

The misdiagnosis of epilepsy in children admitted to a tertiary epilepsy centre with paroxysmal events

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Aims: To determine the proportion of children admitted with difficult to treat paroxysmal events to a tertiary epilepsy centre who did not have epilepsy.

Methods: In an observational retrospective study, all case notes of 223 children admitted in 1997 were examined. The referral was made from the local paediatric department in 51% of cases, other departments in 27%, and from general or specialist practitioners in 22%. Doubt regarding the diagnosis of epilepsy was expressed in the referral note in 17%. On admission, 86% were on antiepileptic drug treatment. During admission all children were subjected to a comprehensive intensive observation and 62% had EEG monitoring.

Results: In total, 39% (87/223) were found not to have epilepsy. In 30% of children (55/184) referred without any doubts about the epilepsy diagnosis, the diagnosis was disproved. Of the 159 children admitted for the first time, 75 (47%) were discharged with a diagnosis of non-epileptic seizures. Of 125 children admitted for the first time with no doubts about the diagnosis of epilepsy, 44 (35%) did not have epilepsy. Staring episodes were the most frequently encountered non-epileptic paroxysmal event. Psychogenic non-epileptic seizures were found in 12 children. A total of 34 (15%) had their medication tapered off; a further 22 (10%) had tapered off medication before admission.

Conclusion: The present study supports the view that misdiagnosis of epilepsy is common. The treating physician should be cautious in diagnosis, especially of staring episodes. A diagnostic re-evaluation should be undertaken in difficult cases with continuing paroxysmal events in order to avoid unnecessary drug treatment and restrictions on the child's lifestyle.

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Epilepsy is a common neurological disorder in children, with a prevalence of about 0.5%. The epilepsies form an array of more or less discrete epilepsy syndromes, characterised by age of onset, hereditary factors, seizure types, electroencephalogram (EEG) abnormalities, and prognosis.¹

The diagnosis of epilepsy is often difficult.^{2–3} A good seizure history depends on descriptions by parents or other observers, mainly staff in day care centres or schools. Direct observations by trained medical staff will add considerably to the value of history, but they are difficult to obtain in a normal paediatric ward setting. Hence, the diagnosis must often be made in the outpatient clinic, based on clinical history taking and interictal EEG. The diagnostic information obtained from a single interictal EEG is low; it is frequently normal in children with epilepsy and 2–5% of children without epilepsy present with epileptiform EEG discharges, especially in the centrotemporal regions.^{4–5} Furthermore, a number of benign variant patterns not related to epilepsy are often misinterpreted as epileptiform.⁶

In specialised units, video-EEG or ambulatory long term EEG monitoring to obtain an ictal recording are very helpful,⁷ but these techniques are not available in most cases. It is therefore not surprising that epilepsy frequently is misdiagnosed in children. Many paroxysmal events may be mistaken for epilepsy, for example, tics, staring, syncope, dystonia, psychogenic seizures, and behavioural disturbances during sleep.⁸

In the UK, it was recently disclosed that one physician had misdiagnosed 618/1948 children (31.7%).⁹ As documented in an evidence report for the Center for Disease Control,¹⁰ our knowledge of the amount of misdiagnosis of epilepsy in children with ongoing paroxysmal events is unknown due to the lack of studies with information on the reasons for

referral, medications, and the degree of representative value of the population studied.

The aim of this observational retrospective study was to describe the results of a diagnostic evaluation in children from a well defined population with difficult to treat paroxysmal events, admitted to a tertiary epilepsy centre.

PATIENTS AND METHODS

The Dianalund Epilepsy Centre is the only tertiary centre of its kind in Denmark (population 5.2 million).¹¹ The case notes of 223 children admitted to the Paediatric Department during 1997 were examined in an observational retrospective study. For children admitted more than once that year, only data from the first admission were included.

The median age was 8 years and 6 months (range 8 months to 17 years and 8 months) and 54% were boys. The pattern of referral was evenly spread from all over Denmark. The rate for the first admission per 100 000 inhabitants was 3.1 (total population). The referral was issued by the local paediatric department in 113 children (51%), other hospital departments in 16 (7%), and general practitioners in 36 (16%); 45 (20%) came from the outpatient clinic of the Epilepsy Hospital and 13 (6%) from non-hospital based paediatricians and neurologists. Table 1 shows the reasons for referral. On admission, 14% of the children had never tried any antiepileptic drug (AED), 34% had been treated with one or two AEDs, 26% three or four AEDs, and 26% more than four AEDs. Drugs used for acute treatment were not included.

During hospital stay all the children were subjected to general observation and recording (including video in the ward) of seizures and other events by trained nurses, nursery

Abbreviations: AED, antiepileptic drug; EEG, electroencephalogram; PNES, psychogenic non-epileptic seizures

Table 1 The main reasons for referral to the Paediatric Department of the Dianalund Epilepsy Centre

	n	%
Improvement of epilepsy treatment	69	31
Doubt about the diagnosis of epilepsy	39	17
Classification of epilepsy	61	27
Psychological problems	17	8
Epilepsy surgery evaluation	10	4
Follow up of EEG, cognitive, and behavioural problems	27	12
Total	223	

staff (kindergarten), teachers, and physicians. All children of school age attended the hospital school. One of the parents was always co-admitted except for some of the older children. In total 56 of the children (34.8%) were examined by a child neuropsychologist.

All children had one or more interictal EEGs performed during the admission, which lasted for an average of three weeks. Furthermore, during admission 62% of the children had intensive EEG monitoring (video-EEG, ambulatory EEG, or cognitive testing during video-EEG while having paroxysmal discharges). A few had a multiple sleep latency test done as part of an evaluation for narcolepsy.

The final decision on whether the child had epilepsy or not was taken based on the comprehensive evaluation during the admission by two of the authors (PU, JB).

RESULTS

On discharge, 87 of the 223 children (39%) were found not to have epilepsy, excluding three children with epilepsy and psychogenic non-epileptic seizures (PNES). As seen from table 2, 30% of the children were diagnosed as non-epileptic, even when the referring doctor had expressed no doubt about the epilepsy diagnosis in the referral note. Of the 159 children admitted for the first time, 75 (47%) were thought to have non-epileptic seizures. Of the 125 children admitted for the first time with no doubts about the diagnosis of epilepsy, 44 (35%) did not have epilepsy. The distribution of the referring doctor's clinic or specialty among these 44 children showed no difference from the total referrals as mentioned in the methods section.

Table 3 shows the diagnoses of non-epileptic events in the 87 children without epilepsy. The most frequently encountered paroxysmal events were staring episodes in mentally retarded children. PNES were found in 12 children (10 girls). Their median age was 14 years (range 8–17). Of these, only three children with concomitant epilepsy were mentally retarded.

Of the 87 children without epilepsy, 35 were treated with AEDs at the time of admission. Among 34 children taken off drugs, seven had been treated with two or more AEDs. In 16 of these cases the referring doctors were in doubt about the

Table 2 Reasons for referral versus diagnosis at discharge among 223 children admitted for possible epilepsy

	Epilepsy confirmed	Epilepsy not confirmed
Doubt about diagnosis of epilepsy in referral note	7 (18%)	32 (82%)
No doubt of epilepsy expressed in referral note	129 (70%)	55 (30%)

Table 3 Diagnosis of 87 children discharged without a diagnosis of epilepsy

Diagnosis	No.
Staring episodes	46
Mental retardation (n = 22)	
Autism/Asperger syndrome (n = 4)	
Learning disorder (n = 3)	
Self stimulation (n = 2)	
Abnormal EEG (n = 7)	
Normal child (n = 8)	
Psychogenic non-epileptic seizures (PNES)	9
Syncope	4
Dystonia	4
Parasomnias	4
Hyperventilation attacks	3
Migraine	3
Breath holding spells	2
Munchausen by proxy	2
Narcolepsy, Gilles de la Tourette, benign tremor, febrile convulsions	4
Not clarified	6

diagnosis of epilepsy. One patient with dystonia was continued on clonazepam because of its muscle relaxant effect. Thus a total of 34 (15%) of the 223 admitted children had their medication tapered off. A further 22 (10%) had previously been treated with AEDs but had been tapered off before admission.

DISCUSSION

In Denmark, most children with epilepsy and other paroxysmal events are treated in the local paediatric departments. Admission to the only tertiary epilepsy centre in Dianalund is free for the patients. All medical doctors can refer a child to the centre. This means that if the parents want a second opinion they can go to their general practitioner for a referral to Dianalund, even though the local paediatrician may not find a referral necessary.

The total annual incidence of childhood epilepsy in Denmark is about 600. Expecting about 25% (150) of these to be difficult to treat, the number of children (159) admitted to Dianalund for the first time in 1997 seems to indicate that the majority of the "intractable" cases in Denmark will be admitted at least once during their lifetime. Furthermore, the geographical distribution of the children was evenly spread from all over Denmark. Even though this is not a strict population based study we believe that the figures in the present study are reasonably representative for Danish children with continuing seizures treated by paediatricians.

The difficulties of obtaining a final decision of the epilepsy diagnosis are illustrated by the fact that 12 of the 87 non-epileptic children had been admitted in previous years. Some of these children had been misdiagnosed at the previous admission; new clinical observations emerged during the admission in 1997 that made it possible to discard the epilepsy diagnosis. Others are thought to have outgrown a previously possible epilepsy. This is in accordance with a prospective study in which experienced child neurologists had to change their first diagnosis of epilepsy to non-epileptic paroxysmal events in 4.6% at later follow up.¹² It has also been shown by the same study group that among child neurologists the agreement was only fair to moderate¹³ on the diagnosis of epileptic seizures based on the description of 100 first paroxysmal events. The agreement improved somewhat using predefined descriptive definitions of epilepsy and panel discussions. In contrast to the Dutch study our results are based on a comprehensive evaluation during admission of children with continuing paroxysmal events. In spite of this

some uncertainty on the diagnosis seems to exist in a small number of cases. In a prospective study it would be reasonable to include a category of children where no firm diagnosis could be made. This might reduce the percentage of misdiagnosis. We doubt, however, that a prospective study with predefined work up of the children would have changed the results. A planned ictal video-EEG would, for instance, seldom be possible to obtain, even during a three week admission.

The incidence of 30% where the referring doctor expressed no doubt about the diagnosis is surprisingly high. We have not found any study calculating the percentage of misdiagnosis where the referral cases all were thought to be epilepsy.

The results of a diagnostic evaluation of suspected epilepsy after a referral to a tertiary epilepsy centre are better documented. In a Scottish study only 54% referred with paroxysmal phenomena had epilepsy.¹⁴ Among 666 Australian children who had intensive EEG monitoring done, 43% had non-epileptic seizures.¹⁵ In a study from the USA, 22.5% of 199 children were discharged without epilepsy diagnosis after video-EEG.¹⁶ However, in these studies the reasons for referral were not specified. Other small observational studies have documented the problem of misdiagnosis in childhood epilepsy.^{2, 17}

Disproving the diagnosis of epilepsy is important from several points of view. Unnecessary drug treatment as well as concerns about development and social coping and restriction imposed on the child's lifestyle can come to an end. In our series, medication could be stopped in 34 children (15% of all admitted). This is a somewhat higher percentage than found in the US study of 883 children referred for EEG monitoring (5%)¹⁶ and children evaluated at the adolescent clinic in the UK (4%).¹⁷ The explanation for their lower figures is probably that more children were referred to these clinics for an early diagnostic evaluation.

The majority of non-epileptic events in the present series were staring episodes, confirming results from other studies.^{15, 16} Most often this is seen in mentally retarded children with non-specific EEG abnormalities which are over-interpreted as "epileptiform". One study showed, however, that it was found just as often in normal children.⁷ Another study found some descriptive features distinguishing epileptic from non-epileptic events; the sensitivity was low, however.¹⁸ PNES were found less often than in other studies,¹⁶ probably because of our strict definition of PNES: paroxysmal events of non-physiological nature, but which are regarded and treated as epileptic and play an important role in the emotional interaction between the child and the parent/environment. This means that the diagnosis was only used if a psychological evaluation could add these positive criteria. Except for gastro-oesophageal reflux, shuddering attacks, paroxysmal torticollis, tonic upward gazing, long Q-T syndrome, and alternating hemiplegia, all the differential diagnoses most frequently mistaken for epilepsy seem to be represented in our material.

The problem of misdiagnosis in epilepsy is not restricted to children. A recent study has shown high figures in adults as well, syncopal episodes being among the most frequent.¹⁹ In the present study, video-EEG monitoring played an important role as 62% of the children had this investigation done. In the remainder, the diagnostic work-up was based on clinical observation combined with careful history taking, and interictal EEG. The role of each diagnostic procedure is difficult to evaluate because each forms part of a comprehensive procedure.

What is already known on this topic

- The diagnosis of epilepsy is difficult
- A consultant paediatrician in England misdiagnosed 618/1948 (31.7%) children as having epilepsy

What this study adds

- The rate of misdiagnosis of epilepsy in a national sample of difficult-to-treat patients from a developed country is extremely high, with more than 30% of those with definite epilepsy not having epilepsy at all

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The co-author Jette Buchholt has passed away since this paper was accepted.

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