalographically as a first step in a prospective evaluation of enuresis as a very early manifestation of convulsive activity.' He had been affected by the finding of Aird *et al.* (1967) that a high percentage of patients with temporal lobe epilepsy had 'previous nocturnal phenomena including enuresis'. The sample seemed inclusive, but 'in no case included within this series did the appropriate urological treatment alleviate the enuresis'. Four of the 39 patients had documented seizure disorders, and fifteen of the EEGs were abnormal. Only two showed 14 Hz positive spikes, and these were in addition to other abnormalities. Only the fullness of time and adequate follow-up will answer the authors' question.

The study by Poussaint and Greenfield (1966) does not confirm Fermaglich's hypothesis. Only 20 of 118 epileptic patients aged between 16 and 79 years recollected wetting the bed after the age of three years. Epileptics in the later years of life might of course have been hazy in their recollections, or have been suffering epilepsy for reasons unconnected with the adequacy of cerebral development in early childhood.

An incidence of enuresis of 17 per cent was, in these authors' view, around the expected level for the general population between the ages of three and fifteen years. Furthermore, 'abnormal tracings are known to occur in 10-15 per cent of the general population', so the finding of EEG abnormalities in other samples of enuretic patients was attributed to selection bias.

Poussaint *et al.* (1967), in a sample of 138 children (from all socio-economic groups), performed EEGs, including recordings during sleep and photic and hyperventilation stimulation, on 68 consecutive children. Only 10 per cent were abnormal. None of these children were mentally retarded or had 'obvious' organic factors contributing to their enuresis. Indeed, none of them had a history of 'any known type of seizure or convulsion'. Considering the rates of these phenomena in childhood, a sample of 138 children without any of them might be considered as unusual as those criticised by Poussaint and Greenfield (see above). These authors' results do not allow them to support the hypothesis that enuresis is an 'epileptic equivalent'.

Little support has come from specific all-night EEG and/or polygraphic studies. The elegant and informative study by Ditman and Blinn (1954) included three young patients and twenty-two naval recruits. In the young children, bedwetting occurred during deep sleep, but in the adults wetting occurred in a state of 'physiological wakefulness'. Pierce *et al.* (1961) confirmed that wetting occurred in deep sleep in young children, and was accompanied by penile erection in the male. Wetting did not accompany dreaming. Pierce (1963) regards the wetting as a 'dream substitute'—another dark room.

Considering the incidence of enuresis—reports indicate rates at five years of approximately 9 per cent in the U.K. and 20 per cent in the U.S.A.—and the incidence of abnormal EEGs amongst enuretics, if reported samples were properly representative of the whole population, one would expect about 6 per cent of children aged five years to have 'abnormal' EEGs under the rubric of enuresis alone. Since this group largely excludes epileptic children, the majority of retardates, children with learning or reading disorders and delinquents, it is evident that the total fringe of 'abnormality' is likely to be very broad. It is for this reason that the distinction between *primary* (life-long) and *secondary* (late-onset) enuresis becomes crucial. The prevalence of EEG abnormalities in secondary enuresis has been reported as a mere fraction of that in primary enuresis (Gunnarson and Melin 1951). If this is a real difference, it is obviously very important.

The ascertainment of secondary enuresis demands a 'dry period', which in some cases may be long. The possibility of an age bias therefore exists. EEG differences in primary and secondary enuresis can only be worked out using samples from each group matched for age and sex.

The difference between the EEGs of children with absolutely nothing wrong with them (so-called 'normal' children), and any other more random or 'diseased' group is exemplified in the papers of Petersén and Eeg-Olofsson (Eeg-Olofsson 1971, Eeg-Olofsson *et al.* 1971, Petersén and Eeg-Olofsson 1971). The group they studied showed a remarkably low level of EEG 'abnormalities'. Nevertheless, their work does reinforce the idea that EEG disturbances, such as slowing, abnormal responses to hyperventilation, photosensitivity, and spikes, occur fairly frequently in the rest of the

child population, and need not signify any specific association. As far as enuresis is concerned, the abnormalities may not even be of prognostic significance. Barbour *et al.* (1963) followed up about 90 per cent of a group of children whose EEGs had been examined by Turton and Spear at least five years before. Their report does not suggest that there had been any symptom substitution. In fact, at the time of the follow-up visit, 60 per cent of the boys and 74 per cent of the girls had become dry and had been so for at least two months. Among the children over 15 years of age at follow-up, three of six with originally normal EEGs were dry, as were four of eight with 'epileptic' records and 27 of 36 with 'immature' records.

The sex ratio in enuresis passes widely unremarked. Where the samples have been drawn from paediatric practice, the ratio of males to females has usually been of the order of 200:100, similar to that in child psychiatry over-all. It is of some interest to note that while in the original sample of Turton and Spear males were over-represented 200:100, amongst those still wet at follow-up the ratio of males to females was 300:100. Over a third of the boys and a quarter of the girls who were over 15 years of age at follow-up were still enuretic. Differential rates of development between the sexes apply in a number of areas. The sex ratio evidence may be adduced to be weakly supportive of the hypothesis that enuresis is a developmental disorder.

Mac Keith (1968) pointed out two important problems relevant to electroencephalographic analysis of enuretic children. Firstly, there is the phenomenon of the child who becomes 'dry' on being hospitalised. This suggests that in some children the necessary mechanisms exist, but are not functioning normally. It would be interesting to know what type of EEG is seen in such children, and whether it is changed by hospitalisation. Secondly, the cause and hence the significance of a symptom is likely to change with age, so that in studying developmental disorders the inclusion of children of different ages is liable to create difficulties in interpreting results.

The Present Study

A prospective electroencephalographic study of children with primary nocturnal enuresis was commenced two years ago, the recordings being taken before, during and after treatment. However, since this particular study will take several years to mature, we report here on a retrospective study of the accumulated EEG records of children with enuresis seen at the Park Hospital for Children, Oxford, over the previous seven years (1963-1969).

Altogether, the EEG records of 103 children (77 boys and 26 girls) have been studied. The sample is a mixed one, comprising 57 patients (42 boys and 15 girls) with primary enuresis, and 46 (35 boys and 11 girls) with secondary enuresis. Their ages at the time of the EEG examinations range from five years six months to sixteen years (Fig. 1).

All the EEGs had been recorded and interpreted before the present investigation was initiated. As a consequence, bias in interpretation may have been reduced. The records had all been interpreted by Douglas Lee, and the results all coded according to the system of Lee and Hutt (1965); this provides a standard, unified system of interpretation.

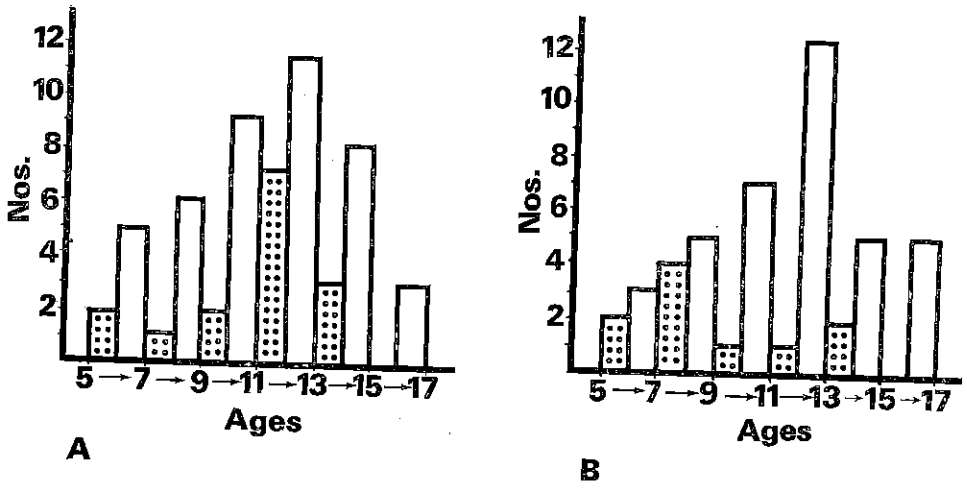

Fig. 1. Distribution of 103 children with nocturnal enuresis by age and sex. **A** (*left*): primary (*i.e.* life-long) enuretics. **B** (*right*): secondary (*i.e.* late-onset) enuretics. *Dotted columns* = females; *plain columns* = males.

TABLE I

Abnormal EEG recordings

EEG abnormality	*Primary enuretics* ($n = 57$)				*Secondary enuretics* ($n = 46$)			
	Males	*Females*	*All*		*Males*	*Females*	*All*	
Diffusely abnormal EEGs	9	2	11	(19%)	1	1	2	(4%)
Abnormal response to 3 mins hyperventilation	21	7	28	(49%)	1	–	1	(2%)
Epileptiform EEGs	3	–	3	(5%)	–	–	–	
'Over-normalised' (= forced normalisation) EEGs	1	1	2	(4%)	3	1	4	(8%)
Atypical wave and spike with photosensitivity	3	1	4	(7%)	–	–	–	
TOTALS	37	11	48	(84%)	5	2	7	(15%)

In all cases, the EEGs had been taken of the fasting child, using a 16-channel Elema-Schönander (Mingograph) electroencephalograph, and the response to photic stimulation and three minutes overbreathing had also been recorded. Children with organic disease of the urinary tract had been excluded. None of the children had been on any form of medication at the time of the recordings, and none of them had ever manifested a clinical seizure.

In 55 patients (53 per cent), the EEGs had been considered abnormal. However, whereas 48 (84 per cent) of the primary enuretics had manifested EEG abnormalities, only 7 (15 per cent) of the secondary enuretics had done so (Table I).

Diffusely Abnormal EEGs

In this group the common finding was a slow dysrhythmical recording, in which there was an unexpectedly large amount of slow wave activity for the patient's age in the resting record. In some recordings there were irregular periods of non-focal, poorly lateralised, sharply contoured waves, often with a bi-occipital emphasis (see Fig. 2). Almost a fifth (19 per cent) of the subjects with primary enuresis, but only 4 per cent of the secondary enuretics, had recordings within this category. These percentage frequencies agree closely with those in the series described by Takayasu *et al.* (1963).

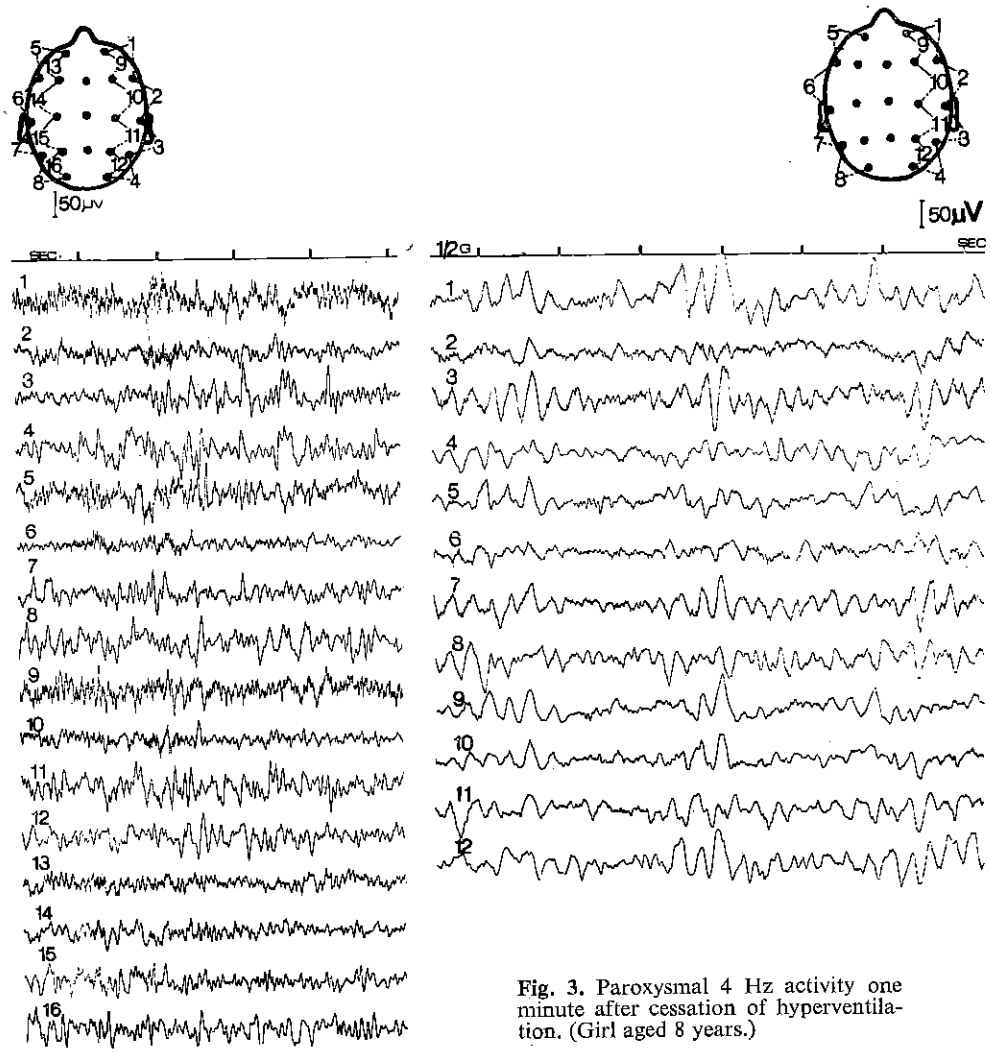

Fig. 2. Diffusely abnormal EEG. Sharply contoured waves with bi-occipital emphasis. (Boy aged 10 years.)

Fig. 3. Paroxysmal 4 Hz activity one minute after cessation of hyperventilation. (Girl aged 8 years.)

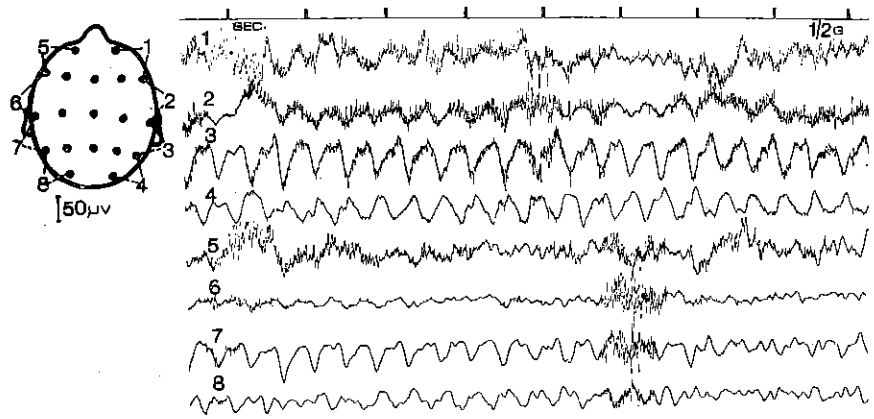

Fig. 4. Regular 3 Hz activity with occasional notching 20 seconds after completion of hyperventilation. (Boy aged 9 years.)

Various authors (*e.g.* Secunda and Finley 1942, Hodge and Hutchings 1952) have described EEGs of this type, and suggested that they reflect cortical immaturity, which might be secondary to inhibition of or delay in maturation.

Abnormal Response to Three Minutes Hyperventilation

Except in subjects with classical petit-mal epilepsy (3Hz spike and wave), paroxysmal activity induced by hyperventilation is rare, and in the large series of so-called 'normal' children studied by Petersén and his colleagues (Kellaway and Petersén 1968) was demonstrated in only 0·3 per cent. An abnormal response to hyperventilation was obtained in 49 per cent (21 boys and 7 girls) of the primary enuretics in the present series and in 2 per cent (one boy) of the secondary enuretics. This abnormal response was easily the most frequent finding of note. The usual abnormality consisted of paroxysmal $2\frac{1}{2}$-$3\frac{1}{2}$ or 4-6 Hz frequencies with bi-occipital maxima. This paroxysmal activity provoked by hyperventilation had been considered excessive at the time of the recording, and had been reported as such (Fig. 3). In one recording occasional notching was seen (Fig. 4). In some recordings shifting rhythmical foci were apparent.

In a few recordings, unusual but non-specific abnormalities were noted on overbreathing. These accord with the 'diffuse abnormalities' of other authors. The abnormalities were continuous or paroxysmal episodes of 3-$3\frac{1}{2}$ Hz high voltage smooth waves, which often persisted for more than 20 seconds after completion of overbreathing. In one child there was a reappearance of such activity following normalisation of the record after overbreathing. These features were first described by Hill and Watterson (1942), in a mixed series of subjects with psychiatric disorders. Although such activity may be regarded as an indication of abnormal cortical instability, there is no definite proof of this, and the non-specificity may reflect no more than an abnormally functioning cortex. In Hill and Watterson's series the subjects were adult, and it was thought that cortical immaturity with failure to reach adult

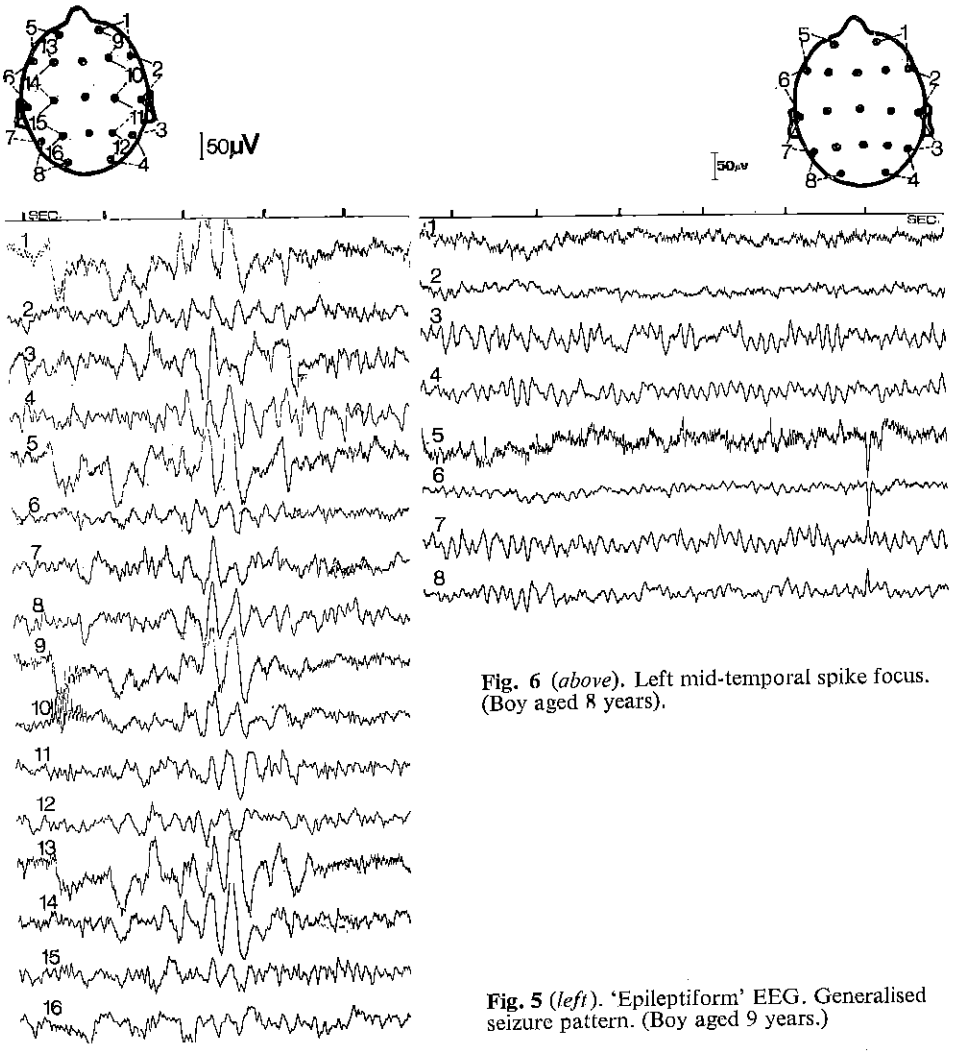

Fig. 6 (*above*). Left mid-temporal spike focus. (Boy aged 8 years).

Fig. 5 (*left*). 'Epileptiform' EEG. Generalised seizure pattern. (Boy aged 9 years.)

control had persisted (= maturation defect). In our series all the subjects showing abnormal response to hyperventilation were over ten years of age.

'*Epileptiform*' *EEGs*

Most authors report 'epileptiform' EEGs with varying frequencies in series of enuretic children. Temmes and Toivakka (1954) found no less than 40 per cent of their series to have such recordings, but they were present in only 5 per cent of our series of primary enuretics (Fig. 5). In one subject, isolated spike foci appeared in the mid-temporal regions (Fig. 6). It must be emphasised that not one of the present series of children had ever manifested overt seizures. Kellaway and Petersén (1968) found spike foci in only 1·5 per cent of almost 1000 'normal' children.

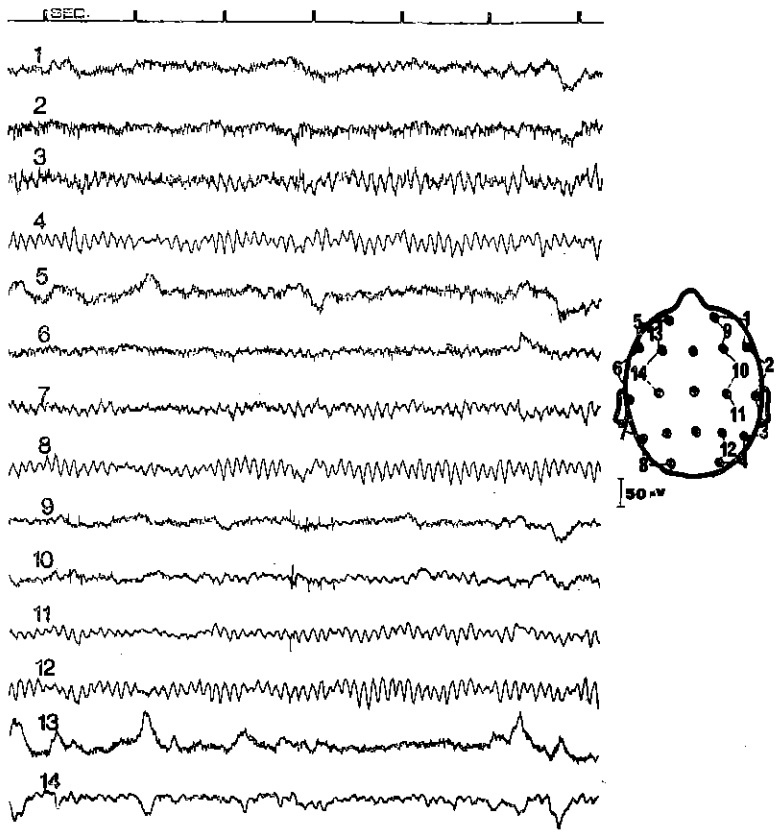

Fig. 7. Marked excess of alpha activity ('over-normal' EEG) in boy aged 12 years.

'Over-normal' (= Forced-normalisation) Recordings

In 4 per cent of the primary enuretics and in 8 per cent of the secondary enuretic children, resting records were consistent with the 'forced-normalisation' recording described by Landolt (1958) (Fig. 7). Not one of these subjects showed focal anomalies, but each manifested instead a monotonous continuity of alpha rhythm which was unexpectedly pronounced for his or her age. This over-normal EEG is regarded by Melin (1958) as an electroencephalographic delay in maturation, sometimes with an inherited component. There is a reported association (Heuyer *et al.* 1956, Landolt 1958) between such EEGs and a predisposition to various psychiatric disorders.

Photosensitivity with Atypical Spike and Wave

Photosensitivity was demonstrated in the recordings of 8 per cent of the primary enuretics, but was not found in those of patients with secondary enuresis. Intermittent photic stimulation induced 3-4 Hz spike and wave formation. Eeg-Olofsson *et al.* (1971) found paroxysmal activity during intermittent photic stimulation in

9 per cent of their large series of 'normal' children, but also found a significantly greater number of girls with such recordings than boys. In the present study three times as many boys as girls were affected.

Discussion and Conclusions

In the light of our introductory review of the literature, our own contribution must be regarded largely as a re-statement of the problems. There can be little doubt that a proportion of children presenting with enuresis show electroencephalograms which, in a child referred with a history of seizures or for support of a clinical impression that he or she might be suffering seizures, would be regarded as reasonably good confirmatory evidence. In fact very few children in any series of enuretics so far examined have suffered from epilepsy. In our view, the term epilepsy must be reserved for an observable behaviour. This behaviour is strongly associated with the finding of cerebral dysrhythmia in the EEG, but the diagnosis of epilepsy overrides the absence of suitably abnormal records. In the absence of a history of seizures, an abnormal EEG in an enuretic child might invite the clinician to take another good look, but does not compel the diagnosis of epilepsy nor suggest that epilepsy and enuresis are in some way equivalent. In the event, EEG research in enuresis is a powerful reminder that there are more people with atypical EEGs than there are people with epilepsy. Indeed, it might be argued, seizure discharges apart, that people with epilepsy merely form part of a larger group of persons showing atypical EEGs. It does not mean that people in this group all suffer from the same thing. Arguments as to the equivalence of phenomena, which seem so popular, simply invite the question 'If they are really the same thing, why are they manifested differently?' Why should some patients wet the bed instead of having fits or dreaming?

The abnormalities reported in our series are, in general, little different from those appearing in other series. Obviously the criteria for diagnosis of abnormality may vary from one centre to another. In most series of enuretic children, especially in those of children with primary or life-long enuresis, the majority of abnormal EEGs have contained diffuse anomalies, with a preponderance of slow-wave activity for the child's age group. In our series we have found a high incidence of subjects with abnormal responses to hyperventilation. If, as has been suggested, these anomalies are a reflection of immaturity of cortical development, then a prospective study of patients with such EEGs is needed in order to demonstrate normalisation of the recording over a given period of time. It might be suggested that primary nocturnal enuresis is a developmental problem associated with maturational delay or inhibition of cortical development.

Early in this review we suggested that confusion has arisen about the significance of the EEG in enuresis, because neither the electroencephalogram nor the bedwetting had been fully investigated developmentally. When the ontogenesis of the electroencephalogram is studied in a properly selected sample of children along the lines which Tanner has so painstakingly done for stature, the meaning of various degrees of dysrhythmia may become clear. From such an analysis, some light may be shed on the tenuous association which is the subject of this review.

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