Clinical and electro-clinical classification of epileptic seizures in West Uganda.

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Résumé : **Classification clinique et électro-clinique des crises d'épilepsie en Ouganda occidental.**

La prévalence de l'épilepsie dans les pays en voie de développement, comparée à celle des pays industrialisés, est relativement élevée, voire extrêmement élevée, avec des taux allant jusqu'a 57 cas pour 1 000 habitants dans certaines régions. Les raisons qui pourraient expliquer les variations demeurent obscures et les données épidémiologiques et cliniques détaillées sont rares, surtout pour l'Afrique rurale. Nous avons mené notre étude dans une région occidentale de l'Ouganda marquée par une prévalence de l'épilepsie élevée et où l'onchocercose est reconnue comme endémique. Les crises des 91 épileptiques diagnostiqués au cours d'une période de deux ans ont été répertoriées selon le système de classification de la Ligue internationale contre l'épilepsie. Si l'on se base seulement sur la description de la crise elle-même, la crise généralisée, chez 57 malades, concernait la majorité des cas (63 %), suivie par la crise partielle chez 22 malades (24%) et par 12 crises non classifiées (13 %). Cinquante cinq des 91 malades ont été examinés par électro-encéphalogramme (EEG), qui indiquait une activité épileptiforme (AE) focale chez 12 personnes, une AE multifocale chez 9 personnes et généralisée chez 6 personnes. Lorsque les résultats de l'EEG des 27 patients avec EA ont été rajoutés aux renseignements cliniques pour la classification de la crise, la proportion de crises partielles s'est élevée à 78 % (n = 21); inversement, la proportion de crises généralisées ne représentait plus que 22 % (n = 6). La prédominance des crises partielles semblerait compatible avec une lésion cérébrale locale comme cause fréquente des crises d'épilepsie dans la zone étudiée. Ces résultats viennent renforcer des observations récentes faites dans plusieurs pays africains, qui associent l'épilepsie et l'onchocercose.

épilepsie
classification
electro-encephalogramme (EEG)
onchocercose
Ouganda
Afrique intertropicale

Summary:

When compared to that of industrialised countries, the prevalence of epilepsy in developing countries has generally been found to be higher and in some areas extremely high rates of up to 57 cases per 1000 inhabitants have been reported. The reasons for this difference are still widely unknown and detailed epidemiological as well as clinical data are scarce, especially from rural Africa. The present study was conducted in western Uganda, in an area of high epilepsy prevalence, known to be endemic for onchocerciasis. The seizures of all 91 epilepsy patients diagnosed in this area over the period of two years were classified according to the criteria of the International League against Epilepsy. Based on seizure description alone, the predominant seizure was classified as generalised in 57 patients (63%), as partial in 22 (24%) and unclassified in 12 (13%). An EEG record was analysed in 55 out of 91 patients, showing focal epileptiform activity (EA) in 12, multifocal EA in 9 and primarily generalised EA in 6 patients. When in addition to clinical information, the EEG results in the 27 patients with EA were taken in consideration for seizure classification, the proportion of partial seizures increased to 78% (n = 21); inversely the proportion of generalised *seizures fell to 22% (n = 6). The predominance of partial seizures would be compatible with a localised brain lesion as a frequent cause for epileptic seizures in the study area. The findings further corroborate recent observations from several African countries of an association between epilepsy and onchocerciasis.*

epilepsy
seizure classification
EEG
onchocerciasis
Uganda
Subsaharan Africa

Introduction

When compared to that of industrialized countries, the prevalence of epilepsy in developing countries has generally been found to be higher and in some areas extremely high rates of up to 57 cases per 1000 inhabitants have been reported (23). Although numerous possible factors are suggested to explain this difference, the underlying causes are still widely unknown and detailed epidemiological and clinical data are scarce, especially from rural Africa (3).

We recently reported on the high prevalence and incidence of epilepsy in an area in West Uganda and its relation to the endemic occurrence of *Onchocerca volvulus*, the causative organism for river blindness (11, 14). Although the

epidemiological data suggest a strong association, it is still unclear whether this represents a causal relationship between infection with *O. volvulus* and epilepsy.

The aetiology of epilepsy can be established clinically only in a small percentage of patients. However, the patterns of seizure characteristics in a population can give important indications as to possible causes of epilepsy in different regions (9). In particular, partial seizure types tend to prevail in regions where symptomatic epilepsies are frequent. The present article gives a description of the epileptic seizures of patients in the afore-mentioned area of West Uganda by use of the ILAE (International League against Epilepsy) classification of epileptic seizures (2).

Patients and methods

All patients originated from the twelve villages of the Kabende parish in the Kabarole district of West Uganda, with a population of 4743 inhabitants in 1994. Details of demography and the epidemiology of epilepsy and onchocerciasis in the study area are presented in our previous articles (12, 14). All patients identified in this area from March 1994 to February 1996 were included in the study: sixty-one patients were seen on the occasion of a population-based prevalence survey for epilepsy in 1994 and another 30 were diagnosed over the following two years during regular 6-monthly follow-up visits to the area (13). Active epilepsy was defined as two or more afebrile seizures over the previous 2 years, not related to alcohol use, drug intake or acute illness (8).

For all patients, case history was taken in the local Rutoro language jointly by a Ugandan health worker (G.A. or Ch.M., both native Rutoro speakers) and a German medical doctor trained in pediatric neurology (Ch.K.). The interviews were held with the patients and a close relative, preferably the mother (n = 38), father (n = 23), brother/sister (n = 15) and in 15 cases with another relative or a neighbour who had witnessed the seizures. No more than five patients were seen on any one day in order to avoid any time constraints. The questionnaire used was similar to the one published by REUTENS D.C. (19) covering issues of seizure description, frequency and provoking factors, as well as a general medical history. If necessary the questionnaire was completed by free exploration.

From those patients seen during the initial prevalence survey, a standard EEG could be recorded with a portable 12-channel EEG machine (Madaus-Schwarzer ED 15, Munich, FRG). Recordings were done with the 10-20 system for placement of electrodes over a minimum time of 20 minutes including 3 minutes of hyperventilation and 2 minutes of photic stimulation, according to the practice at the University Children´s Hospital, Heidelberg. EEG records were analysed independently by two observers (Ch. K. and Ch. B.) with regard to the occurrence of epileptiform activity (EA) using the categories of abnormalities consistent with generalised, focal (one delimited focus) or multifocal (two or more foci) epileptic discharges. Records with differing interpretations were analysed by an additional observer (D.R.) and agreement of all three observers was reached by discussion.

Clinical classification

If a patient had experienced more than one seizure type, the most frequent one was called the predominant and the less frequent one was called the additional seizure. For all patients the predominant and, if applicable, the additional seizure type was classified on the grounds of the seizure description alone, using the proposal for revised clinical and electroencephalographic classification of epileptic seizures (2).

If a patient presented with generalised seizures and in addition to this gave an account of a second seizure type with partial features regularly related to the first seizure type, this was taken as evidence of a partial onset. If a partial and a generalised seizure type were reported to occur only independently, these were classified as two different seizure types. In a partial seizure, consciousness was considered to be impaired or lost, if the eye witness gave an account of a change of the patient's responsiveness and the patient himself could not recall the respective seizure or part of a seizure. In this case the seizure was classified as complex partial. Because an aura has been found to be unreliable in indicating a partial onset of a seizure (25), such a finding was not considered sufficient evidence to classify a seizure as partial. If the patient reported a vague feeling preceding the seizure, such as palpitations or a rising abdominal sensation but the eye witness´ account did not give supportive evidence for a partial seizure, the seizure was classified as generalised.

Electro-clinical classification

For those patients with a finding of EA in the EEG, the seizure type was also classified taking into consideration the EEG results. If the EEG showed abnormalities consistent with focal or multifocal epileptic discharges but the history gave no evidence of a partial onset of a generalised seizure, the seizure was classified as partial, secondarily generalised with undetermined onset as suggested by SENANAYAKE (22).

Results

From March 1994 to February 1996, 91 patients with epilepsy were diagnosed in the study area. The age of the epilepsy patients ranged from 4 to 58 years (median: 15 years). Patients with an EEG record available had a slightly longer duration of seizures since their onset and also presented with a higher seizure frequency than those without an EEG record (Table I). There was however no essential difference in their age at diagnosis or in the ratio of male to female patients.

Table I.

Characteristics of 91 epilepsy patients with and without EEG record
Caractéristiques des 91 malades épileptiques avec et sans EEG.

	patients with EEG (n =55)	**patients without EEG** (n =36)	**all patients** (n =91)
male/female ratio	1:1.1	1:1.3	1:1.2
age (years) **at diagnosis** : mean (95% CL)	15 (13-17)	15 (13-16)	15 (14-16)
age (years) **at first seizure** : mean (95% CL)	10 (9-12)	11 (10-13)	10 (10-12)
seizure duration (years) : mean (95% CL)	3 (2-5)	1 (<1-3)	3 (2-3)
seizure frequency (per month) : mean (95% CL)	8 (4-30)	4 (2-10)	8 (4-10)

Fifty-seven patients presented with a history of generalised seizures without evidence of a partial onset as predominant seizure type (table II). The great majority of these were considered on clinical grounds as tonic-clonic seizures and only two as tonic or atonic. No history was obtained consistent with absence, myoclonic or clonic seizures. In 22 patients an account consistent with a partial seizure was found. Twenty of these were secondarily generalised and only two were not. Seven patients with a history of generalised seizures reported a sensation repeatedly preceding a seizure, which was compatible with an aura. Because in these cases the eye witness had

Table II.

Frequency of predominant seizure type in 91 patients based on seizure description.

Fréquence du type de crise prédominant chez 91 malades selon la description de la crise.

seizure type		number of patients
partial		**22 (24%)**
simple partial	0	
complex partial	2	
partial secondarily generalised	20	
simple onset	12	
complex onset	8	
generalised		**57 (63%)**
tonic	1	
tonic-clonic	55	
atonic	1	
unclassified		**12 (13%)**
total		**91**

not observed a feature indicating a partial onset, they were classified as generalised seizures.

In 12 patients, the predominant seizure could not be classified as partial or generalised and another 7 patients had an unclassifiable seizure in addition to their predominant one. In 15 of these 19 patients, the eye witness gave an account of a seizure characterized by one or several repetitive head movements or "head nodding" which was usually accompanied by an episode of impaired responsiveness lasting from a few seconds up to several minutes. From the histories obtained, it was not possible to decide whether these head nodding movements were a myoclonic, atonic or other feature of the seizure. In two patients complex automatisms were observed in the context of these seizure, in five they were followed by a generalised seizure.

The EEG showed epileptiform activity (EA) in 27 out of 55 patients, which in most cases was focal or multifocal (table III). When based on seizure description alone the proportion of partial and generalised seizure types in these patients was similar to that of all 91 patients. When the seizures were then classified taking into consideration the EEG result, a number of seizures initially classified as generalised or unclassified were re-classified as partial, secondarily generalised with undetermined onset. Accordingly, the proportion of partial seizures rose from 22% to 78% and inversely the percentage of generalised seizures fell from 63% to 22% (table III). An EEG was analysed in 4 out of the 7 patients presenting with the history of an aura, showing focal EA in two cases, generalised EA in one and no EA in the remaining cases.

Table III.

Epileptiform activity (EA) in 27 EEG records related to clinical and electro-clinical seizure classification.

Activité épileptiforme (AE) dans les 27 EEG en fonction de la classification clinique et électro-clinique de la crise.

	clinical classification (nr. of patients)	EA			electro-clinical classification (nr. of patients)
		focal	multifocal	general	
partial	6 (22%)	4	2	0	21 (78%)
generalised	17 (63%)	5	7	5	6 (22%)
unclassified	4 (15%)	3	0	1	0
total	**27**	**12**	**9**	**6**	**27**

In nine cases a seizure could be directly observed during the initial examination, a follow-up visit or on the occasion of the EEG recording, when the patients spent a whole day at the health centre (Table IV). In only one patient was full agreement found for the classification based on seizure description alone, observation alone and classification based on all available clinical and electro-encephalographical information (Pat. Nr. 1). In four others (Pat. Nr. 2-5) the seizure type observed was consistent with the one described, but the EEG

Table IV.

Patients with observed seizures: classification based on description,observation and electro-clinical features.

Malades avec crises observées : classification à partir de la description, de l'observation et des caractéristiques électro-cliniques.

Pat-Nr	clinical classification: description	clinical classification: observation	EA in EEG	electro-clinical classification
1	complex-partial sec. generalised	complex-partial sec. generalised	multifocal	complex-partial
2	GTCS	GTCS	multifocal	partial,sec.generalised
3	GTCS	GTCS	focal	partial sec. generalised
4	unclassified	unclassified	n. d.	(unclassified)
5	GTCS	*generalised tonic	n.d.	(generalised tonic)
6	GTCS	complex-partial	focal	complex-partial, sec. generalised
7	GTCS	*complex-partial	multifocal	complex-partial sec. generalised
8	unclassified	complex-partial with automatisms	no EA	(complex-partial with automatisms)
9	unclassified	complex-partial with automatisms	focal	complex-partial with automatisms

EA = epileptiform activity, GTCS = generalised tonic-clonic seizures,
* =under phenobarbitone, n.d. = not done

revealed partial features in two patients whose seizures initially were classified as generalised. In two patients (Pat. nr. 6 and 7) whose history provided no evidence of a partial onset of a generalised seizure, the seizure observation clearly showed a complex-partial introduction (in both with impairment of consciousness and automatisms) and this was consistent with the EEG result. A seizure could be observed in three patients in whom a history of unclassifiable "head nodding" seizures had been obtained. One of these (Pat. nr. 4, a ten year old boy), when sitting beside his father during the initial interview, had repeated episodes of uttering a short sound ("like a hickup"), which was accompanied by a short single jerk of the upper body and followed by a dropping head movement and a few seconds of impaired responsiveness. In the other patients (Pat. nr. 8 and 9), the seizures were observed when they were lying on the examination table and no head movement was perceived. Unlike in Pat. nr. 4, in these two patients no clonic or atonic feature was observed. Just as in the majority of cases with a seizure observed, the picture was consistent with a complex-partial seizure.

In a few patients, history taking and physical examination revealed a possible risk factor for epilepsy (table V). Two children were reported to have been very small and weak at birth but recovered quickly and were considered healthy until the onset of seizures. Two others had experienced a severe febrile illness with loss of reaction prior to the onset of seizures, which could be consistent with a CNS infection such as meningitis or cerebral malaria. If these findings are taken as evidence of a possible aetiology, epilepsy may be considered as remote symptomatic in 13 out of 91 patients (11%).

Table V.

Risk factors for epilepsy from patients´ history and physical examination.

Facteurs de risque d'épilepsie selon l'histoire et l'examen physique des malades.

risk factor	nr. of patients
perinatal event	2
head trauma	1
suspected CNS infection	2
alcohol abuse	3
impaired hearing	3
microcephaly	2

Discussion

With few exceptions, the epilepsy patients in the Kabende parish presented with generalised tonic-clonic seizures,

with or without evidence of a partial onset. This is probably due to the process of patient identification, which in the introductory house-to-house survey used the local term for epilepsy without a further specification (12, 14). The term designating epilepsy in the local Rutoro language corresponds mainly to the seizure type of generalised tonic-clonic seizures (16, 18). Therefore, patients with other seizure types could not be assessed and those who were actually examined possibly constitute a still incomplete sample out of the whole of epilepsy patients in the study population. In particular, a number of patients with non-generalised partial seizures may have been left out.

History taking revealed a partial onset in about one third of the patients with tonic-clonic seizures and this proportion increased to nearly 80 percent in those patients in whom the EEG revealed epileptiform activity. With a more extensive diagnostic work up, such as repeated recordings and sleep recording, a similar pattern of EEG changes probably would have been detected in those patients who had no epileptiform activity in the standard EEG (4). Direct observation produced additional evidence that classification based on seizure description alone may frequently miss a partial feature, which has not been reported by the eye witness, and this will result in an underestimate of partial seizures.

A frequently described feature of patients with unclassified seizures was repetitive head movements and impaired responsiveness with or without subsequent generalisation. When directly observed, these seizures were classified as complex partial in two cases and in another possibly corresponded to a myoclonic-astatic seizure. Thus, the reported "head nodding" seizures most likely do not represent one distinct but rather a collection of several different seizure types. The clinical description of seizures from two other areas in Africa with a high epilepsy prevalence bears some resemblance to our findings. For a population in Tanzania, JILLEK-AALL *et al.* (10) reported on a frequent seizure type characterised by nodding head movements and VAN DER VAALS *et al.* (26) gave a similar account from Liberia.

So far only a few population-based studies on seizure classification have been published for African countries. Communications from Liberia, Kenya and Tanzania were based on clinical information only (7, 20, 26, 27). Three other reports were also based on EEG recordings (1, 17, 24), although the number of patients examined and the exact valuation of EEG results was stated in only one of these (1). The proportion of partial and generalised seizures in these studies varied widely, with generalised seizures prevailing in Tanzania, Kenya, Tunisia and Ethiopia, and partial seizures in Nigeria, Liberia as well as in our study. In the second Liberian study from the same area, partial and generalised seizures were found to be almost equally distributed (27).

Besides real differences in the distribution of seizure types, this diversity of findings probably reflects differences of the sampling and examination methods used, of the examiner´s interpretation of the seizure classification and of the socio-cultural context in which the study was undertaken. As mentioned, in our study, as in those from Liberia, the use of a sole term for epilepsy as a screening question in the house-to-house survey may produce a bias towards generalised seizures. The other cited reports attempted to avoid this by introducing screening questionnaires which were designed to assess also partial seizures and were applied population-wide after a short training by lay health workers. As demonstrated by our results and those of others (22, 24), the use of an EEG record tends to increase the number of seizures classified as partial. We did not consider the finding of an aura sufficient evidence of a partial onset of a generalised seizure, because the relevance of this finding seems unclear (25). However, such an interpretation in our study would have led also to a further increase in the proportion of partial seizures.

Epidemiological data suggest that epilepsy in the study area is closely linked to the endemic occurrence of onchocerciasis, a filarial helminth known to cause river blindness (12, 14). Anecdotal accounts on such an association had previously been reported from several African countries (5, 28) and recently corresponding observations have been reported from *O. volvulus* endemic areas in Tanzania (11) and Burundi (15). Although the pathomechanism involved is still unclear, it may be speculated that a parasite, which is known to affect various parts of the eye including the optic nerve (21) and has been found in the cerebrospinal fluid (6), possibly can also produce an epileptogenic brain lesion. The predominance of partial seizures found in our patients from Uganda would be compatible with a localised lesion and it would be highly desirable to perform neuroimaging in order to demonstrate a morphological equivalent. However, at present there are no CT or MRI facilities within reach of our patients and this is not expected to be the case in the near future. Further studies on the aetiological background of epilepsy therefore will have to be essentially based on clinical and epidemiological methods. Recently, the transmission of *O. volvulus* in the study area has been successfully interrupted by insecticidal treatment of the breeding sites of the transmitting *Simulium neavei* flies. This will provide the opportunity to test the hypothesis whether the incidence of epilepsy will decline once the putative agent has been removed.

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