Neuropsychological Effects of Konzo: A Neuromotor Disease Associated With Poorly Processed Cassava

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KEY WORDS
konzo, children, Africa, neuropsychology, motor neuron disease, memory, motor function, cognitive ability, cassava

ABBREVIATIONS
BOT-2—Bruininks-Oseretsky Test of motor proficiency (second edition)
CI—confidence interval
CNS—central nervous system
HOME—Home Observation for Measurement of the Environment
KABC-II—Kaufman Assessment Battery for Children (second edition)
MPI—mental processing index
OR—odds ratio
WHO—World Health Organization

Dr Boivin participated in the design of the study, oversight of neuropsychological exam, analysis of the data, and drafting of the manuscript. Drs Okitundu, Bumoko, and Sombo participated in the field testing of the children and drafting of the manuscript. Dr Mumba participated in the study design, konzo diagnosis, and clinical analysis. Dr Tylleskar participated in the design of study, analysis plan, and drafting of the manuscript. Dr Page participated in the statistical analysis and tables, interpretation of study findings, and drafting of the manuscript. Dr Tshala-Katumbay participated in the statistical analysis and tables, interpretation of study findings, and drafting of the manuscript. All authors approved the final manuscript as submitted.

(Continued on last page)

WHAT’S KNOWN ON THIS SUBJECT: Konzo is an irreversible sudden-onset upper-motor neuron disorder affecting children dependent on bitter cassava for food. The neuroepidemiology of konzo is well characterized. Children subsisting on poorly processed bitter cassava without adequate dietary sulfur-based amino acids are especially at risk.

WHAT THIS STUDY ADDS: We found a pervasive subclinical neurocognitive effect in children with konzo. This study provides the first evidence we are aware of that a motor proficiency examination can effectively characterize konzo severity.

abstract

BACKGROUND: Konzo is an irreversible upper-motor neuron disorder affecting children dependent on bitter cassava for food. Although the neuroepidemiology of konzo is well characterized, we report the first neuropsychological findings.

METHOD: Children with konzo in the Democratic Republic of Congo (mean age 8.7 years) were compared with children without konzo (mean age 9.1 years) on the Kaufman Assessment Battery for Children, second edition (KABC-II), and the Bruininks-Oseretsky Test of Motor Proficiency, second edition (BOT-2). Both groups were also compared with normative KABC measures from earlier studies in a nearby nonkonzo region.

RESULTS: Using a Kruskal-Wallis test, children with konzo did worse on the KABC-II simultaneous processing (visual-spatial analysis) (K[1] = 8.78, P = .003) and mental processing index (MPI) (K[1] = 4.56, P = .03) than children without konzo. Both konzo and nonkonzo groups had poorer KABC sequential processing (memory) and MPI relative to the normative group from a nonkonzo region (K[2] = 75.55, P < .001). Children with konzo were lower on BOT-2 total (K[1] = 83.26, P < .001). KABC-II MPI and BOT-2 total were predictive of konzo status in a binary logistic regression model: odds ratio = 1.41, P < .013; 95% confidence interval 1.13–1.69.

CONCLUSIONS: Motor proficiency is dramatically affected, and both children with and without konzo have impaired neurocognition compared with control children from a nonoutbreak area. This may evidence a subclinical neurocognitive form of the disease, extending the human burden of konzo with dramatic public health implications. Pediatrics 2013;131:e1231–e1239
Konzo is a nonprogressive upper-motor neuron disorder documented in African rural areas that are dependent on bitter cassava (manioc), which produces edible carbohydrates in ecologically degraded zones. Bitter cassava is usually soaked for fermentation, and/or sufficiently sun dried to allow for breakdown of linamarin and its cyanogenic compounds. When cassava coquettes are not sufficiently processed (eg, in times of drought or armed conflicts),\textsuperscript{1,2} outbreaks of konzo may occur. Populations are especially vulnerable if shortcuts in processing the cassava are combined with a low dietary intake of sulfur amino acids needed for the detoxification of cyanide in the human body.\textsuperscript{3}

Konzo is defined by World Health Organization (WHO) as a visible symmetric spastic abnormality of gait while walking or running (Fig 1), with a history of onset of <1 week followed by a nonprogressive course in a formerly healthy person and bilaterally exaggerated knee or ankle jerks without signs of disease of the spine.\textsuperscript{4} Because konzo is a pure upper-motor neuron disorder, cognitive effects were deemed absent or minimal.\textsuperscript{4,5} This study is the first to evaluate whether konzo affects neuropsychological function.

**METHOD**

**Study Site**

The Ministry of Health for the Democratic Republic of Congo and the institutional review board for Oregon Health and Sciences University provided study approval. Caregivers of study children were consented orally in the local language with signature or thumb print for those not literate. The study site was a konzo outbreak zone in the district of Kahemba, southern Bandundu Province, Democratic Republic of Congo, in October to November 2011. Kahemba town has a population of \(\sim\)50,000, whereas the surrounding area has a population of \(\sim\)250,000. Residents rely heavily on cassava farming and possess limited livestock for subsistence. This region has been continuously affected by konzo since 1990,\textsuperscript{6} and prevalence is as high as 20% in some villages.\textsuperscript{7–9}

**Study Sample**

From earlier outbreaks in Kahemba, 5000 subjects in Kahemba town had been listed on a WHO surveillance list. From this list, we were able to locate a total of 308 eligible children with konzo in Kahemba town, and these children comprised our study population. From this population, 123 children with konzo were randomly selected for study participation (65 boys, 58 girls; mean age 8.7 years; range 4 to 17 years). Sample size was based on an 80% power calculation for a 2-sided test (.05 level of significance) to detect Kaufman Assessment Battery for Children (second edition) (KABC-II) and Bruininks-Oseretsky Test of motor proficiency (second edition) (BOT-2) global performance differences equal to 0.25 SD between konzo and age-matched control groups.\textsuperscript{10} For all study children with konzo, neurologists did a neurologic examination to confirm konzo diagnosis using the 1996 WHO criteria.\textsuperscript{4} Height and weight were also measured at the time of the neurologic evaluation (Table 1).

For each child with konzo, we attempted to consent a comparison child without konzo (1996 WHO criteria) within 2 years of age, from a neighboring household that met inclusion criteria. Children with a medical history of hospitalization for illness possibly affecting the central nervous system (CNS) (eg, cerebral malaria) were excluded. In total, 87 children without konzo (52 boys, 35 girls; mean age 9.1 years; range 4 to 15 years, Table 1) met the criteria to participate in the study, and completed neuropsychological assessments. The study design was an observational...
study for a cross-sectional 1-time comparison of disease and control groups on neuropsychological outcomes.

All children were screened for retroviruses HIV-1 and -2, and human T-lymphotropic virus-I, and none were positive. Urinary thiocyanate (Bradbury kit, 1999; http://biology.anu.edu.au/hosted_sites/CCDN/five.html) was also measured in all study children (518.59 ± 354.19 μM/mL for the konzo group and 381.04 ± 221.88 for controls). These are high levels of cyanogenic exposure in both groups based on earlier studies by Banea et al of thiocyanate levels in konzo-affected populations in Central Bandundu in Kikongo. 

Socioeconomic Status and Caldwell Home Observation for the Measurement of the Environment

After consent and enrollment, a nurse visited the home of each study child to complete the middle childhood version of the Caldwell Home Observation for the Measurement of the Environment (HOME). 

**Table 1** Subject Characteristics for Children With and Without Konzo

<table>
<thead>
<tr>
<th></th>
<th>Konzo</th>
<th>Nonkonzo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. subjects</td>
<td>123</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>Age, y, mean (SD)</td>
<td>8.7 (2.5)</td>
<td>9.1 (2.6)</td>
<td>.212</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>35 (47)</td>
<td>58 (40)</td>
<td>.320b</td>
</tr>
<tr>
<td>Enrolled in school, n (%)</td>
<td>73 (59)</td>
<td>78 (90)</td>
<td>&lt;.001c,d</td>
</tr>
<tr>
<td>Caldwell HOME score, z-score</td>
<td>−0.1 (−0.7−0.6)</td>
<td>2.3 (1.0)</td>
<td>&lt;.001g</td>
</tr>
<tr>
<td>School grade level, mean (SD)</td>
<td>1.3 (1.6)</td>
<td>2.5 (1.9)</td>
<td>&lt;.001g</td>
</tr>
<tr>
<td>Caregiver with konzo, n (%)</td>
<td>99 (81)</td>
<td>58 (66)</td>
<td>.025d</td>
</tr>
<tr>
<td>Other family with konzo, n (%)</td>
<td>85 (85)</td>
<td>61 (70)</td>
<td>.007d,g</td>
</tr>
<tr>
<td>Weight for age, CDC 2-score^e</td>
<td>−2.9 (−1.0)</td>
<td>−2.1 (1.5)</td>
<td>&lt;.001d</td>
</tr>
<tr>
<td>Height for age, CDC 2-score^e</td>
<td>−3.4 (1.4)</td>
<td>−2.3 (1.8)</td>
<td>&lt;.001g</td>
</tr>
<tr>
<td>Mid-upper arm circumference, cm</td>
<td>15.2 (1.9)</td>
<td>15.7 (1.9)</td>
<td>.122</td>
</tr>
<tr>
<td>Head circumference, cm</td>
<td>49.8 (1.7)</td>
<td>50.2 (1.8)</td>
<td>.178</td>
</tr>
<tr>
<td>Caldwell HOME score, total^f</td>
<td>43.5 (8.1)</td>
<td>47.2 (10.4)</td>
<td>.016d</td>
</tr>
<tr>
<td>Socioeconomic status score^f</td>
<td>2.2 (1.1)</td>
<td>2.8 (3.2)</td>
<td>.645</td>
</tr>
<tr>
<td>Neurologic index score^f</td>
<td>11.4 (4.4)</td>
<td>2.0 (1.7)</td>
<td>&lt;.001d</td>
</tr>
</tbody>
</table>

CDC, Centers for Disease Control and Prevention. Group means and SDs (in parentheses) are presented unless otherwise specified.

- P values based on Kruskal-Wallis analysis of variance test unless otherwise specified.
- P values for χ² statistic between categories (gender, enrolled in school).
- z-score values are from CDC 2000 norms from Epi Info®.
- Based on the Caldwell HOME total score.
- The socioeconomic status score is measured by evaluating the physical characteristics of home dwelling and material and animal possessions during a visit to the home.
- Children with konzo and control children were evaluated for upper-motor neuron signs, which are characteristic of konzo (Table 2). From this examination we computed a total score reflecting the neurologic impairment pertaining to konzo. For each of the neurologic signs listed in Table 2, children were scored as either normal (0 points), mildly abnormal (eg, periodic or mild hyperreflexia and exaggerated clonus or reflexive delay; 1 point), or moderately/severely abnormal (eg, highly exaggerated and/or sustained hyperreflexia or clonus, or sustained reflexive delay; 2 points).

KABC-II

The KABC provides a comprehensive evaluation of core neurocognitive performance domains (see http://ego.thechicagoschool.edu/s/843/index.aspx?sid=843&gid=63&pgid=2050 for powerpoint presentations describing the KABC-II). It has been used previously in the Democratic Republic of Congo,10,12–16 and it has been validated in Uganda.17 Neuropsychological evaluation took place in a quiet room near Kahemba Hospital that afforded privacy.

**Normative Memory Measures (KABC, First Edition)**

The KABC, first edition, was used in validation and intestinal parasite treatment studies in central Bandundu in Kikongo, an area where no konzo has been reported.12,13,16 Kikongo is in a remote rural area on the Wamba River 200 km northwest of the Kahemba outbreak study site. KABC memory subtest and global scores were used from these combined samples as a normative reference base (Kikongo normative group) to compare with the Kahemba children with and without konzo.

Neurologic Index of Konzo Severity

Children with konzo and control children were evaluated for upper-motor neuron signs that are characteristic of konzo (Table 2). From this examination we computed a total score reflecting the konzo neurologic impairment. Quantifying the neurologic severity of the disease allowed us to statistically evaluate its relationship to our cognitive (KABC-II) and motor proficiency (BOT-2) measures. For each of the neurologic signs listed in Table 2, children were scored as either normal (0 points), mildly abnormal (eg, periodic or mild hyperreflexia and exaggerated clonus or reflexive delay; 1 point), or moderately/severely abnormal (eg, highly exaggerated and/or sustained hyperreflexia or clonus, or sustained reflexive delay; 2 points).
TABLE 2 Neurologic Tests for Upper-Motor Neuron Disease

<table>
<thead>
<tr>
<th>Neurologic Signs</th>
<th>Nonkonzo</th>
<th>Konzo</th>
<th>( \Phi ) Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n = 87 )</td>
<td>( n = 123 )</td>
<td></td>
</tr>
<tr>
<td>Patellar reflex</td>
<td>48.3% (42)</td>
<td>0.8% (1)</td>
<td>0.716**</td>
</tr>
<tr>
<td>Ankle reflex</td>
<td>60.9% (53)</td>
<td>2.4% (3)</td>
<td>0.680**</td>
</tr>
<tr>
<td>Babinski's reflex</td>
<td>79.3% (69)</td>
<td>30.1% (37)</td>
<td>0.486**</td>
</tr>
<tr>
<td>Chin-palm reflex</td>
<td>80.2% (69)</td>
<td>69.1% (85)</td>
<td>0.124*</td>
</tr>
<tr>
<td>Oppenheim's sign</td>
<td>82.8% (72)</td>
<td>75.6% (83)</td>
<td>0.089*</td>
</tr>
<tr>
<td>Brachial reflex</td>
<td>89.7% (78)</td>
<td>34.1% (42)</td>
<td>0.553**</td>
</tr>
<tr>
<td>Biceps reflex</td>
<td>92.0% (80)</td>
<td>27.6% (34)</td>
<td>0.636**</td>
</tr>
<tr>
<td>Ankle clonus</td>
<td>96.6% (84)</td>
<td>50.4% (62)</td>
<td>0.495***</td>
</tr>
<tr>
<td>Speech difficulties</td>
<td>98.9% (86)</td>
<td>58.5% (72)</td>
<td>0.460**</td>
</tr>
<tr>
<td>Patellar clonus</td>
<td>98.9% (86)</td>
<td>97.6% (120)</td>
<td>0.233**</td>
</tr>
<tr>
<td>Nyctagmus</td>
<td>98.9% (86)</td>
<td>86.2% (108)</td>
<td>0.233**</td>
</tr>
<tr>
<td>Somatic sensitivity loss</td>
<td>100% (87)</td>
<td>97.6% (120)</td>
<td>0.101*</td>
</tr>
</tbody>
</table>

The tests comprised our neurologic index measures (Table 1). Between-group comparisons consist of konzo groups (nonkonzo, konzo). The neurologic signs were ordered from top to bottom on the basis of the test that had the lowest percentage of normal results in the nonkonzo group (number of children with normal reflex in parentheses). The high percentage of abnormal findings with patellar and ankle reflexes in children without konzo, combined with a very low percentage of normal findings in the children with konzo, \( * P < .05, ** P < .01, *** P < .001 \) on \( \Phi \) coefficient test of relationship between group (konzo or nonkonzo) and percent normal on that neurologic test.

Statistical Analysis

The Kruskal-Wallis 1-way analysis of variance was used for a nonparametric evaluation of between-group differences (nonkonzo versus konzo; or differences among nonkonzo, konzo, and Kikongo normative groups). Neurologic index was correlated to the BOT-2 and KABC-II global measures by group using a Pearson product-moment correlation coefficient test. A binomial logistic regression analysis was used to evaluate the predictive significance of KABC-II total global performance (mental processing index; MPI) and BOT-2 total motor proficiency on nonkonzo versus konzo group status. SPSS version 19 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) was used for statistical analyses and graphs.

RESULTS

Between-Group Descriptive Differences

The konzo and nonkonzo groups were similar in age, gender composition, and socioeconomic status as measured by material possessions in the home; however, the children with konzo were less likely to be enrolled in school (\( \chi^2 [1] = 23.17, P < .001 \)). Children with konzo were more likely to have a care-giver, usually the mother, with konzo (\( \chi^2 [1] = 5.16, P = .023 \)), and another family member in the household with the disease (\( \chi^2 [1] = 7.16, P = .007 \)).

Children both with and without konzo were significantly below Centers for Disease Control and Prevention normative weight-for-age and height-for-age norms, with the children with konzo lower than the nonkonzo group on both weight (\( K[1] = 15.55, P < .001 \)) and height (\( K(1) = 19.94, P < .001 \)) (Table 1). The konzo group was also lower on Caldwell HOME scale total score measuring quality of caregiving (\( K[1] = 5.81, P = .016 \)).

Between-Group KABC-II Differences

Children without konzo were better than children with konzo on the KABC-II global measures of simultaneous processing (\( K[1] = 8.78, P = .003 \)) and the MPI measure of global cognitive performance (\( K[1] = 4.56, P = .033 \)) (Table 3). Other KABC-II global domains had individual subtests that significantly differed between groups, with \( P \) values in bold in Table 3. Table 3 also shows group medians and interquartile ranges for all the KABC-II global scale and subtest measures. When stratifying the between-group differences by gender, all of the statistically significant between-group differences for the KABC-II were consistent for the boys. There were no significant differences between the groups of girls with and without konzo (Table 3).

The nonkonzo and konzo groups were compared with normative group data from Kikongo. The Kikongo control group was significantly better than the nonkonzo and konzo groups on the KABC sequential processing global measure (\( K[2] = 75.55, P < .001 \)), simultaneous processing (\( K[2] = 12.71, P = .002 \)), and MPI global cognitive performance (\( K[2] = 91.57, P < .001 \)). In Fig 2, box and whisker plots are used to visually depict these differences among the 3 groups (nonkonzo, konzo, normative control).
KABC-II planning 57 (11) 51 (16) 3.71 .054 .742 .037
KABC-II delayed learning 72 (14) 74 (14) 0.19 .666 .646 .257
KABC-II learning 70 (14) 70 (11) 0.30 .582 .596 .875
KABC-II MPI 60 (14) 58 (13) 4.56 .033a .420 .087
Rebus delayed 4 (3) 4 (4) 1.19 .275 .317 .464
Atlantis delayed 5 (3) 5 (3) 2.09 .149 .800 .854
Triangles 1 (2) 1 (1) 3.34 .068 .540 .543
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Kikongo control group subtest normative data were available only for the KABC sequential processing domain for comparison with the Kahemba nonkonzo and konzo groups. Kikongo children had better memory than the nonkonzo and konzo groups on the KABC sequential processing subtests of hand movements (K[2] = 93.49, P < .001), number recall (K[2] = 33.69, P = .001), and word order (K[2] = P < .001). For KABC global and memory subtest comparisons, the Kikongo control group performed above both the nonkonzo and konzo groups (see Fig 2).

Between-Group BOT-2 Differences
Children without konzo had higher motor proficiency measures on BOT-2 fine motor control (K[1] = 8.44, P = .004), manual coordination (K[1] = 58.30, P < .001), body coordination (K[1] = 111.43, P < .001), strength and agility (K[1] = 104.13, P < .001), and motor proficiency total (K[1] = 83.26, P < .001). BOT-2 differences between the children with and without konzo were significant for both genders (see Table 3).

Relationship of Neurologic Index to BOT-2 and KABC-II
For the children with konzo, total neurologic signs was highly correlated with BOT-2 total score (r[122] = —0.433, P < .0001). Although total neurologic signs was significantly correlated with all 4 BOT-2 global domains, it has the weakest correlation coefficient with fine manual control (r[122] = —0.225, P = .012), and the strongest correlation with body coordination (r[122] = —0.559, P < .0001) and strength and agility (r[122] = —0.568, P < .0001). Correlations for the control children were significant only for body coordination (r[86] = —0.249, P = .02).

The neurologic index for the children with konzo was significantly correlated only with KABC-II MPI (r[122] = —0.239, P = .008) and the KABC-II global domain of learning (r[122] = —0.244, P = .006), and delayed recall (r[118] = —0.227, P = .013). Neurologic Index was not significantly correlated with any of the KABC-II measures for the children without konzo.

Neuropsychological Predictors of Konzo Group Status
In a binomial logistic regression model, both KABC-II MPI and BOT-2 total motor proficiency significantly predicted konzo group status: odds ratio (OR) = 1.41, P < .013, 95% confidence interval (CI) 1.13—1.69; Nagelkerke R² = 0.51; overall correct classification percentage of 79%. Individually, BOT-2 total
DISCUSSION

Overview of Major Findings

Children with konzo did more poorly than children without konzo on KABC-II simultaneous processing (visual-spatial analysis and problem solving) and on MPI global performance. KABC-II global scale and subtest between-group differences were significant for the boys, but not the girls. The boys with konzo were also less likely to be enrolled in school, perhaps because of social stigma associated with the disorder.5 This may have further contributed to their poorer neurocognitive performance. We are not aware of any published evidence to suggest that boys are more vulnerable to the neuropathophysiological mechanisms of konzo compared with girls. There was not a significant interaction effect between gender and konzo status for either the Neurologic Index or BOT-2 total motor proficiency measures. Both konzo and nonkonzo groups of children were significantly below KABC normative performance of children from a nonkonzo area. These differences were especially apparent on sequential processing (memory) subtests. Weak memory differences between the Kahemba konzo and nonkonzo groups may have been because of more pervasive neurocognitive effects from long-term bitter-cassava low-grade toxin exposure in the Kahemba.

FIGURE 2

Box plots for the konzo groups (nonkonzo, konzo) and the Kikongo normative control group by gender for the KABC global scales (sequential processing, simultaneous processing, mental processing index) and memory subtests (hand movements, number recall, word order). Top and bottom of the box at the third and first quartiles, bisected by the median with outliers plotted as individual data points. American normative mean of 100 at dashed line (SD = 15) for standardized global scores, and a normative mean of 10 (SD = 3) for scaled subtest scores.
outbreak area. Although there was no reported konzo in our Kikongo communities, we do not have urinary thio-
cyanate levels or other cassava toxicity biomarkers from this normative sample. Therefore, other factors apart from 
cassava toxicity may be responsible for the better cognitive performance of these children compared with our 
Kahemba konzo and nonkonzo samples. Children affected by konzo also had significantly lower anthropometric 
measures (weight for age, height for age), indicative of malnourishment. This is perhaps related to the poor 
nutritional intake contributing to risk for konzo, and nutritional malab-
sorption commonly reported with konzo. CNS effects of konzo could 
be compounded by malabsorption and/or malnutrition leading to thiamine and 
other micronutrient deficiencies. Thia-
mine deficiency has been related to 
many of the CNS signs associated with 
konzo, including cerebellar dysfunc-
tion, diffuse electroencephalography 
slowing and evoked response potential 
abnormalities, and pervasive neuro-
cognitive deficits.

Most of the caregivers for both the konzo 
and control groups were affected by 
konzo, but a higher percentage of 
caregivers of children with konzo were 
affected (Table 1). Likewise, a higher 
proportion of households with children 
with konzo had other family members 
affected. Caregivers affected by konzo 
would also be less able to provide for a 
quality caregiving environment for chil-
dren with konzo, explaining the signifi-
cantly lower HOME scores for this group 
compared with the nonkonzo group. This 
is a further significant neurocognitive 
risk factor for children with konzo.

The BOT-2 examination provided a 
comprehensive motor proficiency eval-
uation of the effects of konzo on 
the study children. It was also highly 
correlated to a neurologic index of 
konzo severity. This test quantifies the 
extent of motor impairment, and could 
provide a sensitive neuromotor profile 
of the severity of konzo. Presently, konzo 
severity is categorized as mild, moder-
ate, or severe using the 1996 WHO 
criteria, which is largely based on 
functional mobility. This can improve 
over time, as children develop strategi-
es for overcoming their handicap to 
become more mobile, independent of 
neurologic impairment level. Again, 
our neurologic index was highly pre-
dictive of BOT-2 motor proficiency, as 
well as KABC-II learning and global 
cognitive performance (MPI), for the 
children with konzo only.

In comparing children with and without 
konzo with the BOT-2, fine motor control 
of the upper limbs was comparatively 
more intact in children with konzo than 
other global motor proficiency domains, 
such as strength and agility and body 
coordination. This is consistent with 
what is known in terms of the neuro-
motor pathology of the disease, which 
primarily involves paraparesis to the 
lower limbs. The KABC-II MPI and BOT-
2 total scores together were signifi-
cantly predictive of konzo status among 
our study children.

Evidence for a Subclinical Spectrum for Konzo

Previous electrophysiological studies suggest subclinical deficits in konzo. The structural brain and spinal mag-
netric resonance image of patients 
with konzo can appear normal, yet 
an evoked motor potential response 
from magnetic brain stimulation can 
be completely absent. Transcranial 
electrical stimulation and magnetic 
stimulation fail to evoke motor upper-
limb responses in subjects with konzo 
with preserved voluntary motion. Although patients with konzo can 
have normal voluntary movement and 
strength in their hands and arms, they 
may still lack normal magnetic evoked 
response potential to those limbs.

They may also be unable to make fine 
repetitive and alternating finger and 
hand movements in the absence of any 
cerebellar disease. These fine motor 
deficits of the upper limbs are much like 
the deficits observed with some of the 
items in the BOT-2 fine manual control 
global scale in the current study.

Frontal electroencephalography slowing 
occurs with konzo, as do cortical abnormalities of somatosensory evoked potentials, and abnormalities of visual 
evoked potentials. Because electrophysiological studies failed to find an 
association between their measures of 
abnormality and the severity of the 
disease based on the WHO functioning 
scheme, we proposed a neuro-
psychological evaluation to help gauge 
konzo severity. It is possible that the subtle and yet 
subclinical cassava-associated disease may be progressive in nature even from 
accumulated exposure to low-grade tox-
icity. The neuropsychological profile 
related to long-term toxic cassava exposure 
may differ only in deficit magnitude from 
the neuropsychological and neuromotor 
disabilities that result from abrupt corti-
cospinal damage at konzo onset. Such 
a profile may differ only in deficit mag-
nitude from the neuropsychological and 
neuromotor disabilities that result from 
corticospinal damage related to konzo 
or from a broader damage.

Nigerian tropical ataxic neuropathy, 
another cassava-associated neurologic 
disease, illustrates the possibility of a 
subclinical disease. Detailed neu-
ropsychological studies, combined 
with studies of biomarkers of cassava 
cyanogenic exposure and its bio-
logical effects, will help determine 
whether konzo and tropical ataxic neu-
ropathy are on a cassava-associated 
continuum of neurodegeneration. The 
extent of neurologic and neuropsy-
chological impairments at neurologic 
examination could be used together to 
anchor biomarker findings.
Global Health Importance

Much of sub-Sahara Africa is becoming increasingly dependent on high-yield varieties of cassava that thrive in ecologically degraded zones. Therefore, it is critical to continue brain/behavior research that will help us better understand its neurotoxic properties. The ability to document the more subtle CNS effects of cyanogenic toxicity comprehensive and sensitive neuropsychological batteries is of major public health importance globally and more specifically, in African regions dependent on bitter cassava.

CONCLUSIONS

This study is the first systematic attempt to characterize the neuropsychological profile of children subsisting on bitter varieties of cassava as the main source of food. We have not only documented specific domains of neurocognitive deficits in children with konzo, but have presented evidence for more pervasive neurocognitive effects (e.g., memory) for both children with and without konzo from a similar nutritional environment with pervasive risk factors for konzo onset. Our study is an important step in revealing the extent to which konzo extends into foundational neurocognitive domains providing the basis for critical functional domains for children.

A schematic in Fig 3 portrays how neuropsychological assessment can enhance the contextual understanding of konzo for children in the community. This figure was adapted from Fig 2 in Tshala-Katumbay et al.5 Neuropsychological assessment can bridge the disease severity with the child’s functional status in the community. This model uses a more complete ecological, environmental, agro-economic, and pathophysiologic context for understanding konzo. This framework can provide for a risk-assessment for konzo, leading to better public health surveillance and earlier detection in communities especially in need of targeted public health interventions to prevent konzo outbreaks.

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Neuropsychological Effects of Konzo: A Neuromotor Disease Associated With Poorly Processed Cassava


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