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Research article

The confirmatory factor structure of neurological soft signs in Nigerians with first episode schizophrenia

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HIGHLIGHTS

- We studied the factor structure of neurological soft signs (NSS) in schizophrenia.
- We used a homogenous sample of Black Africans with first episode of the illness.
- We conducted the first confirmatory factor analysis of the NSS in the population.
- 12 of the 26 NSS in the neurological evaluation scale (NES) loaded into categories.
- A 3 factor model overlapping with functionally meaningful categories best fit the data.

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ABSTRACT

We describe empirically derived categories of NSS in first episode schizophrenia among indigenous Africans. A total of 84 Nigerian patients with the disease were assessed using the neurological evaluation scale. An exploratory factor analysis with orthogonal varimax rotation was first conducted and the factors derived based on a priori criteria were subjected to confirmatory analyses using SPSS 18.0 and AMOS 18.0. We tested four different competing models to identify the structure with the best fit to the data. The relationship of the derived NSS structure with the clinical characteristics of schizophrenia was then explored using the Pearson correlation method. The overall clinical status was assessed using the positive and negative syndrome scale and clinical global impression. Additional assessments included the pre-morbid adjustment scale and calgary depression scale for schizophrenia. A three factor structure in which stereognosis is prescribed to load into a 'perceptual and motor sequencing' category (audio–visual integration, fist-edge palm, rhythm tapping, extinction, right–left confusion) provided the best fit to the data (chi-square goodness of fit test = 1.25; comparative fit index = 0.95; root square means error of approximation <0.05). The other two factors were: 'eye movement' (synkinesis, convergence, gaze impersistence) and 'motor co-ordination and graphaesthesia' (Tandem walk, adventitious flow, graphaesthesia). The signs were associated with severe negative ($r = 0.456$, $p < 0.001$), and disorganization ($r = 0.559$, $p < 0.001$) psychopathologies. NSS in this sample are heterogeneous, but aggregates into three correlated categories with significant overlap with previously described classifications.

1. Introduction

One of the most widely accepted classifications of neurological soft signs (NSS) in schizophrenia is their organization into three domains: sensory integration, motor coordination, and motor sequencing NSS [1]. Abnormalities in frontal release, eye movements, and short term memory are the 'other' frequently observed NSS. While this classification is 'meaningful', it has not been confirmed by empirical methods such as exploratory [2] or confirmatory factor analyses (CFA) [3].

Abbreviations: PMS, perceptual and motor sequencing; EYE, eye movement; MCG, motor co-ordination and graphaesthesia; STS, stereognosis; M_1, uni-dimensional model; M_2, two factor model; M_3, three factor model; IFS, incremental fit statistics; RSMEA, root square means error of approximation; GFI, goodness of fit index; TLI, Tucker-Lewis index; CFI, comparative fit index; IFI, incremental fit index; NFI, normed fit index; AIC, akaike information criterion; CAIC, consistent akaike information criterion; ECVI, expected cross validation index.

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Factor analysis is a standard technique for reducing data sets to underlying consistent sub-sets, which can then be used to find principal variables among many observed variables. Out of a dozen reported factor analyses of NSS in schizophrenia [1–12], only one [6] had been based on a sample from the African continent. That exploratory factor analysis (EFA) was based on a sample composed of 21% white, 71% mixed and 8% Black Africans with first episode schizophrenia. Yet there is no previous CFA of NSS in the African population.

In the background of some reports suggesting that race and ethnicity affects the profile of NSS in schizophrenia [4], it remains unclear if the factor structure of NSS in an indigenous African population with first episode schizophrenia would bear similarities with those reported for Caucasian or mixed samples.

In the present study, we conducted EFA, and the first CFA of the neurological evaluation scale (NES) on a sample of mostly medication naïve Black Africans, of Nigerian ancestry, with first episode schizophrenia. Also investigated was the relationship between the component factor structure and a range of clinical characteristics of the disease.

2. Materials and methods

2.1. Subjects

The study was conducted among patients presenting for biomedical treatment for the first time as out-patients or in-patients at two general hospitals with psychiatric units in Ibadan south-Western Nigeria.

The subjects comprised of mostly anti-psychotic naive patients with first episode schizophrenia, schizo-affective disorders, and schizophreniform disorder (6.0% had less than 12 weeks of lifetime oral antipsychotic exposure). The diagnosis of the relevant disorder was verified using criteria from the diagnostic and statistical manual for mental disorders-fourth edition (DSM-IV) [13]. Patients were eligible if they were aged between 16 and 45 years. The procedure of the study was explained to all eligible patients in either English or the local Yoruba language. Participants were those who provided written consent before interviews were conducted. We excluded patients with previous treatment with long acting depot antipsychotics and those with current substance abuse meeting DSM IV criteria. Also excluded were patients with significant physical illnesses. This was determined from the result of a full physical examination and appropriate laboratory investigations. Patients with mental retardation were excluded based on clinical history alone. On the bases of these criteria we recruited a total of 84 patients consecutively over a period of 26 months, between April 2009 and June 2011. They were cross-sectionally evaluated as far as possible before antipsychotic medications were prescribed. A wash-out period of one week was allowed for the 5 (6.0%) participants who had a lifetime exposure to oral antipsychotics. In the few cases where severity of psychopathology prevented immediate assessment, the evaluation was conducted as soon as patients were deemed well enough to co-operate with the examinations. We obtained baseline information on demographic, personal, medical, and psychiatric history, as well as family history.

Ethical approval for the study was obtained from the University of Ibadan/University College Hospital Joint Ethics Committee.

2.2. Measures

The structured clinical interview for DSM-IV- patients edition (SCID-P) [14] was employed in the recruitment of patients. The SCID-P provides for a standardized assessment that generates DSM-IV diagnoses using a semi-structured interview.

2.3. Neurological assessment

The NSS were evaluated using the 26 items neurological evaluation scale (NES) [15]. The NES include neurological tests such as tandem walk, rapid alternation movements, finger to thumb opposition, the finger-to-nose test, audiovisual integration, stereognosis, graphesthesia, extinction, and right to left confusion, first-ring test, the first-edge-palm test, the Ozeretski test, and rhythmic tapping test. The other signs assessed by the NES include cerebral dominance, short-term memory, frontal release signs and eye movement. The NES items are scored with reference to the descriptive anchors provided on a three-point scale (no abnormality = 0; mild, but definite impairment = 1; marked impairment = 2) with the exception of 'suck' and 'snout' reflexes which are scored 0 or 2. In this study, a neurological abnormality was defined as the rating of 2 on any 1 item on the NES. The tests were administered by a psychiatrist who had been trained in the use of the NES. Each item was assessed according to a fixed order.

2.4. Psychiatric assessment

The severity of the baseline psychopathology was evaluated by administering the positive and negative syndrome scale (PANSS) [16]. The model of the PANSS adopted in this study [17] include factors for 'positive symptoms' (delusions, hallucinations, unusual thought content, suspiciousness and grandiosity), 'negative symptoms' (lack of spontaneity, blunted affect, emotional withdrawals, apathetic social withdrawals, motor retardation, poor rapport and active social avoidance), 'disorganization' (stereotyped thinking, poor attention, disorientation, conceptual disorganization and difficulty in abstraction), 'excitement' (poor impulse control, excitement, hostility, and uncooperativeness), and 'emotional distress' (anxiety, depression, guilt, and tension).

The overall clinical status was assessed using the clinical global impression (CGI-Severity) [18], while pre-morbid adjustments and depression in schizophrenia were explored using the pre-morbid adjustment scale (PAS) [19], and the calgary depression scale for schizophrenia (CDSS) [20], respectively. These measures have been used for the assessments of African patients with schizophrenia in previous studies [21].

In this study, duration of untreated psychosis (D.U.P) was defined as the period in months from the onset of psychotic phenomena to first presentation to the psychiatric unit. In line with previous studies, onset of psychosis was defined as the presence for one week or more of one of the following psychotic symptoms; delusions, hallucinations, marked thought disorder, marked psychomotor disorder, and bizarre, grossly inappropriate and/or disorganized behavior, with a marked deterioration of functioning.

2.5. Statistical analysis

Analyses were conducted using SPSS version 18.0 and AMOS 18.0. Descriptive statistics such as means and standard deviations were used to summarize quantitative variables, while frequencies and proportions were used for discrete variables. EFA was conducted on NES items that were abnormal in more than 10% of the entire sample. Items testing for cerebral dominance were excluded. Factors obtained following initial maximum likelihood exploration were further rotated using the varimax procedure. Factors are reported when they have eigenvalues greater than unity and when they contribute at least 10% to the cumulative variance [2].

A four factor loading was generated in EFA. These factors were given conceptual names based on previously published categories: 'PMS', 'EYE', 'MCG', and 'STS'. Following EFA, maximum-likelihood estimation of CFA was conducted. We considered four competing

Table 1
Exploratory factor analyses of the NES Items.

NES items	Factors			
	1	2	3	4
Audiovisual integration	0.6179	0.3813	0.1862	0.0691
Fist-edge-palm	0.8403	−0.0635	−0.0507	0.0175
Rythm tapping	0.6279	0.4463	0.3077	0.0460
Extinction	0.6112	0.2675	0.2758	0.2573
Right/left confusion	0.5355	0.1595	0.3305	0.0876
Synkinesis	−0.0250	0.7128	0.2598	0.2451
Convergence	0.1743	0.7300	−0.0335	−0.0300
Gaze impersistence	0.2665	0.6417	−0.1330	−0.1574
Tandem walk	0.1647	−0.0166	0.6718	0.0700
Adventitious flow	0.1534	0.0558	0.7188	−0.0706
Graphaesthesia	0.0702	0.3899	0.5443	0.2191
Stereognosis	0.2321	0.1389	0.0706	0.8562
Memory	0.4459	0.1318	0.3792	0.3235
Rapid alternating movements	0.3139	0.4897	0.1705	0.3702
Finger/thumb opposition	0.4290	0.4148	0.2145	0.3418
Mirror movement	0.3394	0.3911	0.1305	0.3925
Finger to nose test	0.0312	0.1174	0.1409	0.0929
Grasp reflex	0.3895	0.2048	0.1155	−0.6424
Explained variance (%)	18.1	15.5	10.4	10.1
Severity mean (SD)	6.4 (3.3)	2.4 (2.0)	2.0 (1.6)	0.5 (0.8)

models based on the four categories in EFA which in theory may provide good fit to the data. The first was M_1, where all 12-items loading into the four different factors were combined into a single factor. This was based on an assumption that the NES measures NSS as a uni-dimensional 'trait'. We also investigated M_2; specifying that the MCG and the PMS combines to form a 'motor integration' factor, while the EYE and STS combine to form a 'sensory' factor. Two M_3 models were also considered. The first (M_{3a}) had STS specified to load on MCG while the second (M_{3b}) had STS specified to load on PMS. Similar to Sanders et al., [3], the M_1 model, which assumes that all the NES items are correlated, was used in this study as the 'informed baseline model' on which the other more complex models were compared.

We compared the M_2 and M_3 models with the M_1 model and with each other in order to assess the improvement in model fit. Incremental fit statistics (IFS) were used to provide information on the relative goodness-of-fit of each model. This metric serves to compare each model to that of the informed baseline.

A model is considered an adequate fit to data if the following conditions are satisfied [22]: the chi-square statistics divided by the degrees of freedom (χ^2/df) is less than 3 and the root square means error of approximation (RSMEA) is less than 0.05. RSMEA examines the level of variation between the proposed model and the true population model.

Also, the following fit indices: goodness of fit index (GFI), Tucker-Lewis Index (TLI), comparative fit index (CFI), incremental fit index (IFI), and normed fit index (NFI) should be greater than 0.90 for the model to be considered a good fit [22]. These indices serve to ensure that the hypothesized model is not incongruous with the study sample. Furthermore, the Akaike information criterion (AIC), consistent Akaike information criterion (CAIC), and expected cross validation index (ECVI) were used for model comparisons. These indices examine the discrepancy between the predicted and observed models within the context of the study sample. They are also able to penalize inadequate sample sizes and signpost the reliability of the results assuming other similar samples. In this regard, smaller values indicate better metrics.

In subsequent analyses, the correlations between NES total and factor derived scores and indices of clinical characteristics were tested using the Pearson's correlation method.

Table 3
Relative improvement in fit using normed fit indexes calculated using a one-factor baseline model.

Comparison	χ^2 difference	df	*p*-value	NFI
M_1–M_{3a}	19.34	3	<0.001	0.232
M_1–M_{3b}	19.92	3	<0.001	0.239
M_1–M_2	8.4	1	0.004	0.101
M_2–M_{3a}	10.94	1	0.001	0.146
M_2–M_{3b}	11.52	1	0.001	0.153
M_{3a}–M_{3b}	0.58	0	1.00	0.009

$^{**}p < 0.01$

3. Results

The mean age at presentation and at onset of schizophrenia was 28.7 (±6.4) years and 24.6 (±8.2) years, respectively. The mean duration of untreated psychosis was 38.9 (±47.7) months, with a median of 26.0 months. The mean NES score of the subjects was 21.5 (±11.1). NSS were elicited in 81 (96.4%) subjects.

The first 4 factors accounted for 54.1% of the total variance. Table 1 shows the results of the principal component matrix with the factor loadings after orthogonal varimax rotation. Factor 1 (PMS) is comprised of items which are known to test for motor and sensory integration [6]. Factor 2 (EYE) represents eye movement abnormalities in schizophrenia. Factor 3 (MCG) include items that test for primary motor functions and graphaesthesia, while Factor 4 (STS) comprised of stereognosis.

In Table 2, fit indices for four competing models are presented. These indices were improved for the M_3 models. However, with a χ^2/df = 1.25, CFI = 0.95, and RMSEA = 0.05, the M_{3b} appeared better when compared to the M_{3a} model. In addition, the AIC = 457.43 and CAIC = 700.14 for the M_{3b} was smaller than that of all other competing models.

In Table 3, the two M_3 models provided a better fit to the data compared with the M_1 and M_2 models as indicated by the alpha values. However, M_{3b} do not provide a substantially better fit than M_{3a}.

In Table 4, the inter-item correlation matrix shows that the twelve items extracted in the EFA were relatively correlated. Table 5 summarises the relationship between the derived factors of NSS and the clinical characteristics of schizophrenia.

4. Discussions

In this Nigerian sample of patients with first episode schizophrenia, NSS loaded into a four factor structure in EFA; 'perceptual and motor sequencing', 'eye signs', 'motor co-ordination and graphaesthesia', and 'stereognosis'. However, a three factor structure provided the best fit to the data in CFA. The signs were

Table 2
Confirmatory factor analyses, goodness of fit and fit indices.

Models	χ^2/df	TLI	CFI	IFI	GFI	NFI	RMSEA	AIC	CAIC
One-factor model (M_1)	83.45/54**	0.85	0.87	0.88	0.87	0.72	0.08	131.45	213.79
Two-factors(M_2)	75.05/53*	0.88	0.91	0.91	0.87	0.75	0.07	125.05	210.82
1st three-factors model (M_{3a})	64.11/51	0.93	0.94	0.95	0.89	0.79	0.06	118.11	210.74
2nd three-factors model (M_{3b})	63.53/51	0.93	0.95	0.95	0.89	0.79	0.05	117.53	210.16

Table 4
The inter-item correlation matrix.

	NES 1	NES 2	NES 6	NES 7	NES 8	NES 10	NES 13b	NES 17	NES 18	NES 19	NES 20	NES 21
NES 1	1	.367[b]	0.173	0.15	.258[a]	0.184	.306[b]	.254[a]	.360[b]	0.1	0.176	0.088
NES 2	[b]	1	.261[a]	0.195	0.185	0.21	.243[a]	.262[a]	.330[b]	.317[b]	0.129	0.193
NES 6		[a]	1	.268[a]	.395[b]	.419[b]	.501[b]	.455[b]	.390[b]	.283[b]	.368[b]	.289[b]
NES 7			[a]	1	.266[a]	0.21	.295[b]	.350[b]	.261[a]	.300[b]	0.14	0.053
					0.014	0.056	0.007	.001[b]	0.016	0.006	0.203	0.631
NES 8	[a]		[b]	[a]	1	0.018	.368[b]	.291[b]	0.127	.337[b]	0.158	0.057
NES 10			[b]			1	.412[b]	.464[b]	.383[b]	0.013	0.176	.306[b]
NES 13b	[b]	[a]	[b]	[b]	[b]	[b]	1	.511[b]	.514[b]	.355[b]	.423[b]	.306[b]
NES 17	[a]	[a]	[b]	[b]	[b]	[b]	[b]	1	.530[b]	.402[b]	.291[b]	.284[b]
NES 18	[b]	[b]	[b]	[a]		[b]	[b]	[b]	1	.237[a]	.326[b]	.282[b]
NES 19		[b]	[b]	[b]	[b]		[b]	[b]	[a]	1	.326[b]	.302[b]
NES 20			[b]				[b]	[b]	[b]	[b]	1	.519[b]
NES 21			[b]			[b]	[b]	[b]	[b]	[b]	[b]	1

NES 1. Tandem walk, 2. Rhomberg test, 6. Audio–visual integration, 7. Stereognosis, 8. Graphaesthesis, 10. Fist-Edge-Palm test, 13. Rhythm tapping, 17. Face-Hand test (extinction), 18. Right/left confusion, 19. Synkinesis, 20. Convergence, 21. Gaze impersistence. Listwise $N = 84$.

[a] Correlation is significant at the 0.05 level (2-tailed).

[b] Correlation is significant at the 0.01 level (2-tailed).

generally associated with severe negative and disorganization psychopathologies.

Apart from the work by Sanders et al., [3], relying on 13 items extracted from the NES [8], CFA of the NES appear scarce in the literature. To increase the reliability of our findings, we have applied a range of fit indices than have been used previously.

We observed that the factor structure of the NES in this sample bear considerable similarities with the categories identified in the studies by the Sanders group [3,5,7,8,23]. Firstly, we identified four factors in EFA with considerable overlap with the factors identified previously. Secondly, the fourth factor in this study had a single item loading. Thirdly, our CFA established that a three factor solution provided the best fit to the data as previously reported [3]. Fourthly, the PMS factor of this study is very similar to the 'cognitive perceptual' factor in the analyses by the Sanders' group, in so far as 80% of the items loading into the previously described 'cognitive perceptual' factor [3] were represented in the PMS category of this study. Similarly, the difference between the MCG factor of this study and the previously reported 'balance' factor lie in the replacement of abnormal 'Rhomberg test' with 'adventitious flow' [3,8]. This difference may not be substantial as it did not change the conceptual meaning of the balance/MCG categories of both studies.

While considering studies, all exploratory, that have used samples different from those of the Sanders' group, we note that the EYE category of this study mirrors the 'sensory integration' factor of the study by Malla et al. [10] in so far as all 3 items testing for eye movements loaded together in both studies. Also, similar to the theoretical classification by Heinrich's and Buchanan [1], we note that the PMS category of this study bore considerable similarities with the sensory integration 'functional' category conceptualised in that taxonomy, since four out of five items were represented in the PMS factor of this study. Differences observed between the results of the present investigation and previous report may be a reflection of the heterogeneous nature of both NSS and schizophrenia. In line with this indication, it has often been difficult to provide exact replications of empirically derived categories of NSS, even when the same sample had been re-analysed, or when the same NES items had been used [2,5–7].

The pattern of relationship between NSS and severe negative and disorganization psychopathology in this study is not surprising given previous documentation in samples around the world [24]. It provides additional validity to the proposed factor structure. Also, such association may be relevant in assessing the prognosis of schizophrenia. Abnormal NSS may originate from defects in the fronto-basal ganglia circuitry [25]. Disturbances in similarly interconnected areas of the brain have been associated with the neuro-developmental process of schizophrenia [26]. In this regard, the absence of a significant relationship between the age at onset of schizophrenia and NSS in this study was unexpected.

In interpreting the results of our analyses, it is important to note that the investigators were not blind to the clinical state of the subjects.

Table 5
Pearson correlation of baseline NSS and the clinical characteristics of schizophrenia.

Characteristics	1 Perceptual and motor sequencing	2 Eye signs	3 Motor coordination/graphaesthesia	NES Total
Baseline profile				
Age at onset	−0.079	0.023	−0.05	−0.004
D.U.P	0.037	−0.021	0.116	−0.005
Pre-morbid adjustment				
CHILDHOOD (social/academic)	0.019/0.123	0.075/0.120	0.003/−0.051	0.034/0.101
ADOLESCENT (social/academic)	0.067/−0.011	0.045/−0.132	0.109091	0.039/−0.081
PANSS				
Positive	−0.058	0.01	−0.072	−0.075
Negative	0.472**	0.328**	0.239*	0.456**
Disorganized	0.525**	0.384**	0.305**	0.559**
Excited	0.238*	0.224*	0.204	0.228*
Depression	0.157	0.09	0.113	0.169
CGI-severity	0.558**	0.506**	0.228*	0.566**
CDSS	0.065	0.02	0.134	0.095

PANSS: Positive and Negative Syndrome Scale, CGI: Clinical Global Impression, CDSS: Calgary Depression Scale of Schizophrenia, DUP: Duration of untreated psychosis.

* $p < 0.05$.

** $p < 0.01$.

In concluding, NSS in this sample loaded into a three factor structure with overlaps with previously described categories. Differences observed across studies may be a reflection of the heterogeneous nature of NSS measured using the NES in schizophrenia. Therefore, the 26 item NES may be too diverse to tell any specific story about the process of the disease.

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