Table 3: Mean cognitive error scores of patients by domains

	Mean cognitive error scores by domains (*N*=56)						Total error score	Total correct score
	Year	Month	Time	Count 20-1	Name months (December-January)	Memory (recall)		
At baseline	0.9	1.1	0.1	1.6	2.6	4.6	11 (SEM 1.7)	17 (SEM 1.7)
At 6 weeks	0.6	0.4	0.1	0.9	1.6	3.2	6.7 (SEM 1.6)	21.3 (SEM 1.6)
At 12 weeks	0.4	0.4	0.0	0.7	1.1	2.9	5.4 (SEM 1.5)	22.6 (SEM 1.6)
F value	31.4	4.5	NA	16.2	7.2	9.0	29.8	29.8
P	<0.001*	<0.01*		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

NA: Not applicable, SEM: Standard error of the mean, **P* values significant (<0.05)

Table 4: Mean cognitive correct scores by patient's category

Time frame	Mean cognitive total correct scores			
	PWE (*n*=28)	Dementia (*n*=28)	*t*	*P* values
Baseline	20.9 (SD 6.4; range 9-28)	13.1 (SD 9.3; range 0-28)	3.6	<0.001*
At 6 weeks	25.4 (SD 3.5; range 18-28)	17.2 (SD 9.7; range 2-28)	4.2	<0.001*
At 12 weeks	26.9 (SD 2.6; range 20-28)	18.3 (SD 8.9; range 6-28)	4.9	<0.001*
F	29.3	7.7		
P	<0.001	0.12		

SD: Standard deviation, PWE: Patients with epilepsy, Student *t*-test analysis yielded *t* values, *Significant *P* values (<0.05)

Despite the improvement in the cognitive performances of patients with dementia observed with 12 weeks therapy of vinpocetine, this did not reach statistical significance ($P = 0.12$; 95% CI: 0.8-11.2). On the other hand, however, the PWE showed sustained statistically significant improvement in cognitive performance during the 12 week therapy ($P < 0.001$; 95% CI: 3.1-8.9). The mean total error scores of the PWE gradually declined from the baseline score of 7.1 (SD: 6.4) (95% CI: 4.6-9.6); range 0-19 to 2.6 (SD: 3.5) (95% CI: 1.2-4.0); range: 0-10 at 6 weeks then to 1.1 (SD: 2.6) (95% CI: 0.1-2.1); range: 0-8 at 12 weeks. Contrariwise the initial decline from baseline error score of 14.9 (SD: 9.3) (95% CI: 11.3-18.5); range: 0-28 to10.8 (SD: 9.7) (95% CI: 7.0-14.6); range: 0-26 at 6 weeks in patients with dementia, which was initially significant ($P = 0.04$; 95% CI: 9.2-0.9) was not sustained at 12 weeks when the mean error score was 9.7 (SD: 8.9) (95% CI: 6.3-13.2); range: 0-22 and the *t* value obtained when compared with the 6-week score yielded 0.6 and *P* value of 0.53 (95% CI: 4.9-7.2) [Figure 3].

The analysis of the various cognitive domains revealed that the more remarkable improvement in recall ability (memory) was observed in the first 6 weeks and among the PWE [Figure 4]. This was revealed in the likelihood ratios for lack of improvement (i.e., chances of committing errors on testing) in recall ability after 6 weeks of vinpocetine therapy among the PWE and the dementia patients, which were 7.3 ($P < 0.01$) and 20.7 ($P = 0.01$) respectively. The same trend was observed for concentration abilities [Figure 5].

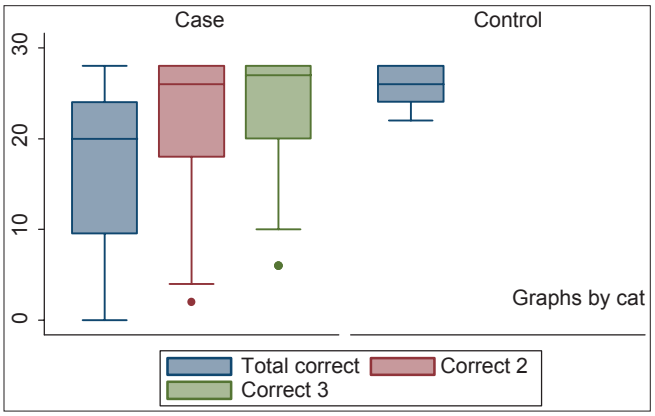

Figure 2: Box plot showing correct scores of study participants. Total correct 1: Mean correct scores at baseline; correct 2: Mean correct scores at 6 weeks; correct 3: Mean correct scores at 12 weeks

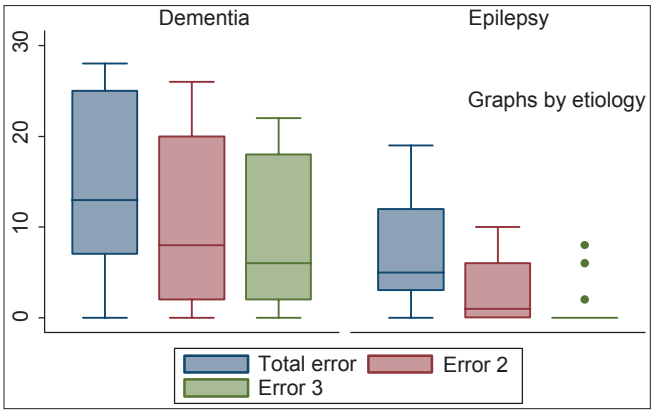

Figure 3: Box plot showing total error scores of patients with epilepsy and dementia. Total error 1: Mean error scores at baseline; error 2: Mean error scores at 6 weeks; error 3: Mean error scores at 12 weeks

Impact of disease variables on cognitive performances

The analysis of the relative impact of clinical variables of the patients on their cognitive performances revealed that the age categories, duration of epilepsy and seizure frequency of the PWE had no significant impact on the trend of cognitive performance with vinpocetine therapy. Similarly, among patients with dementia, the type of dementia and their age categories had no influence on the trend of their performances. Details of analysis are presented on Table 5.

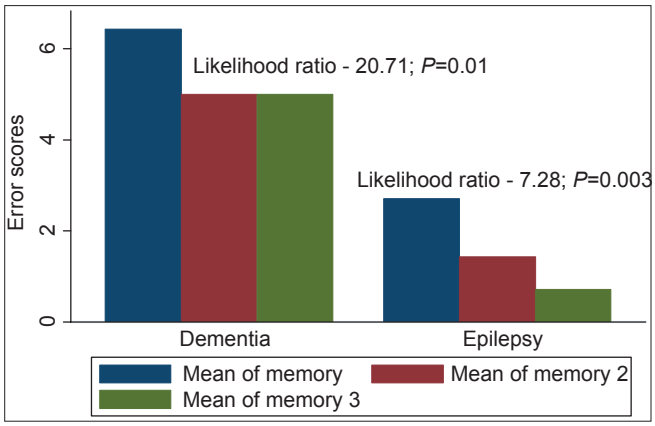

Figure 4: Bar chart showing memory error scores for patients with epilepsy and dementia. Mean of memory 1: Mean error scores at baseline; mean of memory 2: Mean error scores at 6 weeks; mean of memory 3: Mean error scores at 12 weeks

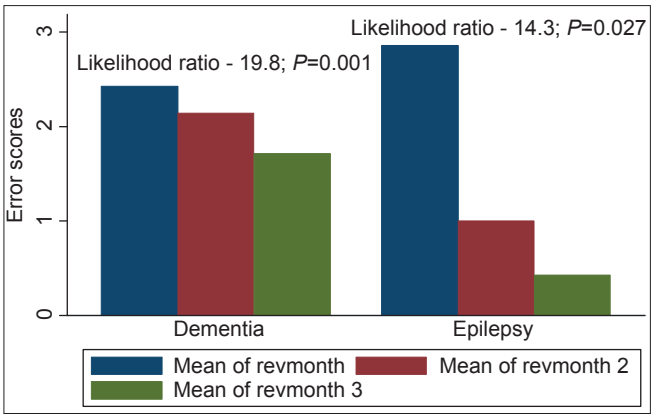

Figure 5: Bar chart showing concentration error scores for patients with epilepsy and dementia. Mean of revmonth 1: Mean error scores at baseline; mean of revmonth 2: Mean error scores at 6 weeks; mean of revmonth 3: Mean error scores at 12 weeks

Table 5: Clinical characteristics of patients and effects on cognitive performance

Variables	Frequency (%)	Patients with epilepsy (PWE)-mean total correct scores (*n*=28)				*F* (*P*)[#] values
		Baseline	6 weeks	12 weeks	Mean (SD)	
Age groups						
20-30	14 (50)	21.8 (4.2)	25.4 (1.8)	26.3 (1.1)	24.5 (2.6)	1.4; (0.27)
31-40	6 (21.4)	18.8 (2.3)	22.7 (1.1)	24.4 (1.7)	22.0 (1.9)	
41-50	4 (14.4)	22.1 (5.2)	26.8 (2.7)	27.1 (1.0)	25.3 (3.1)	
51-60	2 (7.2)	18.2 (6.3)	23.2 (3.7)	25.7 (2.6)	22.4 (4.2)	
61-70	2 (7.2)	19.7 (4.1)	23.5 (3.2)	25.9 (2.9)	23.0 (3.7)	
71-80	0 (0)	0	0	0	0	
Duration of epilepsy						
Less than 1 year	4 (14.4)	19.3 (2.2)	22.8 (2.1)	26.3 (1.2)	22.8 (1.7)	0.4 (0.75)
1-5 years	12 (42.9)	20.4 (3.7)	24.9 (1.8)	25.8 (2.6)	23.7 (1.9)	
6-10 years	7 (25)	19.6 (1.6)	25.1 (2.1)	25.7 (1.5)	23.5 (2.4)	
>10 years	5 (17.8)	18.4 (2.7)	24.2 (1.9)	25.3 (2.5)	22.6 (2.6)	
Frequency of seizures						
Several fits/day	3 (10.9)	17.6 (1.7)	19.4 (2.7)	21.1 (2.3)	19.4 (2.4)	3.2 (0.09)
Once-thrice/week	9 (32.1)	18.9 (2.1)	24.7 (3.6)	26.1 (3.9)	23.2 (4.2)	
Once twice/month	6 (21.4)	19.2 (3.2)	25.2 (4.1)	27.0 (2.8)	23.8 (3.7)	
Once 3-6 months	5 (17.8)	20.4 (3.4)	24.9 (3.2)	26.3 (2.9)	23.9 (2.8)	
Less than 1/year	5 (17.8)	20.1 (2.3)	25.0 (1.1)	26.7 (3.3)	24.0 (2.9)	
		Patients with dementia-mean total correct scores (*n*=28)				
Age groups						
20-30	0 (0)	0	0	0		0.1 (0.95)
31-40	0 (0)	0	0	0		
41-50	4 (14.4)	11.3 (5.2)	15.2 (6.2)	15.7 (4.2)	14.1 (5.7)	
51-60	8 (28.6)	12.7 (3.8)	16.7 (7.2)	17.7 (5.9)	15.7 (6.1)	
61-70	6 (21.4)	12.9 (6.1)	16.3 (5.1)	17.9 (4.8)	15.7 (5.2)	
71-80	10 (35.7)	12.3 (5.9)	16.1 (4.7)	17.4 (8.2)	15.3 (6.8)	
Type of dementia						
Alzheimer's	19 (67.9)	12.8 (4.1)	16.7 (6.3)	17.7 (7.1)	15.7 (6.6)	0.7 (0.51)[*]
Vascular	9 (32.1)	14.6 (7.2)	18.4 (7.6)	19.7 (6.3)	17.6 (7.8)	

[#]Trend analysis yielded *F* (*P*) values, [*]Analysis done with Student *t* test yielded *t* (*P*) value, PWE: Patients with epilepsy, SD: Standard deviation

Adverse reactions

There was no significant adverse effect reported among the study participants. Two of the 56 patients (3.6%) reported transient period of drowsiness which lasted for 2-3 days after the commencement of the drug. Patients were reviewed on a two-weekly basis to assess for any adverse effect. Numerous clinical studies have demonstrated the safety of vinpocetine during long-term administration.[30,31] It has not been shown to change

laboratory tests or produce allergic symptoms.[32] Furthermore, no serious drug-drug interactions have been reported.

Discussion

This prospective interventional study showed the beneficial effects of vinpocetine on the cognitive performances of patients with demonstrable disturbances in their cognitive abilities prior to administration of the drug. In addition, the pilot study demonstrated the utility of the SBT in routine cognitive assessment of patients with medical diseases that may be complicated by cognitive deterioration as shown by its acceptable accuracy of 83.9%. It is important to point out that the SBT can only suffice as a screening tool as it is limited in the scope of cognitive domains it can detect. It tests for concentration and memory. The cut-off error score of 6 obtained by the test designers was also obtained in this study,[21] implying that the cut-off value of six can be used for categorizing Nigerians into those who are and are not cognitively impaired.

Though the findings of this preliminary study revealed significant improvement in cognitive abilities of affected patients with vinpocetine treatment, the improvement observed with patients who had severe impairments was not statistically significant. It thus implied that vinpocetine needs to be commenced early once mild cognitive dysfunction is noted in any patient to achieve significant improvement in cognitive performance. Furthermore, it is not obvious from this study why the cognitive improvement plateau out after 6 weeks in patients with dementia. It may be that the drug needs to be continued for more than the 12 week-period of this study to achieve additional benefits. It is not certain if continuing vinpocetine would ensure sustain improvement over time. This requires further studies design to assess cognitive functioning in patients on this therapy for more than 12-24 months.

Previous studies that assessed the effect of vinpocetine on the cognitive abilities of patients with ischemic disturbances of cerebral circulation showed considerable improvement in memory functions in most of the patients, thus corroborating the findings of this study.[26,27,31-33] One of the studies used the Mini-Mental Status Questionnaire, Sandoz Clinical Assessment-Geriatric scale and Clinical Global Impression scale and showed that vinpocetine caused improvement of memory functions of patients with chronic cerebral dysfunction at a higher dose of 30 mg a day without any significant untoward effects.[31] In our study, a better improvement, though insignificant, in cognitive ability of patients with vascular dementia was observed compared to those with Alzheimer's dementia. This observation may be related to the role of underlying chronic cerebrovascular changes in the pathogenesis of the vascular type, which makes vinpocetine more effective considering its modes of action.

The probable mechanism by which vinpocetine achieved improvement in memory has been allied to its ability to boost the cerebral metabolism by increasing cerebral blood flow thus enhancing both oxygen and glucose utilization, increasing the rate of neuronal utilization of ATP and consequently improving cerebral functions. It is also believed that this drug maintains neuronal electrical conductivity and protect from damage caused by excessive intracellular release of calcium. It also inhibits abnormal platelet aggregation that may interfere with cerebral hemodynamics.[5,6,26,27,32,33]

The results of this preliminary study have shown the benefits of Vinpocetine (Cognitol™) in the treatment of cognitive impairments especially memory and sustained attention deficits in Nigerian Africans. Furthermore, it has also demonstrated the usefulness of the SBT for the screening of memory and sustained attention impairments in our patients.

Limitation of study

The use of the SBT for cognitive assessment is a limitation because of the restricted cognitive domains that it covers. However, the simplicity of the test and its utility in resource poor settings makes it valuable for screening. Furthermore, the 12 week duration of therapy precludes the assessment of the long-term effects of vinpocetine on cognition. Though the sampling technique has an appreciable power, studies with larger sample sizes involving patients with other chronic medical diseases are needed for further evaluation of cognitive benefits of vinpocetine.

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How to cite this article: Ogunrin AO. Effect of vinpocetine (cognitol™) on cognitive performances of a Nigerian population. Ann Med Health Sci Res 2014;4:654-61.

Source of Support: Nil. **Conflict of Interest:** None declared.