Factors associated with behavioral problems and cognitive impairment in children with epilepsy of Kinshasa, Democratic Republic of the Congo

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Abstract

Background: Behavioral problems and cognitive impairment are common in children with epilepsy (CWE). In sub-Saharan Africa, little is known about these comorbidities particularly their relationships with socioeconomic features. The goal of this study was to identify clinical and socioeconomic factors associated with behavioral problems and cognitive impairment in CWE of Kinshasa (Democratic Republic of the Congo).

Methods: This cross-sectional hospital-based study had included 104 CWE aged 6 to 17 years. Behavioral problems were assessed by the child behavior checklist. The Wechsler nonverbal scale of ability was used to assess cognitive impairment.

Results: At least one behavioral problem was found in 34.6% of CWE. Internalized problems were increasing with father's age (p=0.034). Externalized problems were increasing with the decreased of mother's age (p=0.009) and with a previous antiepileptic treatment (p=0.032). Total behavioral problems were increasing with a previous antiepileptic treatment (p=0.029). Cognitive impairment was present in 73.3% of CWE. It was more common in boy (p=0.013), and it was increasing with a low household daily expenses (p=0.034), with a previous antiepileptic treatment (p=0.041), with an early onset of epileptic seizures (p=0.042) and with a high frequency of epileptic seizures (p=0.011).

Conclusion: Behavioral problems and cognitive impairment are common in CWE. Multivariate analysis has shown that behavioral problems were associated with socioeconomic features only. Contrariwise cognitive impairment was associated with both socioeconomic factors and clinical features. There is a need of more studies to improve knowledge of these comorbidities in the sub-Saharan Africa context.

Key words: Epilepsy; Children; sub-Saharan Africa; Behavioral problems; Cognitive impairment; Democratic Republic of the Congo.

1. Introduction

Psychopathological disorders and cognitive impairment are common in children with epilepsy (CWE). Psychopathological disorders, including psychiatric disorders, behavioral problems and emotional problems, may affect up to three quarters of CWE [1-2]. Cognitive impairment may affect one third of CWE [3]. These disorders are more common in CWE than in children without epilepsy [1,4].

In developed countries, psychopathological disorders and cognitive impairment are the subject of numerous publications. In sub-Saharan Africa, very few studies have been devoted to behavioral disorders [5-9] and/or to cognitive impairment [5-6,10-14] in CWE. These sub-Saharan Africa researches have been focused primarily on the relationship between these disorders and the clinical characteristics of epilepsy. Relationships between these disorders and socioeconomic aspects specifics to the sub-Saharan Africa are rarely addressed [6]. However, sociocultural and economic features may have an influence on both the epilepsy and the behavioral disorders and cognitive impairment.

To our knowledge, in the Democratic Republic of the Congo (DRC) as elsewhere in the rest of the Central Africa, no study has been conducted nor on behavioral problems nor on cognitive impairment in CWE. This article is the first of two studies that integrate socioeconomic conditions and the care pathway of the CWE in Kinshasa (capital of DRC). The goal of this first study was to identify clinical and socioeconomic factors associated with behavioral problems and cognitive impairment in CWE of Kinshasa.

2. Participants and methods

2.1. Site and period of the study

This research was conducted from April to May 2013 and from November to December 2013. The Centre de santé mentale Telema (CSMT), a mental health center of the primary level of the DRC's care system, was the site of the study. This health facility is devoted to cares of neurological and psychiatric diseases of outpatients. The CSMT works daily with 4 or 5 nurses who provide consultations based on guidelines. A neuropsychiatrist (in DRC the training in neurology and psychiatry are combined) is reachable at any time and, once a week,

he conducts consultations of patients referred by nurses. The CSMT has two EEG-videos. The EEG protocols are made by the neuropsychiatrist.

In terms of attendance and infrastructure, the CSMT is the most important of the scarce mental health centers of Kinshasa (capital of the DRC). This city has more than 6 million inhabitants with an average income per capita of 1 United States Dollar (USD) per day. Kinshasa has only one hospital that has both a department of neurology and a departement of psychiatry, the Centre Neuro-Psychopathologique de l'Université de Kinshasa (Neuro-Psychopathological Centre of the University of Kinshasa). Besides these two structures there are nearly a dozen of neurological-psychiatric private clinics with a capacity of 10 to 20 beds. The CSMT plays an important role in the field of mental health because it performs more than 30,000 consultations each year. Price of the consultation is accessible to almost every budget: 5 USD for the first consultation and 2.5 USD for the ulterior consultations. The EEG is performed at a cost of 20 USD for patients treated to CSMT and 30 USD for others. In comparison, in the other neurological-psychiatric clinics of Kinshasa the price of each consultation usually varies between 15 USD and 50 USD, and the EEG between 20 USD and 80 USD.

2.2. Participants

Children aged 6 to 17 years with active epilepsy were included by a convenience sampling on their arrival at the CSMT. Epilepsy was defined as the occurrence of at least two unprovoked epileptic seizures separated by an interval of at least 24 hours [15]. Epilepsy was active when at least one epileptic seizure had occurred in the last 5 years [15]. Epileptic seizures were classified according to the recommendations of the International League against Epilepsy [16]. The diagnosis of epilepsy was established on the basis of the clinical history told by an eyewitness of the seizures.

2.3. Assessment of behavioral problems

French version of the child behavior checklist (CBCL) for children aged 6 to 18 years was used to assess behavioral problems. This scale has been used in many different cultural contexts. It was especially used in a study in Uganda [17], a bordering country of DRC. As in that study (Bangirana et al., 2011), a team formed by two authors and two french-lingala interpreter-translators, have provided translation of the scale in Lingala, the main language spoken in Kinshasa. All members of this team have lingala and french as mother tongues.

The parents' version of the CBCL used includes 113 items that help to diagnose 8 behavioral problems: anxiety/depression, withdrawal/depression, somatic problems, social problems, problems of thought, attention problems, rules-breaking and aggressive behavior. These behavioral problems can be grouped in the internalized problems (anxiety/depression, withdrawal/depression and somatic complaints) and the externalized problems (rules-breaking

and aggressive behavior). Total problem behavior evaluates overall behavioral problems. The clinical threshold of the CBCL was chosen as the cut-off to define both the existence of a behavioral problem and of the different syndromic groupings.

2.4. Assessment of cognitive impairment

A psychologist blind of clinical data has assessed cognitive performance by using the short version (2 subtests) of the Wechsler Nonverbal (WNV) scale of ability. This test was designed, among others, for children of non-Western culture. The nonverbal nature of this test, the short duration of its administration and the results in our daily practice have guided its choice. A score below 70 in the total scale was considered as a cognitive impairment. Similarly, the inability to perform the tasks of WNV coupled with suggestive clinical observation of mental disability was considered as a cognitive impairment. Test was postponed for children who have a seizure the day before or the day of the test.

2.5. Neurological impairment

Pyramidal syndrome was synonym of a neurological impairment. Results of neurological examination of CWE that had presented a seizure the day of inclusion were not recorded. In this case, a further meeting was proposed.

2.6. Other variables

Sociodemographic variables had include age, gender, religion, father's age, mother's age, household size and an estimation of the amount of money (equivalent in USD) usually spent on the daily needs of the household in which the child lives most often.

Epilepsy variables had included age at the first crisis, duration of epilepsy, type of epileptic seizures, monthly epileptic seizure frequency (< 2 crises per month versus ≥ 2 crises per month) and type of antiepileptic treatments before the first consultation to the CSMT. Depending on the previous type of treatment, the CWE were divided in 2 groups: i) CWE not treated and ii) CWE treated with antiepileptic treatment either by antiepileptic drugs (AEDs) or by the traditional treatment (TT) whatever its form (herbal medicine, ritual scarification, etc.).

2.7. Missing data

Telephonic calls were conducted to relatives of CWE for incomplete sociodemographic and clinical data. For the CWE who had already consulted at the CSMT the missing data were looking for in the medical files. CWE who could not be examined (neurological examination) and/or tested (NVW) on the day of inclusion were invited to come back an ulterior day. In this case their transportation was refunded. The CSMT had authorized that these CWE be reviewed for free. Finally, missing data were not replaced and are indicated in the tables of results.

2.8. Ethical approval

The research protocol was approved by the Ethic Committee of the School of Public Health of the University of Kinshasa (approval number ESP/CE/018/13). Caregivers of CWE were informed about the research and gave their signed consent before the inclusion in the study.

2.9. Statistical analyses

Statistical analyzes were performed with SPSS 20 and Statistica 12. Normality of quantitative data was determined by the Shapiro test. Homoscedasticity was evaluated by Levene's test. The Grubbs test was used to treat outlier data. The groups were compared by the Fisher's exact test and the Student's t-test. Multivariate logistic regressions were performed by the forward stepwise based on to the likelihood ratio. The variables included in the models were those for which the p-value was less than 0.10 in the univariate analysis.

3. Results

3.1. General characteristics of CWE

Sociodemographic and clinical features of 104 CWE are presented in table 1. The average age was 12.0±3.2 years. Boys (n=61 or 58.7%) outnumbered girls (n=43 or 41.3%) with a boy/girl sex ratio of 1.4. These CWE lived in a household of 7.2±2.8 people. The daily expenditures of these households were 8.04±4.15 USD or 1.24±0.72 USD per person. All CWE lived in a christian household.

Table 1. General characteristics of CWE

Variable	n (%) or mean±SD
Age (year)	12.0±3.2
Girls	43 (41.3%)
Age of fathers (year), N=91	48.9±8.0
Age of mothers (year), N=97	41.5±7.0
Household size, N=102	7.2±2.8
Household daily expenses (USD), N=98	8.04±4.15
Daily expenses per person (USD), N=98	1.24±0.72
Age of onset (year)	6.9±4.1
Duration of epilepsy (year)	5.1±4.2
≥ 2 crisis/month, N=103	59 (57.3%)
Seizure types	
- Generalized	35 (33.6%)
- Focal	58 (55.8%)
- Epileptic spasms	3 (2.9%)
- Unclassified (due to lack of information)	8 (7.7%)
Prior antiepileptic treatment, N=102	
- None	45 (44.1%)
- AED	14 (13.7%)
- AED and Traditional	13 (12.8%)
- Traditional	30 (29.4%)
Neurological impairment, N=98	12 (12.2%)

AED : Antiepileptic Drug. USD: United States dollar.

3.2. Frequency of behavioral problems and cognitive impairment

At least one behavioral problem was present in 36 (34.6%) CWE (table 2). The different behavioral problems varied between 14% and 2% with a predominance of social problems (14.4%) and aggressive behavior (14.4%, Table 2) followed by depression/withdrawal (13.5%). Internalized, externalized and total behavioral problems were present, respectively, in 23%, 27% and 29% of CWE.

Table 2. Behavioral problems and cognitive impairment of CWE

Variables	n	%
Anxiety/depression	7	6.7
Withdrawal/depression	14	13.5
Somatic problems	5	4.8
Social problems	15	14.4
Problems of thought	8	7.7
Attention problems	2	1.9
Rules-breaking	2	1.9
Aggressive behavior	15	14.4
Internalized problems	24	23.1
Externalized problems	28	26.9
Total problems	30	28.8
Cognitive impairment, N=90	66	73.3

Of the 104 CWE included, 90 (86.5%) had undergone the WNV test. A CWE had refused to pass the second subtest. Thirteen others CWE had experienced epileptic seizures the day before or the day of the test and either they did not return for the test or they had presented others epileptic seizures the day before or the day of the appointment proposed. Of the 90 CWE who had undergone the WNV test, 18 were unable to respond to the test items and had clinical signs and/or clinical history of mental disability. At the threshold of the score of 70 on the total WNV scale or according to the clinical features, 66/90 (73.3%) CWE had a cognitive impairment.

3.3. Factors associated with behavioral problems and cognitive impairment

Fathers of CWE who had an internalized behavioral problem were older than the fathers of the other CWE (52.2±8.9 years versus 47.9±7.5 years; t=2.22; p=0.029; table 3).

CWE who had an externalized behavioral problem were younger than the others (10.8±3.1 years versus 12.4±3.1 years; t=-2.46; p=0.016). They had younger mothers (38.6±6.5 years

versus 42.7±6.9 years; t=-2.67; p=0.009) and had begun epilepsy earlier (5.5±3.5 years versus 7.4±4.2; t=-2.14; p=0.035) than children who had not externalized behavioral problem.

Table 3. Factors associated to behavioral problems and cognitive impairment

Variable	Yes	No	p
	n/N (%) or mean±SD	n/N (%) or mean±SD	
Internalized problems			
Age of father (year)	52.2±8,9	47.9±7.5	0.029
Externalized problems			
Age (year)	10.8±3.1	12.4±3.1	0.016
Age of mother (year)	38.6±6.5	42.7±6.9	0.009
Age of onset (year)	5.5±3.5	7.4±4.2	0.035
Total problems			
AED and/or TT	21/29 (72.4%)	36/73 (49.3%)	0.046
Cognitive impairment			
Girl	22/66 (33.3%)	15/24 (62.5%)	0.016
Household daily expenses (USD)	7.41±3.79	9.86±4.88	0.018
Daily expenses per person (USD)	1.15±0.67	1.54±0.84	0.031
Age of onset (year)	6.6±3.7	9.2±4.2	0.006
≥ 2 crisis/month	42/66 (63.6%)	6/23 (26.1%)	0.003

AED : Antiepileptic drug. TT : Traditional treatment. USD: United States dollar.

Total behavioral problems were more common in CWE who had previously received antiepileptic treatment than for the other CWE (21/29 or 72.4% versus 8/29 or 27.6%, p=0.046).

Cognitive impairment was more common in boys than in girls (44/66 or 66.7% versus 22/66 or 33.3%, p=0.016). Daily household expenditures of families of CWE with cognitive impairment were lower than those of other CWE (7.41±3.79 USD versus 9.86±4.88 USD; t=-2.42; p=0.018). Similarly, household expenditures per person in the household of these CWE were lower than those of CWE that did not exhibit cognitive impairment (1.15±0.67 USD versus 1.54±0.84 USD; t=-2.19; p=0.031). Compared to the others, CWE with cognitive impairment had begun epilepsy earlier (6.6±3.7 years versus 9.2±4.2 years; t=-2.8; p=0.006). Cognitive impairment was more common in CWE who had at least 2 seizures per month

compared to CWE with fewer than 2 seizures per month (42/66 or 63.6% versus 24/66 or 36.4%, p=0.003).

3.4. Multivariate analyzes

Logistic regression had retained only fathers' age as predictor variable for internalized behavioral problems (p=0.034) with a Nagelkerke pseudo-R² of 0.077 (table 4). The proportion of these problem was increasing with the age of the fathers.

Table 4. Multivariate analyzes

Variables	B	OR (IC à 95%)	p
Internalized problem			
Father's age	0.068	1.070 (1.050-1.139)	**0.034**
Externalized problem			
Mother's age	-0.104	0.901 (0.834-0.974)	**0.009**
Antiepileptic treatment (none =1)	1.141	3.130 (1.103-8.850)	**0.032**
Total problem			
Antiepileptic treatment (none =1)	1.055	2.872 (1.116-7.407)	**0.029**
Cognitive impairment			
Gender (female=1)	1.817	6.151 (1.462-25.883)	**0.013**
Household daily expenses	-0.163	0.849 (0.730-0.988)	**0.034**
Antiepileptic treatment (none =1)	1.491	4.444 (1.066-18.519)	**0.041**
Age of onset	-0.183	0.832 (0.698-0.993)	**0.042**
Crisiss/mounth (< 2 = 1)	1.811	6.115 (1.513-24.710)	**0.011**

The mathematical model was predicting that the externalized behavior problems was decreasing with the increase in the age of the mothers of the CWE (p=0.009). And this problem was three times more common in CWE who have previously received an antiepileptic treatment (p=0.032). This model has a Nagelkerke pseudo-R² of 0.171.

Logistic regression had retained only the type of antiepileptic treatment as a predictor variable of the existence of total behavioral problems (p=0.029) with a Nagelkerke pseudo-R² of 0.074. Total behavior problems were three times more common in CWE who previously have benefited of an antiepileptic therapy than in other CWE.

Cognitive impairment was six fold more often in boy than in girls (p=0.013). It was four fold more common in CWE who previously had received antiepileptic treatment than in those who had not received this treatment (p=0.041). The frequency of cognitive impairment was increasing with the decrease of age at first epileptic seizure (p=0.042). Also, it was increasing with the decrease of household expenditures (p=0.034). Cognitive impairment was six fold

more common in CWE with at least two seizures per month than in other CWE (p=0.011). The Nagelkerke pseudo-R² of this mathematical model with these five variables is 0.452.

4. Discussion

The aim of this study was to identify factors, including socioeconomic ones, associated with behavioral problems and cognitive impairment in CWE.

4.1. Frequency of behavioral problems

In sub-Saharan Africa researches on mental disorders in CWE are scare. To our knowledge, only 2 prevalence studies are available. These two studies conducted in rural areas of Tanzania and Kenya found high prevalences, respectively, 66% [8] and 49% [6]. Identical inclusion criteria between these two studies would probably have brought their results closer together. But, operational definitions are not sufficient to explain differences between these two studies and the present one. With the same definitions of active epilepsy this study has found a frequency almost half of the prevalence that Burton et al. [8] have observed. Differences of populations studied and of psychometric instruments used probably have played a role. Nevertheless, much of the difference between this study and the two others could be attributed to the types of studies. Burton's [8] and Kariuiki's [6] teams investigated whole populations in rural areas while this clinical study was performed in an urban city. Therefore the present study enlisted only subjects for whom families could pay for consultation and that their families knew that epilepsy is medical condition.

4.2. Factors associated with behavioral problems

In this study, frequency of internalized behavior problem was increasing with age of the fathers. Perhaps oldest fathers are less tolerant toward their children. Ulterior studies are needed to confirm this result and to understand its meaning.

As other authors [18], this study has observed that externalized behavioral problems were increasing with the decrease of age at the first epileptic seizure. Such association between behavioral problems and clinical features is related to intellectual disabilitie [1]. Logistic regression has showed that externalized behavior problems of CWE were increasing with the decrease of mothers' ages. Externalized behavior problems reflect the valuation by caregivers the inability of their CWE to observe social rules. But they can also reflect difficulties of relatives to enforce social rules. Oldest mothers could have more resources to manage their children's difficulties.

This study has found a link between behavioral problems, both externalized and total, and an antiepileptic treatment prior to the consultation at the CSMT. In non epileptic patients, Kinyanda et al. [19] and Abbo et al. [20] had found that type of treatment, biomedical and/or traditional, influences psychological issues. In the present study, behavioral problems were less frequent in CWE who had not received antiepileptic treatment prior to the consultation at

the CSMT. This paradoxical result agrees with the results of an anterior study carried out in the same center [21]. This study had shown that CWE who had received none antiepileptic treatment had better clinical features than CWE who had received it. The socioeconomic level [21-23], educational level [24] and cultural beliefs of parents [25-26] could explain differences between groups. Although their role is often mentioned, the results of this study did not show a link between socioeconomic factors and behavioral problems. It is possible that the general context of great poverty in which live the CWE has masked the influence of socio-economic level.

The different predictive models have shown a weak contribution of the factors studied in the explanation of the presence of behavioral problems. Further studies are needed to identify other factors associated with the presence of these problems. The role of antiepileptic drugs, particularly phenobarbital, which remains the main molecule used in countries with low incomes [10], must be evaluated.

4.3. Frequency of cognitive impairment

The results of this study have shown a great proportion of children with cognitive impairment. These results are very different from those observed in CWE in countries with high incomes. In sub-Saharan Africa, very few studies are available on cognitive impairment of CWE. These studies have revealed that 27% to 69% of CWE have cognitive impairment. These studies conducted in rural area can be distinguished by the countries where they were performed, the psychometric instruments used, the operational definitions of cases of epilepsy and the criteria for the inclusion of CWE. In Kenya, Munyoki et al. [12] had found a prevalence of 27% of cognitive impairment to children with active epilepsy (two or more unprovoked epileptic seizures with at least one crisis in the last 12 months). By evaluating clinically the ability of CWE to interact with investigators, these authors have probably underestimated the prevalence of cognitive impairment, particularly of CWE with mild cognitive impairment. Kariuki et al., again in Kenya, with the same inclusion criteria and definition of active epilepsy, had observed a prevalence of 43% [6] by using a validated test for Kenyan children and 23% [10] by evaluating clinically the ability of CWE to interact with investigators. For this 23%, Kariuki's team as Munyoki et al. [12], has probably underestimated the real prevalence of cognitive impairment. Elsewhere, a Tanzanian team, using the Goodenough-Harris Drawing Test, had found that 64% of CWE (two or more unprovoked epileptic seizures with at least one crisis in the last 5 years) have cognitive impairment [11]. After a follow-up of 3 years of these CWE this team had found 69% of cognitive impairment [5]. The frequency of cognitive impairment observed in the present study is close to these latters. Two reasons could explain the similarity of results. On the one hand, the operational definitions of the

latter studies are identical to those used in this study. On the other hand, tanzanian team [5,11] had used a test which has good concordance with the Wechsler group tests. Nevertheless, another reason may explain the high frequency of cognitive impairment observed in this study. This hospital-based study was conducted in a structure dedicated to the care of neurological and psychiatric disorders. It is highly likely that cognitive impairment was one of the reasons for which the CWE were taken to the CSMT.

The high frequency of cognitive impairment in CWE raises questions. Is this the consequence of the use a test that is not yet validated and/or calibrated in Congolese children that gives an incorrect picture of the real situation? Or would it be the consequence of a delayed and inapropriate care of epilepsy? Berg et al. [27] have shown that delay in diagnosis and management has an impact on the cognitive abilities of CWE.

4.4. Associated factors to cognitive impairment

Results of this study corroborate the literature by observing that age at first epileptic seizure, seizure frequency, and low socioeconomic status were associated with cognitive impairment [11,28]. As observed by Kariuki et al. [10] cognitive impairment was more common in boys than in girls. Numerous literature on child's cognitive shows that girl have better abilities than boys [29]. Factors that explain gender differences are numerous and complex [30].

This study has found that CWE who had not received previously an antiepileptic treatment had less cognitive impairment than other CWE. Various reasons could explain this result which again seems surprising. CWE who had received an antiepileptic treatment before the first consultation at the CSMT had a longer duration of epilepsy than other CWE [21]. Thus, compared to other CWE, this group could have more children with pharmacoresistance to antiepileptic drugs which is frequently associated with cognitive impairment [31]. In addition, families of CWE who previously had benefited of an antiepileptic treatment could have less financial resources than other CWE. Families of CWE who had previously benefited for an antiepileptic treatment, compared to others, could have more financial difficulties to treat properly their children. For the traditional treatment this is the subject of an abundant literature [25]. For CWE treated with antiepileptic drugs it is known that they receive inappropriate and non-preventive treatments [32]. These CWE are cared for in financially more affordable structures than hospitals but by a medical or a nursing staff untrained for the diagnosis and the treatment of epilepsy. Moreover, privious antiepileptic treatment is associated with high frequency of epileptic seizures, long duration of epilepsy and early onset of epileptic seizures [21]. In this study all these factors were associated with cognitive impairment. Other factors that influence the choice of the type of treatment, such as that

culture, beliefs and parent's educational attainment, may have had an influence, either directly or indirectly, on cognitive impairment.

4.5. Limitations

The main limits of this study is to be a hospital-based study and the use of psychometric tools not yet validated in Congolese children. Nevertheless, results echoes others studies performed elsewhere in sub-Saharan Africa.

5. Conclusion

The aim of this study was to identify clinical and socio-demographic factors associated with behavioral problems and with cognitive impairment in CWE. In multivariate analyzes behavioral problems were associated only with socioeconomic factors. Cognitive impairment was associated both with clinical characteristics of epilepsy and with socioeconomic factors. Further studies are needed to identify other specific factors to sub-Saharan Africa that could be associated with behavioral problems and/or with cognitive impairment.

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