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Classification of Idiopathic Generalized and Localization-Related Epilepsies

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ÖZET

İdyopatik Jeneralize ve Lokalizasyonla İlişkili Epilepsilerin Sınıflandırılması

Epilepsilerin sınıflandırılması ilk kez 1960'larda uluslararası bağlamda anlaşmayı kolaylaştırmak, yanlış anlamaları engellemek ve değişik ülkeler ve okullar arasında karşılaştırmalar yapabilmek amacıyla başlatılmış ve son hali 1989'da Uluslararası Epilepsi ile Savaş Ligi (ILAE)'nin genel kurulunda kabul edilmiştir. Sınıflamada etyolojiye dayanan üç bölüm vardır: semptomatik, idyopatik ve kriptojenik. İdyopatik epilepsiler bir başka bozukluk nedeniyle değil tamamen kendine özgü etyoloji ve patogenezle gelişen durumlardır ve hemen tümünde genetik bir bozukluk suçlanmakta olup tutulan genlerin yerini belirlemek için yoğun çalışmalar sürdürülmektedir. Bu makalede idyopatik epilepsilerin ana özellikleri görülme yaşları da gözönüne alınarak sınıflamaya göre incelenmiştir.

Anahtar kelimeler: *epilepsi, sınıflama, idyopatik epilepsi*

SUMMARY

The classification of epilepsies was started in the 1960's to improve the communication of epileptologists, to avoid the misunderstandings and to be able to compare data from different countries and schools. The revised proposal was accepted by the General Assembly of the International League Against Epilepsy (ILAE) in 1989. This classification has three classes refering to the etiology: symptomatic, idiopathic and cryptogenic. Idiopathic epilepsies are those which are known not to be caused or occasioned by another disorder but diseases with specific etiology and pathogenesis. Almost all of them supposed to be related to a genetic defect and intense research is going on to identify the involved genes. In this paper the idiopathic epilepsies are given according to the international classification in order to the age of manifestation.

Key words: *epilepsy, classification, idiopathic epilepsy*

INTRODUCTION

The development of an International Classification of Epilepsies was begun in the 1960's, and the first aim of this initiative was practical, to improve the possibility of an international exchange of ideas in epileptology, to avoid the misunderstandings which arose from using the same names for different things, and different names for the same things, and to ensure comparability of data from different countries and schools.

It is appropriate to state that the international classification as it was accepted by the General Assembly of the International League Against Epilepsy in 1989, reasonably fulfills these purposes. In addition, it has had some unexpected but equally important results:

- the development of the classification and the publications accompanying it brought a wave of new epileptological knowledge to countries with little tradition in epileptology;

- the classification divided the vast field of epileptology up in more manageable and more homogeneous subentities which was a necessary precondition to the important developments in epilepsy genetics of the past years;

- the discussion of the correctness of the classification and the terms and entites included in it favoured the development of theories in epileptology;

- this in turn improved the interchange between clinicians and theoreticians in epileptology.

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On the other hand, it would be wrong to expect from the classification what it is not meant to give. In particular, the international classification does not contain what should be considered the definite truth about epilepsy. The reason for this is that a definite truth about epilepsy does not exist and will probably never exist. Ongoing research will always change our views of epilepsy and reveal new information and insight which will probably also have its influence on the classification as time goes on.

Thus, the international classification should only be considered as a useful systematic order of those diagnoses included under the heading of epilepsy which were accepted in 1989 by a significant number of international epileptologists. A perfect agreement of all experts could neither be expected nor was it reached. The accepted classification is a fair and reasonable compromise between different views. It is also non compulsory in the sense that everybody is supposed to use every item which is included in the classification. If some researcher finds in the classification an entity which he does not believe to exist he is not compelled to use it. He will know, however, that he will find this entity mentioned in the literature, and that a significant number of international researchers do use it. The international classification is, then, supposed to provide an accepted definition.

IDIOPATHIC EPILEPSIES

The international classification has three classes referring to the etiology: symptomatic, idiopathic and cryptogenic. There are clear definitions of all three. Symptomatic epilepsies or those which are known to be the consequence of some disorder, disease or lesion affecting the brain or parts of it. Idiopathic epilepsies are those which are known not to be caused or occasioned by another disorder but diseases sui generis with a specific etiology and pathogenesis. Cryptogenic epilepsies are those where the etiology is unknown, not clarified.

The idiopathic epilepsies included in the international classification are almost all supposed to be rooted in a genetic defect, and intense research is going on to localize and identify the involved genes.

They have also in common that they have specific ages of manifestation. They are therefore given in the international classification, and in this paper, in order of manifestation age differentiating, however, between generalized and localization-related epilepsies.

IDIOPATHIC GENERALIZED EPILEPSIES

Benign familial neonatal convulsions

This is an autosomal-dominantly inherited rare disease, and in various but not all families, a relevant gene has been located to chromosome 20. The onset is mostly on the second to third day of life, and the duration rarely exceeds one week. The hallmark are multilocal clonic seizures, and apnoic spells are a typical potential additional seizure type. In about 11 % of cases, seizures recur later in life, mostly as isolated events. The EEG shows rhythmic spikes or slow waves, and a pattern known as théta pointu alternant. Treatment is not necessary as far as known.

Benign neonatal convulsions

This is, strictly speaking, a cryptogenic and not an idiopathic disorder with an onset mostly on the fourth to sixth day of life, lasting for not more than 2 weeks. The hallmark is a status of clonic and apnoeic seizures. The EEG is similar as in the previous disorder, and treatment is not necessary.

Benign myoclonic epilepsy in infancy

This syndrome starts at the age of 4 months to 3 years, in children who often have a family history of seizures. The hallmark are bilateral jerks of the axial, facial and limb muscles. The EEG shows generalized spike-waves and poly-spike-waves. The prognosis of well-treated children is excellent, otherwise developmental delay may occur. The drug of choice is valproic acid.

Childhood absence epilepsy or pyknolepsy

Onset is in the age 3-12 years, and a positive family history is frequent. The hallmark are frequent (daily) absences of all types. Potential additional seizure types are generalized tonic-clonic (frequently, and

usually of the awakening mode) and myoclonic jerks (rarely). The EEG is characterized by frequent 2.5-3.5 Hz bilateral Spikes and Waves. The seizures are typically precipitated by lack of sleep and, in subsets of the syndrome, intermittent lights and eye closure, the latter especially in absences with eyelid myoclonia. Appropriate drugs are valproic acid, ethosuximide (for absence only), and lamotrigine. The prognosis is usually excellent with correct treatment.

Juvenile absence epilepsy

A syndrome with frequent positive family histories, and an onset at 14.8±8.3 years. The hallmark are infrequent (sporadic) absences of all types. Potential additional seizure types are GTC (on awaking) and myoclonic jerks, the letter more frequently than with childhood absences. The EEG presents bilateral 3.5 - 4 Hz spikes and waves. The seizures are sensitive to sleep withdrawal. Photosensitivity seems to be less common than in childhood absences. Treatment is the same, and the prognosis is excellent provided the absences are treated.

Juvenile myoclonic epilepsy (Janz syndrome)

This is a presumably polygenic syndrome where a candidate gene is suspected on chromosome 6p. The onset is mostly in the age of 12-19 years. The hallmark are bilateral jerks, mostly in the arms distally, rarely in the legs, not in the face, in clear consciousness. Potential additional seizure types are GTC, usually on awakening, and these are often the presenting symptom; absences may also occur. The EEG shows bilateral spikes and waves usually faster than 3 Hz, and the ictal pattern is always generalized poly-spike-wave. The seizures are sensitive to lack of sleep and, often, to intermittent light stimuli. The role of praxis-induction, perhaps in a subset of patients, needs further clarification. The drug of choice is valproic acid, phenobarbital being a possible alternative. Clonazepam seems only to be effective against the myoclonic seizures. Response to treatment is usually excellent, but long-term therapy is mostly required.

Epilepsy with grand mal on awakening

Onset is mostly in the second decade of life, and positive family history is frequent. The hallmark is the namegiving feature, but there is a subset with seizures occuring predominantly in the evening leisure hours. Common additional seizure types are absences and myoclonic jerks of the type described above. The EEG shows any type of bilateral spike-wave and poly-spike-wave. The seizures are typically sensitive to lack of sleep, and photosensitivity is frequent. The drug of choice is valproic acid, with phenobarbital and primidone as possible alternatives. The prognosis is usually very good.

LOCALIZATION-RELATED IDIOPATHIC EPILEPSIES

Childhood epilepsy with occipital paroxysms

The age of onset has been reported to stretch from 15 months to 17 years, with a mean of 7.5 years. There is a family history of epilepsy in 37 %, and of migraine in 16 % of the patients. The hallmark are visual auras which may evolve into focal motor seizures, often followed by a headache. In the EEG, bilateral occipital spike-waves and sharp waves are found. A typical sensitivity exists to sudden changes of illumination. No specific preference for a particular AED has been described, and the results of therapy are not quite as good as in the following syndrome.

Benign epilepsy of childhood with centro-temporal spikes ("benign rolandic epilepsy")

The age of onset is from 3 to 13 years, and a family history of epilepsy is frequent. The syndrome also has a typical age of offset which is puberty. The hallmark are simple focal motor seizures of the upper body quadrant. GTC seizures often are an additional or the only seizure type. Most seizures occur during sleep. The typical EEG finding is the namegiving feature. Drug treatment is only necessary when the seizures are too prominent to be accepted by the patient and family. In that case, good results have been reported with valproic acid, carbamazepine or sulthiame. The prognosis is excellent independent from therapy.

Reading epilepsy

The onset is between 12 and 25 years of age, and a positive family history is frequent. The hallmark are focal speech motor seizures provoked by reading which may evolve into a GTC seizure if the patient continues to read. Potential other seizure types are visual or ocular auras. The EEG presents bilateral or unilateral sharp waves in the temporo-parietal or the fronto-central derivations. The treatment is often behavioural with avoidance of excessive reading, valproic acid being the drug of choice if pharmacotherapy is required. The prognosis is excellent, with no tendency to develop spontaneous seizures.

GENERALIZED VERSUS LOCALIZATION-RELATED IDIOPATHIC EPILEPSIES

What is the difference, in idiopathic epilepsies, between "generalized" and "localization-related"? This question can also be put differently: if idiopathic epilepsies mostly have a genetic background as the basis of their pathogenesis: why is its expression not always generalized but sometimes localized or regional? The probable answer to this question is that the expression is always regional but sometimes in a bilateral, more or less symmetric way, and sometimes asymmetric or unilateral. At present we are unable to tell the reasons for this difference. But we know that the difference has some significance beyond the question of symmetry or asymmetry. Thus, the localization-related idiopathic epilepsy syndromes seem never to overlap either with each other or with generalized idiopathic syndromes. Quite to the contrary, there is an important overlap between some of the idiopathic generalized epilepsy syndromes.

The clarification of these questions where we can expect much from molecular genetics and from the study of receptors and ion channels is perhaps the most important challenge for a better theoretical understanding of the variability of epilepsy as it is visible in the syndrome classification.

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