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Psychomotor function in children with epilepsy seen at a tertiary hospital in southern Nigeria: does treatment with anti-epileptic drugs have any effect?

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Abstract

Background: Psychomotor slowing is more commonly reported in children with epilepsy (CWE) compared to healthy controls. The effect of anti-epileptic drug (AED) treatment on psychomotor abilities of CWE remains controversial. In Nigeria, psychomotor abilities of CWE are scarcely investigated and the impact of AEDs is not known. The present study sought to assess psychomotor performance of CWE compared to healthy controls and to determine any association with seizure characteristics and treatment.

Method: A comparative cross-sectional study involving 160 children with idiopathic epilepsy and 80 controls aged 6–16 years. Psychomotor function was assessed using reaction times and tapping task of the Iron psychology computerised test battery. The criterion for impairment was fixed at two standard deviations (SD) worse than the mean of age-matched controls. The relationship between seizure variables and psychomotor function was assess with the one-way analysis of variance (ANOVA).

Result: Fifty-nine (36.9%) CWE had impaired auditory reaction, 50 (31.3%) with impaired visual reaction and 11 (6.9%) had fine motor control impairment. There was no significant difference in psychomotor performance between CWE on AED and the newly diagnosed counterparts yet to start AED treatment (auditory reaction time—$p = 0.226$; visual reaction time—$p = 0.349$; tapping task—$p = 0.818$). AED treatment duration over 5 years was associated with better auditory reaction time ($F = 4.631$, $p = 0.034$) in CWE. Also, seizure onset before 5 years of age was associated with slower auditory reaction ($F = 4.912$, $p = 0.028$) and verbal reaction ($F = 14.560$, $p < 0.001$).

Conclusion: Nigerian CWE perform less favourably on tests of psychomotor function than healthy controls. The performance of children on AED is not significantly different from those not on AED. Longer duration of AED treatment may result in psychomotor improvement in CWE. CWE should be closely monitored for psychomotor slowness so that deficits can be identified and appropriate interventions instituted.

Keywords: Psychomotor function, Children with epilepsy, CWE, Auditory reaction, Visual reaction, Hand dexterity, Tapping task, Anti-epileptic drug, AED, Cognition

Background

Psychomotor ability refers to the capacity to perform physical motor movements with precision, coordination and strength [1]. They involve a combination of precise stimulus perception, processing and motor response. In

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a fast-paced world where academic and non-academic activities are time bound, limitation of psychomotor functions have far-reaching effect in children. Impaired psychomotor function can impact negatively on learning, school performance and psychosocial interactions [2]. Murrihy et al. [3] in a study of 133 children aged 8–12 years, showed that psychomotor ability significantly affected learning outcomes—reading and mathematics achievements, through its effect on short-term memory.

Psychomotor slowing is more commonly reported in children with epilepsy (CWE) compared to healthy controls [4–6]. Boelen et al. [4] in Netherland (2007) found statistically significant slowing in newly diagnosed children with idiopathic epilepsy compared to healthy controls using the Iron Psychology computerised test battery. In terms of magnitude of the effects, the difference in prevalence of psychomotor slowing between CWE and healthy controls was 12% for auditory reaction and 18% for visual reaction [4]. The prevalence of impaired hand dexterity, however, was comparable with controls. Reijs et al. [5] also found psychomotor impairment in 35.8% of children with cryptogenic lateralisation related epilepsy (CLRE) compared to 21.9% of healthy controls using the Movement Assessment Battery for Children (mABC). Other authors have reported significantly slower reaction times in CWE compared to healthy controls [6]. In spite of reported high prevalence, psychomotor slowing is usually understudied and undiagnosed in CWE [7]. Its impact on the quality of life and contribution to their morbidity is therefore, not fully understood.

The effect of anti-epileptic drug (AED) treatment on psychomotor abilities of CWE remains controversial. It is generally believed that psychomotor speed and fine motor coordination is the domain most commonly affected by AEDs [2, 8]. Although this position has been supported by studies involving adults with epilepsy [9, 10], the findings in children have been unconvincing. For example, Rathouz and colleagues [6] in a 6-year longitudinal study of 69 CWE found that psychomotor speed abnormality detected at or near the time of epilepsy diagnosis largely remained unchanged without evidence of progressive worsening or recovery. Similar conclusion was made by Garcia-Ramos and colleagues [7] in a 2-year longitudinal study involving 78 American children with idiopathic epilepsy. The observations suggest that AEDs might not have significant modifying effect on psychomotor performance of CWE. This view challenges the generally held opinion that the domain of cognition most commonly affected by AED was psychomotor speed. Perhaps with more research, better insight will be gained into the effect of AED on psychomotor function in CWE.

In developing countries like Nigeria, psychomotor abilities of CWE are scarcely investigated. A few works on cognitive performance in Nigerian CWE have focused on intelligence [11] and academic performance [12, 13]. Furthermore, unrecognised psychomotor problems in CWE may negatively impact on their capacity to engage in timed task and ultimately their self-esteem. Early recognition and management is thus mandatory in clinical practice. The present study therefore sought to assess psychomotor performance of CWE compared to healthy controls. We hypothesised the following: (a) CWE will perform more slowly than healthy control in all tasks; (b) impairment would be worse in CWE on AED treatment than the newly diagnosed group.

Methods

Study design

We conducted a comparative cross-sectional study of children with epilepsy (CWE) recruited from the Paediatric Neurology Clinic and General Practice Clinic of a tertiary hospital in southern Nigeria. A total of 240 research participants were recruited for the study including 80 newly diagnosed CWE, 80 CWE on anti-epileptic drugs (AEDs) and 80 healthy controls. Selection criteria for CWE include (a) chronological age 6–16 years; (b) idiopathic epilepsy; (c) no other neurologic or psychiatric disorder. Idiopathic epilepsy was defined as epilepsy with no underlying cause other than a possible hereditary predisposition [14]. The controls were children without epilepsy attending the general practice clinic for medical examinations for school entry and placement as well as those presenting for follow-up visit after brief illnesses within the study period. Selection criteria for controls included: (a) chronological age 6–16 years, (b) no current neurologic or psychiatric disorder. 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. [15] Patients were examined by a qualified medical doctor who documented all the findings.

Assessment of psychomotor function

The measures for psychomotor speed were assessed with the Iron Psychology (Fepsy) computerised test battery. Participants completed three motor tasks including auditory reaction time, visual reaction time and tapping task. Simple reaction times were measured using auditory stimuli (loud 800-Hz tone) and visual stimuli (white square on the screen) presented at random intervals by the computer. The test score is measured in milliseconds. The time to complete each task was recorded and used as the dependent variable in all analyses. The finger-tapping test (a measure of hand dexterity and fine motor control) required the participant to tap as fast as possible using

the index finger of the dominant hand. The participant was given five consecutive trials. The average number of tapping in a 10-s trial was recorded.

Data analysis

The collected data were organised, tabulated and statistically analysed using the Statistical Package for Social Sciences (Version 21.0; IBM SPSS statistics, Chicago, IL, 2011). The auditory reaction times, visual reaction times and the average number of tapping were summarised as mean ± standard deviation (SD) and compared using the Student's *t*-test. The times were further dichotomised into impaired and normal. The criterion for impairment on the tasks was fixed at two standard deviations (SD) worse than the mean of age-matched controls. One-way analysis of variance (ANOVA) was used to assess the relationship between seizure variables (age at seizure onset, duration of epilepsy, type of seizure and seizure frequency) treatment variables (duration of treatment and number of AEDs) and psychomotor function. Chi-squared tests were used to analyse differences in prevalence of impairment. Differences were considered to be statistically significant if their two-tailed *p*-values were less than 0.05.

Table 1 Demographic and clinical characteristics of study population

	CWE	Controls
Age (mean ± SD)	10.65 ± 2.90	11.01 ± 2.61
Sex		
Male	81 (50.6%)	41 (51.3)
Female	79 (49.4%)	39 (48.7)
Socio-economic class		
Upper	68 (42.5)	62 (77.5)
Middle	44 (27.5)	13 (16.3)
Lower	48 (30.0)	5 (6.2)
Age of epilepsy onset		
< 5 years	74 (46.3)	
≥ 5 years	86 (55.7)	
Type of seizure		
Focal	35 (21.9)	
Generalised	125 (78.1)	
Duration of epilepsy		
< 5 years	105 (65.6)	
≥ 5 years	55 (34.4)	
Seizure frequency		
> 1/month	46 (28.8)	
< 1/month	87 (54.4)	
Yearly/none in 2 years	27 (16.8)	
Duration of treatment		
< 5 years	67 (83.8)	
> 5 years	13 (16.2)	
Number of AEDs		
Monotherapy	71 (88.8)	
Polytherapy	9 (11.2)	

Results

The demographic and clinical characteristics of the CWE and controls are presented in Table 1. CWE had slower auditory and visual reaction times than control, but significantly better hand dexterity than controls (Table 2). CWE on AED did not significantly differ from the newly diagnosed counterparts yet to start AED treatment (Table 3). Fifty-nine (36.9%) CWE had impaired auditory reaction, 50 (31.3%) with impaired visual reaction and 11 (6.9%) had fine motor control impairment. Among the controls, four children (5.0%) had auditory reaction impairment; three (3.8%) had visual reaction impairment and eight (10%) had impaired tapping task (Fig. 1). The prevalence of psychomotor impairment in CWE was significantly higher than the controls on test of auditory reaction ($\chi^2 = 33.900$; $p < 0.001$) and visual reaction ($\chi^2 = 23.441$; $p < 0.001$), but not on fine motor control (finger tapping task) function ($\chi^2 = 0.08$; $p = 0.779$). Longer duration of treatment [F (1,156) 4.631, $p = 0.0341$] was only significantly associated with better auditory reaction time task. Earlier age at onset of seizure was significantly associated with poorer auditory reaction [F (1,156) 4.912, $p = 0.028$] and verbal reaction [F (1,156) 14.56, $p < 0.001$] (Table 4).

Table 2 Psychomotor performance of children with epilepsy and controls

Test (dominant hand)	CWE	Controls	*F*	*p*
Auditory reaction time[α]	493.3 (156.5)	393.0 (80.6)	28.983	< 0.001*
Visual reaction time[α]	474.0 (143.7)	364.1 (96.5)	38.118	< 0.001*
Tapping task[β]	49.2 (8.0)	45.2 (19.4)	4.987	0.026*

*Significant at $p < 0.05$; α—lower values indicate better performance; β—higher values indicate better performance

Table 3 Psychomotor function in CWE on AED treatment and CWE yet to commence treatment

Test (dominant hand)	AED treatment	No treatment	*F*	*p*
Auditory reaction time[α]	478 (138)	508 (173)	1.476	0.226
Visual reaction time[α]	463 (136)	484 (151)	0.882	0.349
Tapping task[β]	49.1 (9.2)	49.3 (6.7)	0.053	0.818

α—lower values indicate better performance; β—higher values indicate better performance

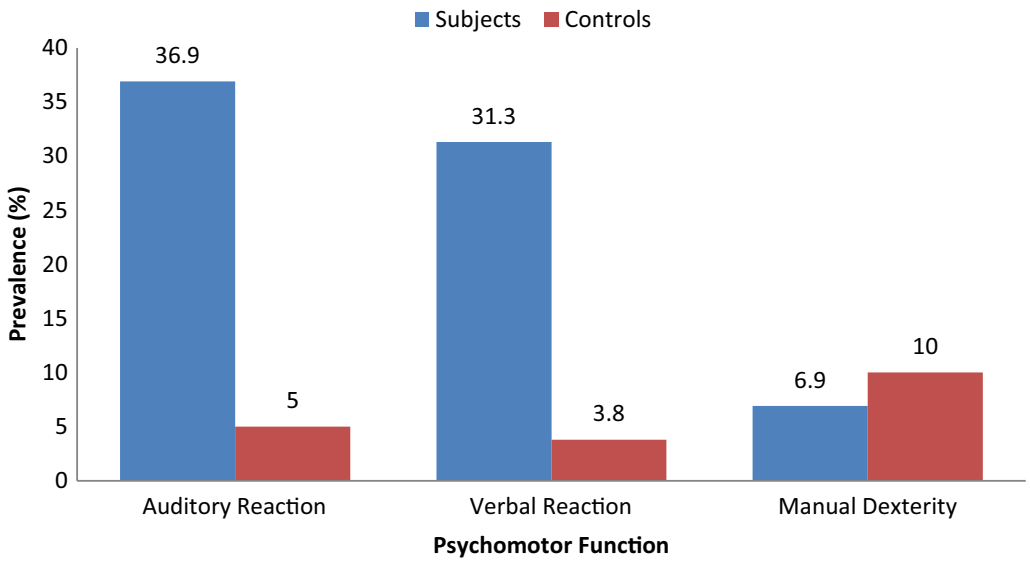

Fig. 1 Prevalence of psychomotor function impairment in study population

Table 4 Association of psychomotor test scores with seizure and treatment characteristics

Characteristics	Auditory reaction[α]			Visual reaction[α]			Tapping Task[β]		
	Duration (SD)	*F*	*p*	Duration (SD)	*F*	*p*	Duration (SD)	*F*	*p*
Age at epilepsy onset									
< 5 years	523 (171)	4.912	0.028*	519 (159)	14.560	< 0.001*	48.49	1.028	0.312
≥ 5 years	469 (139)			435 (117)			49.78		
Duration of epilepsy									
≤ 5 years	501 (152)	0.790	0.375	483 (149)	1.195	0.276	48.54	2.031	0.156
> 5 years	478 (164)			456 (132)			50.44		
Type of seizure									
Focal	536 (220)	3.401	0.067	472 (30)	0.007	0.932	49.67	0.157	0.693
Generalised	481 (132)			475 (12)			49.06		
Seizure frequency									
0–1 in 2 years	481 (126)	0.098	0.906	440 (117)	1.026	0.361	50.99	1.367	0.258
≤ 1 seizure/month	495 (177)			476 (157)			49.36		
> 1 seizure/month	495 (130)			489 (129)			47.83		
Duration of treatment									
< 5 years	497 (144)	4.631	0.0341*	477 (145)	2.335	0.131	47.96	3.244	0.076
≥ 5 years	424 (97)			424 (99)			52.10		
Number of AEDs									
Monotherapy	478 (142)	0.002	0.960	460 (137)	0.305	0.583	49.01	0.010	0.922
Polytherapy	480 (85)			487 (125)			49.33		

*Significant at $p < 0.05$; α—lower values indicate better performance; β—higher values indicate better performance

Discussion

Our findings indicate that children with epilepsy had slower auditory and visual reaction times, but significantly better finger tapping speed than controls. There was no significant difference in psychomotor performance between CWE on AED and the newly diagnosed counterparts yet to start AED treatment. Duration of treatment beyond 5 years was associated with better auditory reaction time. Seizure onset before 5 years of

age was associated with poor auditory reaction and verbal reaction.

In the current study, CWE performed significantly worse than controls on measures of auditory and visual reaction. This finding agrees with the conclusion of Rathouz et al. [6] and Boelen et al. [4] showing longer reaction time in CWE, compared to controls. Slower reaction in CWE may be attributed to general cerebral inhibition and disruption of neural transmission by the epileptic seizure as well as the effect of anti-epileptic medications. Psychomotor impairment has also been demonstrated in newly diagnosed children around or before onset of seizure [7]. Thus psychomotor slowing in CWE might be a marker for abnormal brain development rather than the effect of seizures themselves.

An interesting observation in the present study was that finger tapping speed, a measure of hand dexterity and fine motor control, was higher in CWE compared to controls. Boelen et al. [4] also observed better fine motor control among CWE compared with control group. They, however, considered it a chance effect. It is likely that the better performance by CWE is behavioural. Tanner and colleagues have shown that intentional sub-optimal performance of tapping task can be simulated by persons motivated to perform less than optimally [16]. It may also be true that people who were more motivated to perform optimally will tap faster than those who were not. Children with epilepsy might have been more enthusiastic about the test being a part of their management than were controls. Henkin et al. [17] however, reported worse finger tapping in CWE compared to healthy controls. The reason for the difference in the current study is not clear. This observation, however, may need further investigation and possibly a prospective approach.

Anti-epileptic drug treatment may not significantly impair psychomotor function as previously suggested [8, 18–21]. In the present study, the performance of children on AED was not significantly different from the result of their counterparts who were recently diagnosed and not on AED treatment on all tests. This observation is in agreement with the findings of Boelen et al. [4] among 87 Dutch children with uncomplicated epilepsy. They observed that AEDs drug load (defined as the ratio of prescribed daily dose to defined daily dose) did not significantly affect psychomotor function in CWE. Similarly, Rathouz et al. [6] in a 6-year prospective study of 69 children with epilepsy reported that the psychomotor impairment noted at the onset of seizures did not change with treatment at 6 years follow-up. Some studies assessing psychomotor performance of CWE following discontinuation of AEDs have reported significant improvement with re-testing [22, 23]. It is probable that the improvement in psychomotor performance was due to test–retest advantage (practice effect) rather than reversal of AED-induced psychomotor slowing.

In the current study, the duration of treatment appears to be associated with improved psychomotor performance. Children who have been on AED treatment for more than 5 years had a better profile for auditory reaction than those with lesser duration of treatment. Similar observations were made with respect to visual reaction and fine motor control although both were not statistically significant. Studies on the effect of AED treatment on psychomotor performance have been inconclusive. A few authors have however, reported improvement in psychomotor abilities following commencement of AED treatment [2, 7]. It is likely, that the improvement of psychomotor function is as a result of reduced disturbance from recurrent seizures.

In the present study, psychomotor slowing was more prominent in children whose seizure started before their fifth birthday compared to those whose seizure onset was later. While this is plausible, most studies of psychomotor function in children have not considered the influence of age of onset on psychomotor performance. Younger age at onset of epilepsy has been associated with poorer cognitive function in CWE [8, 24–26]. Epileptiform discharges at young age could disrupt brain circuits' formation and negatively affect neurodevelopmental processes including synaptogenesis and apoptosis [26]. These interferences would ultimately result in slow impulse generation and transmission and commonly manifest as slow reaction times. Similarly, earlier seizure may suggest more severe neuronal injury and thus greater functional abnormality.

Conclusion

In conclusion, psychomotor slowing is common in Nigerian CWE. Children with epilepsy perform less favourably on tests of reaction time than healthy controls. The performance of children on AED is not significantly different from those not on AED. On the contrary, the present study suggests that AED treatment might improve psychomotor impairment in CWE. Care givers should monitor CWE closely for psychomotor slowness and other motor impairments. Early psychomotor assessment should be done so that deficits can be identified and appropriate interventions instituted.

Limitation of study

In terms of study limitations, the study utilised a hospital-based sample, thus, selection biases may have affected study inclusion and limit the generalisability of results to all children with epilepsy. Secondly, the use of cross-sectional design limits its ability to establish causality.

However, the results of this study provide evidence that psychomotor problems are common in CWE.

Abbreviations
CWE: Children with epilepsy; AED: Anti-epileptic drug; Fepsy: Iron psychology computerised test battery; CLRE: Cryptogenic lateralisation related epilepsy; mABC: Movement assessment battery for children; SD: Standard deviation; ANOVA: Analysis of variance.

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Authors' contributions
PEI conceptualised the work and designed the study. He also participated in data collection, data analysis, interpretation of data as well as drafting of the article. He approved the final the version to be published. OPO—study design, data collection, interpretation of data, revision of draft critically for important intellectual content; and final approval of the version to be published. BIA—study design, data analysis and interpretation, drafting the article and final approval of the version to be published. GEO—conceptualisation and study design, interpretation of data, revision of draft critically for important intellectual content and final approval of the version to be published. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The research was reviewed and approved by the University of Benin Teaching Hospital ethics and research committee (protocol number: ADM/E22/A/VOL.1457). Signed informed consent was obtained from participants' parents after the nature and purpose of the test was explained to their understanding. Participation was completely voluntary and participant could withdraw at any time.

Consent for publication
Not applicable.

Competing interest
The authors declare that they have no competing interests.

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