Niger J Paediatr 2021; 48 (3):128 – 134

ORIGINAL

Ikhurionan Paul E
Okunola Olusola P
Ofovwe Gabriel E
Abhulimhen-Iyoha Blessing I

Determinants of cognitive impairment in children with epilepsy in Benin City

DOI:http://dx.doi.org/10.4314/njp.v48i3.3

Accepted: 9th May 2021

Ikhurionan Paul E (✉)
Department of Paediatrics,
Lily Hospitals Limited, Benin City, Nigeria
Email: paul_ehi@yahoo.com, paulikhurionan1@gmail.com

Okunola, Olusola P
Ofovwe, Gabriel E
Department of Child Health,
University of Benin Teaching Hospital, Benin City, Nigeria

Abhulimhen-Iyoha, Blessing I
Specialty Doctor in Paediatrics,
St. Mary's Hospital, Isle of Wight NHS Trust, Wessex, England

Abstract: *Background:* Seizures during the critical period of cerebral maturation in children may interfere with neuro-developmental changes in their brain. This may lead to widespread impairments in a child's neurological development and manifest as cognitive problems.
Objective: The aim of the study was to determine the prevalence of cognitive impairment as well as its determinants in children with epilepsy (CWE) attending the Child Neurology Clinic of the University of Benin Teaching Hospital, Benin City, Nigeria.
Subjects and Methods: One hundred and sixty CWE (comprising 80 treatment naive and 80 on treatment) aged 6-16 years were recruited for the study. Cognitive functions were evaluated using the Wechsler's intelligence scale for children (4th edition).
Results: Prevalence of cognitive impairment was 55%. Children with epilepsy on treatment had a higher prevalence of cognitive impairment (63.8%) compared to the newly diagnosed who were not on antiepileptic drug (AED) treatment (46.3%).Twenty-nine (18.1%) of the subjects had scores consistent with a diagnosis of intellectual disability (FSIQ<70). Age group ($p<0.01$), socio-economic class ($p<0.01$), age at onset of seizure ($p<0.01$) and type of seizures ($p<0.01$) were significantly associated with cognitive impairment in bivariate analysis. However, in a multivariable logistic regression model, only socio-economic class and age at onset of seizure remained significant.
Conclusion/Recommendation: The findings of this study highlight the need for evaluation of cognitive performance of CWE periodically, especially those on AED treatment. Early intervention programs to improve the cognitive function would be beneficial for the overall development of CWE. In addition, future longitudinal studies should shed more light on the influence of AED on cognitive performance of CWE.

Introduction

Cognitive impairment occurs more frequently in children with epilepsy (CWE) than those without.[1] It is believed that early seizures and prolonged abnormal neural activity during the critical period of cerebral maturation disrupt unique processes that occur in the brain and/or interfere with neuro-developmental trajectories.[2–4]Interruption of these processes may manifests as poor intelligence, learning disabilities, poor academic performance, behaviour problems, language stagnation or deterioration and other cognitive problems. [5–7]A prevalence of cognitive impairment ranging between 26.4% and 64.3% has been reported in with CWE [8,9,10,11,12] In Ibadan, South west Nigeria (2016), Lagunju and colleagues[8] in a study of 40 children newly diagnosed with idiopathic epilepsy reported global intellectual impairment in 47.5% of the subjects.

Although the cause of cognitive impairment in epilepsy is multifactorial; these factors appear to be inter-related in a complex way[1,9–11]. Epilepsy related factors including underlying aetiology of epilepsy, seizure type, frequency or control, age at onset of epilepsy, on-going subclinical epileptiform discharges, and the duration of epilepsy as well as use of antiepileptic drugs (AED) are among the important causes. Studies have described below average performance in children with symptomatic epilepsies compared to idiopathic epilepsies and those without epilepsy.[12,13]Similarly, the age at onset of disease seem to be one of the most important predictor of cognitive outcome.[12–15] Early onset seizures, especially before the fifth birthday have been identified as an increased risk for cognitive impairment.[13,16,17] Long duration of epilepsy,[11]generalised seizures[11,18] and greater seizure frequency[19] have also been described in several studies as predisposing factor for low intelligence quo-

tient (IQ) scores. To understand the exclusive effect of underlying seizure condition on cognitive function, idiopathic epilepsy not due to any brain lesion would give a better insight. The purpose of this study is to determine the prevalence and predictors of cognitive impairment in children with epilepsy seen in a tertiary institution in Nigeria.

Method

Participant

Subjects included children with epilepsy (CWE) who were recruited from the Child Neurology Clinic of the University of Benin Teaching Hospital (UBTH) between October 2017 and November 2018 and were classified based on the International League Against Epilepsy (ILAE) criteria. A researcher-administered proforma was used to obtain information including age at onset of epilepsy, frequency of seizures, type of seizures and treatment. Subjects were selected based on the following criteria: a) age 6 – 16 years, b) idiopathic epilepsy and c) absence of other known neurologic diagnosis. The socio -economic class of study subjects and controls were classified into the high, middle and low socio-economic class based on the fathers' profession and mothers' level of education according to the method described by Olusanya*et al*[20]

Procedures and assessment of Intelligence

The children were recruited during their clinic appointment. The aim and procedures involved in the study were explained in detail to them and/or their parents/ carers. After informed consent was obtained from the parents/carers, the children were scheduled for their psychological assessment. Ethical approval was obtained from the Ethics Committee of UBTH.

Intellectual function was assessed using the Wechsler's intelligence scale for children fourth edition (WISC IV). Scores for full scale intelligence quotient (FSIQ) were estimated from four index scores Verbal comprehension index, Perceptual reasoning index, Working memory index and Performance speed index. The study population was categorised according to their composite Full scale scores (FSIQ) for age into normal and impaired. The cut off FSIQ score was set at 85. Scores greater than or equal to 85 were categorised as normal while scores less than 85 were categorised as impaired.[21]Results obtained from the neuropsychological assessment of the children were communicated to them and their parents. Those who were found to have impaired intelligence were counselled along with the neuropsychologist and offered professional help and guide.

Statistical analysis

The collected data were organised, tabulated and statistically analysed using the International Business Machines Corporation (IBM) Statistical Package for the Social Sciences (SPSS) version 21.0 (SPSS for Window Inc; Chicago, LL, USA) Statistical Software. The performance on the WISC IV (FSIQ) was used to determine the prevalence of cognitive impairment. Level of cognitive function was dichotomised into normal (FSIQ $\geq$ 85) and impaired (FSIQ < 85). The associations between cognitive impairment and variables such as age group, sex, socioeconomic class, age at onset of seizure, type of seizure, etc., were investigated using Chi square statistics. A logistic regression analysis was used to determine the variables that were independently associated with cognitive impairment. Variables considered included age group, sex, socioeconomic status, age at seizure onset, duration of epilepsy, type of seizure, seizure frequency, duration of treatment and number of AEDs. Difference was considered to be statistically significant if the two-tailed p-value was less than 0.05.

Result

A total of 160 children with epilepsy (CWE) were enrolled into the study. Eighty of the subjects were already on antiepileptic drug (AED) treatment for at least 3 months while 80 were newly diagnosed, and not yet commenced on AED treatment.

Socio-demographic and clinical characteristics

The children's age ranged from 6 – 16 years with a mean age of 10.65 years (SD 2.60). The children were categorized into preadolescent (56), early adolescent (70) and mid adolescent (34). The male to female ratio was 1.03 and majority of the children (42.5%) were from the lower socioeconomic class.

Prevalence of cognitive impairment

The overall prevalence of impaired cognitive function was 55% (N = 88), of which 63.8% (51) of those on AED and 46.3% (37) of the newly diagnosed subjects not on AED had impaired cognition. The prevalence of mental retardation (FSIQ < 70) was 18.1% (29) in the subjects. Fourteen (17.5%) of the newly diagnosed children who were yet to commence AEDs had FSIQ results consistent with mental retardation and fifteen (18.8%) of those who were already on AEDs had FSIQ scores less than 70.Cognitive impairment was more prevalent in the early-adolescence group (44.3%), followed by themid-adolescence age-group (34.1%) and was least in the pre-adolescence group (21.6%). More female (51.1%) participants than males (48.9%) had impaired cognition. The prevalence of cognitive impairment was 29.4% among the upper social class, 65.9% among participants in the middle social class, while 81.3% of participants from the lower social class had cognitive impairment.

Clinical characteristics of subjects

The clinical characteristics (age at onset, duration of epilepsy, type of seizures, seizure frequency, number of antiepileptic drugs [AEDs] and duration of treatment) of the subjects are presented in Table 1. The frequencies of

cognitive impairment according to the age at seizure onset were 33.3% (onset before their first birthday); 64.5% (1-5years); 32.2% (5-10 years of age) and92.6% (onset after 10years of age). Ten (28.6%) of participants with focal seizure had cognitive impairment while 78 (62.4%) of children with generalised epilepsy had impaired cognition. Other distributions are highlighted in Table 2.

Bivariate Analysis

To identify if there was an association between cognitive impairment and the socioeconomic and clinical characteristics, bivariate analysis was done. Significant association was found between cognitive impairment and chronological age group (χ^2 = 25.24, p < 0.01), socio-economic class of participants (χ^2 = 33.469, p <0.01), age at seizure onset (χ^2 = 32.350, p <0.01) and type of seizures (χ^2 = 12.643, p < 0.01). There was however, no significant association with sex, duration of epilepsy and seizure frequency (Table 2).

Multivariate Logistic Regression (Table 3)

In multivariable analysis the only associations that remained significant were socioeconomic class and age at onset of seizure. Children from a high socioeconomic class and those with seizure onset before one year were less likely to have cognitive impairment compared to a lower socioeconomic class and seizure onset after five years respectively

Table 1: Clinical characteristics of children with epilepsy

Age at onset of epilepsy	Frequency (%)
< 1 year	12 (7.5)
1 – 5 years	62 (38.8)
5 – 10 years	59 (36.9)
> 10 years	27 (16.8)
Duration of illness	
< 2 years	74 (46.2)
2 – 5 years	30 (18.8)
> 5 years	56 (35.0)
Type of seizure	
Focal	35 (21.9)
Generalised	125 (78.1)
Frequency of seizures	
> 1/month	46 (28.8)
< 1/month	87 (54.4)
Yearly/ None in 2 years	27 (16.8)
No of AEDs	
Monotherapy	71 (88.8)
Polytherapy	9 (11.2)
Duration of treatment	
< 2 years	40 (50)
2-5 years	27 (33.8)
>5 years	13 (16.2)

Table 2: Association between cognitive function and seizure-related characteristics of subjects

Characteristics	Cognitive Function		χ^2	P
	Normal	Impaired		
Age at onset of epilepsy				
< 1 year	8 (11.1)	4 (4.5)	32.35	<0.01*†
1 - 5 years	22 (30.6)	40 (45.5)	0	
6 – 10 years	40 (55.5)	19 (21.6)		
>10 years	2 (2.8)	25 (28.4)		
Duration of Epilepsy				
< 2 years	38 (52.8)	36 (40.9)	2.248	0.33
2-5 years	12 (16.6)	18 (20.5)		
>5 years	22 (30.6)	34 (38.6)		
Type of seizure				
Focal	25 (34.7)	10 (11.4)	12.64	<0.01*
Generalised	47 (65.3)	78 (88.6)	3	
Seizure frequency				
Yearly/2 years freedom	12 (16.7)	15 (17.0)	1.421	0.49
≤ 1 seizure/ month	36 (50.0)	51 (58.0)		
> 1 seizure/ month	24 (33.3)	22 (25.0)		
Number of AEDs				
Monotherapy	28 (96.6)	43 (84.3)	2.773	0.10†
Polytherapy	1 (3.4)	8 (15.7)		
Duration of treatment				
< 2 years	13 (44.8)	27 (52.9)	5.422	0.14
2-5 years	11 (37.9)	16 (31.4)		
> 5 years	5 (17.3)	8 (15.7)		

*significant at p < 0.05; † = fishers exact two-tailed p value,

Table 3: Multivariate logistic regression analyses for factors associated with impaired cognition in children with epilepsy

	Univariate		Multivariate	
	p	OR(95% C.I. of OR)	p	OR(95% C.I. of OR)
Seizure type				
Focal	0.01	0.24(0.11-0.55)	0.13	0.28(0.05-1.48)
General		1.00		
Sex				
Male	0.62	0.86(0.46-1.60)	0.15	0.36(0.09-1.44)
Female		1.00		
Seizure frequency				
Yearly/2 year seizure freedom	0.52	1.36(0.53-3.54)	0.03	7.95(1.25-50.56)
≤ 1 seizure/month	0.24	1.55(0.76-3.17)	0.01	7.80(1.51-40.32)
> 1 seizure/month		1.00		
No of AED				
Monotherapy	0.13	0.19(0.02-1.62)	0.14	0.06(0.00-2.37)
Polytherapy		1.00		
Social Class				
High	0.01	0.10(0.04-0.24)	0.02*	0.06(0.01-0.35)
Middle	0.10	0.45(0.17-1.16)	0.05	0.15(0.02-0.98)
Low		1.00		
Duration of Illness				
< 2 years	0.17	0.61(0.30-1.24)	0.23	0.31(0.04-2.12)
2 - 5years	0.95	0.97(0.39-2.40)	0.87	0.85(0.12-5.84)
> 5 years		1.00		
Duration of Treatment				
< 2 years	0.17	0.61(0.30-1.24)	0.08	7.91(0.77-81.32)
2 - 5 years	0.95	0.97(0.39-2.40)	0.62	1.72(0.20-15.02)
> 5 years		1.00		
Age group				
6-9 years	<0.01	0.07(0.02-0.22)	0.20	0.36(0.07-1.74)
> 9 years		1.00		
Age at onset of epilepsy				
< 1 year	0.24	0.51(0.17-1.56)	0.03*	0.23(0.06-0.83)
1-5years	0.19	1.70(0.77-3.73)	0.40	1.47(0.06-3.56)
> 5 years		1.00		1.00

*significant at $p < 0.05$

Discussion

The present study assessed intellectual functioning in relatively large samples of children with idiopathic epilepsy. As many as one in two CWE (55%) had impaired intelligence from this study. This prevalence is comparable with the findings of Park *et al*[22] in Korea (54.7%), Cormack *et al*[15] in United Kingdom (57%) and Rantanen*et al*[13]in Finland (59%). The prevalence is however lower than that reported by Powell *et al*[23] (69%) and Burton *et al*[24](64%) both in Tanzania. These authors studied a mixed population of idiopathic and symptomatic epilepsies. It is well known that causes of symptomatic epilepsy could affect cognition independent of the seizures and hence account for higher prevalence found in such children. Hypoxic ischaemic encephalopathy (HIE) for instance can impair cognitive function independent of the epilepsy induced by the condition.[3] The study of a homogenous population provides a more realistic estimate of the prevalence of seizure related cognitive impairment than that of a heterogeneous group.

Eighteen percent of CWE had FSIQ scores consistent with a diagnosis of intellectual disability. The observation was similar to the findings by Rantenan and colleagues[13] (16.7%) among Finnish preschool-aged children with idiopathic epilepsy. The prevalence of intellectual disability was similar in those on treatment and those recently diagnosed with epilepsy not on treatment. This may suggest that serious cognitive impairment present at time of diagnosis remains static and unaffected by treatment or the course of the disease. It is also likely, that the effects of treatment on cognition are quite modest and not significant to cause serious cognitive problem. This observation might however, be better evaluated with a longitudinal study design in our locale. Jones *et al*[19] in a 2-year longitudinal study of 94 American children with epilepsy also suggested that there was no significant change in FSIQ of children with epilepsy over time.

When compared with each other, children on AED treatment appear to have a higher prevalence of cognitive impairment than those not on AED treatments. The effect of medication on cognitive functions in children with epilepsy remains controversial. Mandelbaum and Burack[25] reported that there was improvement in cognitive function of children with epilepsy following treat-

ment. Other authors, however, suggest that medications may cause cognitive deterioration through both dose-dependent and type-specific adverse effect.[13,25,26] The effect of treatment on cognitive performance would be better studied with a longitudinal or case-control study. The presence of association in this study however, provides a base for further evaluations.

In this study, socio-economic class was significantly associated with cognitive impairment in CWE. The frequency of cognitive impairment was higher in children from the lower socio-economic class compared to those from the upper classes. This finding is in concord with reports by other authors.[10,27]Low socioeconomic class is associated with economic and social deprivation.[28] This may result in limited cognitive stimulation and poor cognitive performance. Similarly, the poor cognitive performance of children from low socio-economic class may reflect the inability for children from low socio-economic class to afford care and treatment for epilepsy. Delay in seeking and commencing appropriate epilepsy treatment will result in progressive detrimental effect of seizure on cognition.

The relationship between seizure variables and cognitive functioning in children with epilepsy is not clearly understood. Some studies support a causal relationship and others do not. In our sample, age at seizure onset and type of seizure were associated with poor cognitive test performance in CWE. Younger age of onset was associated with poorer performance on cognitive tests. This observation compares with reports from the United Kingdom,[15] Finland,[13] Canada[29] and the United States of America[12]. Lopes *et al*[11] in Portugal and Lagunju *et al*[8] in Nigeria however found no significant association between age of seizure onset and cognitive impairment. It is possible the disparity in our finding might be related to the fact that this study had significantly higher proportion of children with onset of first seizure at younger ages compared to the studies by Lopes *et al* and Lagunju *et al*.

Children with generalised seizures had significantly higher prevalence of cognitive impairment compared to those with focal seizures in the bivariate analysis. Generalised seizures originate at some point and rapidly engage, bilaterally distributed cortical and sub-cortical networks. Focal seizures on the other hand have their effect localised to the locus of origin. It is predictable therefore, that the effect on cognition would be worse in children with generalised seizure compared to those with localised seizure. This is similar to the findings by Kernan *et al*[30] in a study involving children with complex partial seizure and childhood absence epilepsy. Lopes and colleagues[11] also showed that the type of epilepsy had significant effect on the cognitive performance of CWE in a study involving three common childhood epilepsy syndromes – frontal lobe epilepsy (FLE), childhood absence epilepsy (CAE) and benign epilepsy with centro-temporal spikes (BECTS).

The duration of epilepsy was not significantly associated with cognitive performance of children with epilepsy. This was unlike the study by Lordo *et al*[31]in the United States where longer lifetime seizures were shown to be significantly associated with impairment of cognitive function in children with epilepsy. It however accords with studies by Cormack *et al*[32]in London, United Kingdom; Rantanen *et al*[13] in Tampere, Finland and Lagunju *et al*[8] in Ibadan, Nigeria. With a median duration of epilepsy of 3 years and most of the subject with duration of epilepsy less than five years in this study, it is likely that the cumulative effect of seizures on cognition might not be apparent yet nor become significant. Lordo and colleagues had a significant proportion of children with epilepsy duration longer than five years in their cohort.

Age below one year at onset of seizures and higher socioeconomic class were negatively associated with cognitive impairment in CWE. The impact of seizure onset before one year on cognition is not fully understood. Younger age of seizure onset has been strongly linked with symptomatic cause and epileptic encephalopathy which are both associated with cognitive impairment.[12] However, some benign epilepsy with onset in infancy have good cognitive profile.[1]Similarly, some authors have suggested that good cognitive profile in children with seizure onset in infancy may be due to plasticity of the immature brain.[31,33]The number of subjects in this study with seizure onset in infancy was quite small and thus, it may be difficult to draw conclusions from our finding. Higher socioeconomic class may be protective against cognitive impairment in CWE because of associated better psycho-social stimulation and access to prompt and appropriate care in these children.

Conclusion

This study indicates that cognitive impairment is common in children with epilepsy and as much as one in two children with idiopathic epilepsy has cognitive impairment. Children on AEDs appear to have worse cognitive outcome than those newly diagnosed and yet to commence treatment. The age at onset of seizures and the socioeconomic class play significant roles in determining cognitive impairment in children with epilepsy.

Recommendation

It is therefore recommended that children with epilepsy be evaluated for cognitive impairment periodically considering the high prevalence of cognitive impairment in them. It may be necessary to have more frequent assessment in children on treatment.

Conflict of interest: None
Funding: None

References

1. Kim E-H, Ko T-S. Cognitive impairment in childhood onset epilepsy: up-to-date information about its causes. *Korean J Pediatr. 2016;59(4):155-164. doi:10.3345/kjp.2016.59.4.155*
2. You SJ. Cognitive function of idiopathic childhood epilepsy. *Korean J Pediatr. 2012;55 (5):159-163. doi:10.3345/ kjp.2012.55.5.159*
3. Hermann B, Seidenberg M. Epilepsy and cognition. *Epilepsy Curr. 2008;7(1):1-6. doi:10.1111/j.1535-7511.2007.00151.x*
4. Hermann BP, Jones JE, Sheth R, et al. Growing up with epilepsy: a two-year investigation of cognitive development in children with new onset epilepsy. *Epilepsia. 2008;49 (11):1847-1858. doi:10.1111/ j.1528-1167.2008.01735.x*
5. Bompori E. b, Niakas D., Nakou I., Siamopoulou-Mavridou A., Tzoufi MS. Comparative study of the health-related quality of life of children with epilepsy and their parents. *Epilepsy Behav. 2014;41:11-17. doi:10.1016/ j.yebeh.2014.09.009*
6. Reilly C, Atkinson P, Das KB, et al. Academic achievement in school-aged children with active epilepsy: A population-based study. *Epilepsia. 2014;55 (12):1910-1917. doi:10.1111/ epi.12826*
7. Fastenau PS, Jianzhao Shen, Dunn DW, Austin JK. Academic underachievement among children with epilepsy: proportion exceeding psychometric criteria for learning disability and associated risk factors. *J Learn Disabil. 2008;41 (3):195-207. doi:10.1177/002221940831754 8*
8. Lagunju IA, Adeniyi YC, Olukolade G. Cognitive function in Nigerian children with newly diagnosed epilepsy: A preliminary report. *Pan Afr Med J. 2016;24. doi:10.11604/ pamj.2016.24.113.8995*
9. Bourgeois BF. Antiepileptic drugs, learning, and behavior in childhood epilepsy. *Epilepsia. 1998;39(9):913-921. http:// www.ncbi.nlm.nih.gov/ pubmed/9738670*
10. Melbourne Chambers R, Morrison-Levy N, Chang S, Tapper J, Walker S, Tulloch-Reid M. Cognition, academic achievement, and epilepsy in school-age children: A case-control study in a developing country. *Epilepsy Behav. 2014;33:39-44. doi:10.1016/ j.yebeh.2014.02.002*
11. Lopes AF, Simões MR, Monteiro JP, et al. Intellectual functioning in children with epilepsy: Frontal lobe epilepsy, childhood absence epilepsy and benign epilepsy with centro-temporal spikes. *Seizure. 2013;22(10):886-892. doi:10.1016/ j.seizure.2013.08.002*
12. Berg AT, Langfitt JT, Testa FM, et al. Global cognitive function in children with epilepsy: A community-based study. *Epilepsia. 2008;49 (4):608-614. doi:10.1111/ j.1528-1167.2007.01461.x*
13. Rantanen K, Eriksson K, Nieminen P. Cognitive impairment in preschool children with epilepsy. *Epilepsia. 2011;52 (8):1499-1505. doi:10.1111/ j.1528-1167.2011.03092.x*
14. Smith ML. Epilepsy and cognition. In: Prasher V, Kerr M, eds. *Epilepsy and Intellectual Disabilities. Springer Science + Business Media; 2008:193-208. doi:10.1007/978-1-84800-259-3_12*
15. Cormack F, Helen Cross J, Isaacs E, et al. The development of intellectual abilities in pediatric temporal lobe epilepsy. *Epilepsia. 2007;48 (1):201-204. doi:10.1111/ j.1528-1167.2006.00904.x*
16. Cormack F. Early-onset epilepsy, cognition, and behaviour: Continuity and challenge. *Dev Med Child Neurol. 2013;55(10):963-964. doi:10.1111/dmcn.12185*
17. Lagae L. Cognitive side effects of anti-epileptic drugs. The relevance in childhood epilepsy. *Seizure. 2006;15(4). doi:10.1016/ j.seizure.2006.02.013*
18. Ibekwe RC, Ojinnaka NC, Iloeje SO. Factors influencing the academic performance of school children with epilepsy. *J Trop Pediatr. 2007;53 (5):338-343. doi:10.1093/ tropej/fmm034*
19. Jones JE, Siddarth P, Gurbani S, Shields WD, Caplan R. Cognition, academic achievement, language, and psychopathology in pediatric chronic epilepsy: Short-term outcomes. *Epilepsy Behav. 2010;18(3):211-217. doi:10.1016/ j.yebeh.2010.03.015*
20. Olusanya O, Okpere E, Ezimokhai M. The Importance of Social Class in Voluntary Fertility Control in a Developing Country. *West Afr J Med. 1985;2:205-212.*
21. Wechsler D. Administration and Scoring Manual for the Wechsler Intelligence Scale for Children (4th Ed.). The Psychological Corporation.; 2003.
22. Park J, Yum M, Choi H, Ko T, Kim HW. Cognitive function in childhood epilepsy-a single center study. *Epilepsia*. 2012;2:169. doi:http:// dx.doi.org/10.1111/j.1528-1167.2012.03677.x
23. Powell K, Walker RW, Rogathe J, et al. Cognition and behavior in a prevalent cohort of children with epilepsy in rural northern Tanzania: A three-year follow-up study. *Epilepsy Behav. 2015;51:117-123. doi:10.1016/ j.yebeh.2015.06.034*
24. Burton K, Rogathe J, Whittaker RG, et al. Comorbidity of epilepsy in Tanzanian children: a community-based case-control study. *Seizure. 2012;21(3):169-174. doi:10.1016/ j.seizure.2011.10.011*

25. Mandelbaum DE, Burack GD. The effect of seizure type and medication on cognitive and behavioral functioning in children with idiopathic epilepsy. *Dev Med Child Neurol. 1997;39(11):731-735.* http://www.ncbi.nlm.nih.gov/pubmed/9393886
26. Sherman EMS, Brooks BL, Fay-mcclymont TB, Macallister WS. Detecting epilepsy-related cognitive problems in clinically referred children with epilepsy : Is the WISC-IV a useful tool ? *Epilepsia. 2012;53(6):1060-1066. doi:10.1111/j.1528-1167.2012.03493.x*
27. Bioh R, Durowaa R, Kumasenu B, Asiedu BY. Cognitive and Psychological Deficits in Children with Epilepsy at the Korle-Bu Teaching Hospital in Ghana. *Int Neuropsychiatr Dis J. 2018;12(1):1-9. doi:10.9734/indj/2018/44437*
28. Ahmed GK, Darwish AM, Khalifa H, Khashbah MA. Comparison of cognitive function, socioeconomic level, and the health-related quality of life between epileptic patients with attention deficit hyperactivity disorder and without. *Middle East Curr Psychiatry. 2020;27 (1). doi:10.1186/s43045-020-00054-9*
29. Smith M Lou, Elliott IM, Lach L. Cognitive Skills in Children with Intractable Epilepsy: Comparison of Surgical and Nonsurgical Candidates. *Epilepsia. 2002;43(6):631-637. doi:10.1046/j.1528-1157.2002.26101.x*
30. Kernan CL, Asarnow R, Siddarth P, et al. Neurocognitive profiles in children with epilepsy. *Epilepsia. 2012;53 (12):2156-2163. doi:10.1111/j.1528-1167.2012.03706.x*
31. Lordo DN, Van Patten R, Sudikoff EL, Harker L. Seizure-related variables are predictive of attention and memory in children with epilepsy. *Epilepsy Behav. 2017;73:36-41. doi:10.1016/j.yebeh.2017.05.017*
32. Cormack F, Cross JH, Isaacs E, et al. The development of intellectual abilities in pediatric temporal lobe epilepsy. *Epilepsia. 2007;48(1):201-204. doi:10.1111/j.1528-1167.2006.00904.x*
33. Gleissner U, Sassen R, Schramm J, Elger CE, Helmstaedter C. Greater functional recovery after temporal lobe epilepsy surgery in children. *Brain. 2005;128(12):2822-2829. doi:10.1093/brain/awh597*