Cognitive impairment and quality of life of people with epilepsy and neurocysticercosis in Zambia

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Abstract

Cognitive impairment and quality of life (Qol) are important to assess the burden of epilepsy and neurocysticercosis (NCC), which are common but neglected in Sub-Saharan Africa. The aims of this study were to assess cognitive performance and Qol of people with epilepsy (PWE) in Zambia and to explore differences in PWE with and without NCC.

In this community based, cross-sectional case-control-study, 47 PWE and 50 healthy controls completed five neuropsychological tests (Mini Mental State Examination, Digit Span, Selective Reminding Test, Spatial Recall Test, Testbattery of Attentional Performance) and a WHO questionnaire of Qol. Comparisons were made between PWE (n=47) and healthy controls (n=50) and between PWE with NCC (n=28) and without NCC (n=19), respectively, using Analysis of Covariance (ANCOVA) and Linear Models (LM) while correcting for confounders such as age, sex and schooling years and adjusting for multiplicity.

Working memory, spatial memory, verbal memory, verbal learning, orientation, speech and language reception, visuo-constructive ability, and attentional performance were significantly reduced in PWE compared to healthy controls (ANCOVA and LM, $p<0.05$). Qol of PWE was significantly lower in three domains (psychological, social, environmental) and in overall Qol compared to healthy controls (ANCOVA, $p<0.05$). There were no significant differences between PWE with NCC and PWE without NCC detected by ANCOVA. Using LM, significant differences between the groups were detected in four tests, indicating worse performance of PWE without NCC in MMSE, Digit Span, SPART, and lower physical quality of life.

Epilepsy was found to be associated with cognitive impairment and reduced QoL. PWE due to NCC had similar cognitive impairment and Qol compared to PWE due to other causes. Further studies should investigate the role of different conditions of NCC and the role of seizures on cognition and Qol.

Key Words: Epilepsy; Neurocysticercosis; Cognitive impairment; Quality of life; Sub-Saharan Africa

Abbreviations

AED: Antiepileptic drug

ANCOVA: Analysis of Covariance

CT: Computed Tomography

BRB: Brief Repeatable Battery

EITB: Enzyme-linked immunoelectrotransfer blot

LM: Linear Model

MMSE: Mini Mental State Examination

mm: millimeter

ms: milliseconds

NCC: Neurocysticercosis

PWE: People with epilepsy

Qol: Quality of life

RHC: Rural Health Center

SD: Standard deviation

SPART: Spatial Recall Test

SPSS: Statistical Package for Social Science

SRT: Selective Reminding Test

SSA: Sub-Saharan Africa

T. solium: Taenia solium

TAP: Test Battery of Attentional Performance

WHOQOL-BREF: short WHOQOL questionnaire

1. Introduction

1.1. Neurocysticercosis and epilepsy: aspects of the burden of disease

Neurocysticercosis (NCC) is a parasitic infection of the central nervous system with a high prevalence in Sub-Saharan Africa (SSA) [1-3]. It has been identified as a frequent cause of epilepsy [4; 5]. Cognitive impairment is an important and very common co-morbidity of epilepsy in this region [6]. Two case-control studies in SSA found significantly impaired cognitive functions of people with epilepsy (PWE) in comparison to healthy controls, ranging from decreased intellectual abilities to mental retardation and dementia [7; 8]. However, cognitive impairment is also associated with NCC. Attentional and executive functions, visuo-constructive ability and memory skills are reported to be significantly more impaired in people with NCC compared to PWE and to healthy controls [9-11]. So far, there are few studies on the degree of cognitive impairment in people with NCC and epilepsy. All previous studies were conducted in Latin America and the examined PWE were treated with antiepileptic drugs (AED), so the effect of epileptic seizures might be obliterated.

Quality of life (Qol) is another aspect of the burden of disease. The few reports on Qol of PWE in Africa show considerably low scores and negative correlations with seizure frequency, seizure severity and living in a rural area [7; 12-14]. People with NCC also showed significantly lower scores of Qol compared to healthy controls in two studies in Latin America [11; 15]. To our knowledge, there are no reports from SSA on Qol for people with NCC who have epileptic seizures in comparison to PWE due to other reasons.

1.2. Aim of the study

The aim of the present work was to broaden the knowledge on cognitive impairment and Qol in PWE in general, as well as in PWE with and without NCC in SSA. Due to missing test norms for African populations, different cultural backgrounds and lack of habituation to testing situations, cross-cultural neuropsychological testing in SSA is challenging. Accordingly, one further aim of our work was to add experience in cross-cultural neuropsychological testing of PWE in a rural African area.

More specifically, in this study, cognitive performance and Qol of PWE with and without NCC in rural Zambia were assessed.

2. Methods

2.1. Study area and study setting

The study was conducted in the Mtandaza community of Katete district in the Eastern province of Zambia. Previous studies have suggested a high prevalence of *Taenia solium* (*T. solium*) cysticercosis in this area [16; 17]. Health care in this community is provided by the Mtandaza Rural Health center whose catchment population is approximately 20,000. The people in this area are predominantly Christians and practice subsistence agriculture raising animals like cattle, goats, pigs and chickens and growing crops like maize, groundnuts, bananas and cotton. Pigs are kept free-range and have access to the bushes that are used as latrines. The people's homes are of adobe, have few sanitary facilities with hand pumps being the source of water for most villages. This rural community was selected because of free-range pig keeping, reports of PWE, and the common observation of cysticerci in slaughtered pigs.

The Mtandaza Rural Health Center (RHC), that services the community, provided separate quiet rooms for the study. The study was conducted by a team of five local health workers (CB, CP, HT, MM, RT), three biomedical scientists (KEM, SG, NP), a neurologist (JB), and a psychologist (JW).

2.2. Recruitment of PWE and healthy controls

Fifty-two PWE were recruited and diagnosed as described by Mwape et al. (2015) in detail [5]. In short, 4443 people (above 5 years of age) in the Mtandaza Rural Health Centre catchment area were screened with an epilepsy questionnaire (added as Supplement File 1 in [5]) adapted from Birbeck and Kalichi [18] and Placencia et al. [19]. People with the highest probability of epilepsy were invited for further evaluation until 52 people were diagnosed with epilepsy according to the criteria of Winkler et al. [20] by a neurologist (JB).

Among the 52 PWE the proportion of people with NCC was assessed using the Del Brutto criteria [21] adapted by the use of serum antigen detection as major criterion as suggested by Gabriel et al. [22]. Serum for detection of specific antigen using B158/B60 monoclonal antibody-based enzyme-linked immunosorbent assay and anticysticercal antibodies using enzyme-linked immunoelectrotransfer blot (EITB) was available for all participants and computed tomography (CT) images in 48 PWE. PWE with "definite NCC" or with "probable NCC" were combined into one group (PWE with NCC). The serum analysis and the CT scans were performed several days after the neuropsychological tests and assessment of quality of life. Therefore the status of NCC was not known at the examination day.

Fifty healthy controls living in the same area as the PWE were recruited stepwise by matching them to groups of PWE with similar age, sex distribution, and schooling years. Information about the health status and demographic data was acquired either by a short questionnaire or by interview. All neuropsychological tests were administered between the 8th and 25th of September 2012.

Fifty PWE and 50 healthy controls completed all neuropsychological tests and the Qol questionnaire. All participants lived in Katete district in the Eastern province of Zambia. Two PWE were later diagnosed with inactive epilepsy, so they were excluded from the analysis. One person with epilepsy was excluded from the neuropsychological part of the study due to

a seizure during the examination. The results of remaining 47 PWE and 50 healthy controls were evaluated. Twenty-eight (59.6%) of the 47 PWE were diagnosed with NCC according to the adapted Del Brutto criteria [21; 22]. Fifteen had the diagnosis of “Probable NCC” and 13 “Definitive NCC”.

2.3. Tests and instruments

The Mini Mental State Examination (MMSE) [23] is a short test that assesses cognitive functions like orientation to time and space, memory and recall, alertness, speech, and language reception. It was chosen because it is used very often in clinical practice and was found to reliably differentiate between people with and without cognitive impairment [24]. The MMSE was modified following the suggestions of Kabir et al. [25] for the use with less educated participants. Some extra adaptations to local circumstances were made (see supplement material, table S1).

The Selective Reminding Test (SRT) and the Spatial Recall Test (SPART) from the Brief Repeatable Battery (BRB) were used to assess verbal learning and memory (SRT) and spatial memory (SPART) [26]. The SRT word list was translated into the local language Chewa and some words were adapted to local circumstances (see supplement material, table S2). The participants were asked to repeat twelve unrelated words immediately after listening to them. For the SPART, participants were asked to remember the location of ten crown caps on a checkerboard. Between the first six trials of the SRT respectively three trials of the SPART and their delayed recall conditions was a time gap of about 20 minutes.

The Digit Span from the Wechsler Memory Scale [27] was used to assess non-verbal short term memory. To assess basic attentional performance, the test “Alertness” from the computer-based Test Battery of Attentional Performance (TAP) [28] was used. Participants were asked to react as quickly as possible to a visual stimulus on the screen by pressing a button (test without warning tone assessed tonic alertness). In a second test, a warning tone is presented before the visual stimulus and again participants were asked to react as quickly as possible to the visual stimulus by pressing a button (test with warning tone assessed phasic alertness). All participants performed test trials until they understood how to perform this computer-based test.

Qol was assessed by the short version of the WHOQOL questionnaire (WHOQOL-BREF) [29]. The WHOQOL-BREF is an international, cross-culturally applicable instrument that consists of 26 items. It assesses overall Qol and four domains of Qol, namely “physical” and “psychological health”, “social relationships”, and “environment”. The questions were translated into Chewa by local health workers who assisted with completing the questionnaire. In addition, participants were asked to mark their overall Qol on a visual analogue scale (Qol scale). The test score of the Qol scale was the millimeter distance from the left pole (0 mm = Qol 0) to the point the participant marked on the scale (e.g. 67 mm = Qol 67), the maximum was 100.

The tests were conducted in the following order: MMSE, SRT (six trials), SPART (three trials), Digit Span (forward and backward), TAP Alertness, SRT Delayed Recall (one trial), SPART Delayed Recall (one trial).The WHOQOL-BREF was completed either before or after the neuropsychological examination. In total, the neuropsychological examination lasted around 40 minutes.

2.4. Data analysis

Results of all neuropsychological tests and all scores of the WHOQOL-BREF questionnaire as well as the Qol scale were compared between PWE and healthy controls. Before the analyses, missing values were imputed using Multiple Imputation [30].

Data were analyzed by one-way Analysis of Covariance (ANCOVA) and Linear Models (LM) to determine statistically significant differences between the two groups on all test scores while controlling statistically for confounding by age, sex and school years. Differences between PWE with NCC and PWE without NCC were tested in a similar way. To control the false discovery rate, a Benjamini-Hochberg adjustment was conducted [31]. Demographic data were analyzed by t-tests and Fisher's exact tests. Statistical significance was arbitrated at the 5% level for all calculations. All analyses were performed using the software packages SPSS 19 (Statistical Package for Social Science) [32] and R 3.3.1 [33; 34]. For all scores of the TAP Alertness test T-values were calculated and compared with the given norms. Data are presented as means ± standard deviation (SD).

2.5. Ethical considerations

The study obtained ethical approval from the University of Zambia Biomedical Research Ethics Committee (IRB0001131) and the Ethical Committee of the University of Antwerp, Belgium (ITG:12084813).All PWE and healthy controls participated in the study voluntarily. Confidentiality of information was guaranteed. Participants were informed about their right to refuse to participate at any time without giving reasons. Written informed consent was obtained from all participants who took part in the medical and neuropsychological examinations. To the less educated participants, study information was read. Persons who could not write their name gave their consent by fingerprint. Under age children gave assent and written consent was obtained from their parents. In collaboration with the regional health center Mtandaza all patients received free medical follow up and antiepileptic drugs according to national guidelines.

3. Results

3.1. Demographics

The demographic characteristics of PWE (n=47) and healthy controls (n=50) are presented in table 1. There were no statistically significant associations between the epilepsy status and gender distribution (Fisher's exact test, $p>0.5$), age (t-test, $p>0.9$), and educational level (t-test, $p>0.1$). Likewise, there were no significant associations between epilepsy status and marital status (Fisher's exact test, $p=0.254$) and number of children (t-test, $p>0.9$).

Table 1 also presents the demographic characteristics of PWE with NCC (n=28) in comparison with PWE without NCC (n=19). No significant differences in age (t-test, $p=0.87$), sex (Fisher's exact test, $p=0.24$), school years (t-test, $p=0.23$), number of children (t-test, $p=0.51$) and marital status (Fisher's exact test, $p=0.59$) were found between PWE with NCC and those without NCC.

3.2. Clinical characteristics and CT scan results

The age of epilepsy onset was 17.9 years in average in PWE. There were no significant differences (t-test, $p=0.97$) between PWE with NCC (mean age of epilepsy onset: 18 years) and PWE without NCC (mean age 17.8 years). Earlier age of onset was significantly correlated with lower Qol physical ($r(47)=-0.479$, $p<0.01$) and lower scores in Qol rated by the Qol scale ($r(45)=0.403$, $p<0.01$). No other correlations were statistically significant.

Regarding seizure frequency, PWE reported a mean of 4.8 seizures per month. No significant differences between PWE with NCC (4.1 seizures per month) and PWE without NCC (5.6 seizures per month) were found (t-test, $p=0.41$). No statistically significant correlation between seizure frequency and cognitive impairment was found. There was a significant correlation between psychological Qol and seizure frequency ($r(40)=-0.443$, $p<0.01$). Higher seizure frequency was associated with lower psychological Qol.

AED use was reported by 21 PWE (44.7%) altogether, 9 PWE with NCC (32.1%) and 12 PWE without NCC (63.2%). The dose of AED of all patients was lower than recommended for the respective drug. There were no significant differences in test performance and Qol between PWE using AED and PWE not using AED (t-test, $p>0.5$).

In the group of PWE without NCC 16 had a normal CT scan, one a hydrocephalus, one posthemorrhagic defects occipital in both sides, one a probably postischemic lesion in the capsula right side and two had single hyperdense lesions that could be a calcification due to NCC (one right temporal, one next to posterior horn of left side ventricle) but other differential diagnosis are possible. In the group of PWE with NCC two had active cysts and inactive NCC lesions combined, 12 had only calcifications highly suggestive of NCC, one had an ischemia in the border zone of the middle and anterior cerebral artery, 9 had a normal CT scan, one had a possible calcification left temporal but other differential diagnosis were possible and one CT scan had many movement artifacts so the interpretation was difficult. Of the 12 patients with calcifications highly suggestive of NCC 4 had more than 10 lesions, one had 10 lesions, one had 7 lesions, one had 4 lesions, 3 had three lesions and 2 had two lesions. The two patients with active and inactive lesions had 1 right occipital cyst and more than 10 calcifications on both sides and 3 cysts and 4 calcifications on both sides, respectively.

3.3. Neuropsychological performance and Qol of PWE and healthy controls

PWE had lower overall means than healthy controls in all neuropsychological tests and Qol scores, as presented in table 2.The comparisons indicated significant differences between PWE and healthy controls on MMSE, Digit Span, all scores of SRT, all scores of SPART, and all TAP Alertness scores after controlling for age and school years (ANCOVA, $p<0.05$) and after controlling for age, school years, and sex (LM, $p<0.05$ see table 2).

PWE showed lower scores in the WHOQOL_BREF scales psychological Qol, social Qol, environmental Qol, and overall Qol. The analyses revealed statistically significant differences between PWE and healthy controls in psychological Qol, social Qol, environmental Qol, and overall Qol after controlling for age and school years (ANCOVA, $p<0.05$) and after controlling for age, school years, and sex (LM, $p<0.05$).

No significant effects of epilepsy were found on physical Qol after controlling for age and school years (ANCOVA, $p>0.05$), however, results of LM indicated a significant effect of epilepsy on physical Qol after controlling for age and school years as well as after controlling for age, school years, and sex (LM, $p<0.05$, see table 2). No significant effects of epilepsy were found on Qol rated by the Qol visual analogue scale after controlling for age and school years (ANCOVA, $p>0.05$) and after controlling for age, school years, and sex (LM, $p>0.05$ see table 2).

3.4. Neuropsychological performance and Qol of PWE with and without NCC

The results for the comparisons between PWE with NCC and PWE without NCC are also presented in table 2. LM found significant differences in the neuropsychological tests MMSE ($p=0.04$), Digit Span ($p=0.01$), SPART ($p=0.02$), both when controlling for age and school years and for age, school years, and sex. PWE with NCC performed better than those without NCC in these tests. No significant differences were found by LM in the other tests. Based on the results from ANCOVA, no significant differences between PWE with NCC and those without NCC in neuropsychological test performances were found.

Regarding Qol, one significant difference in physical Qol was found by LM($p=0.01$), both when controlling for age and school years and for age, school years, and sex. PWE with NCC reported better physical Qol than PWE without NCC. In all other Qol scores, no significant

differences were detected by LM. Based on ANCOVA, no statistically significant differences in Qol were found between the groups.

3.5. Comparison of standard values with European norms

The standardized T-scores were calculated from the TAP Alertness raw scores. All mean T-scores were lower than 40, which indicates that the reaction times and standard deviations of reaction times of both PWE and healthy controls are more than one standard deviation below average compared to European test norms ($T<40=z<-1$). No other test scores were compared to European test norms because of the use of adapted versions of tests and lack of test norms.

4. Discussion

In this study, cognition and Qol in PWE and healthy controls in a rural area in Eastern Zambia were assessed. Additionally, the role of NCC in neuropsychological performance and Qol was analyzed.

The results (see 3.3.) indicate that PWE in Eastern Zambia show significantly lower cognitive performance than healthy controls after controlling for influences of age and education as well as age, education, and sex. These findings are consistent with previous results showing that cognitive impairment in PWE is severe in SSA [6]. However, in several studies from Latin America, PWE and healthy controls showed similar results in cognitive performance [9-11]. All patients with epileptic seizures in the aforementioned studies were treated with AED whereas in the current study, no participant was on sufficient antiepileptic medication. Seizure control might improve cognition in PWE [35].Another factor that might play a role in the degree of cognitive impairment in PWE is the age of onset [36]. In the current study, the age of onset of epilepsy was not significantly associated with cognitive impairment.

PWE without NCC showed significantly worse performance in MMSE, Digit Span and SPART compared to PWE with NCC, as detected by one of the analysis methods (see 3.4.). By the second analysis method (ANCOVA) there were no significant differences in test performance found between PWE without NCC and those with NCC. This is in accordance with the results of another study revealing similar cognitive performances of PWE without NCC and those with NCC [37]. In contrast, two previous studies in Latin America found that people with NCC were more impaired in cognition than PWE without NCC [9; 11].

It is still unknown what factors of NCC might account for cognitive impairment. So far, no significant associations between cognitive performance and number of cysts, localization of cysts in the brain, or type of lesion were found [9; 10], however, studies including all types of NCC are needed to further evaluate causes of cognitive impairment.

Assessing neuropsychological performance in a cross-cultural setting is difficult, especially with a high proportion of less educated participants. The use of standardized tests that were developed in North America and Europe might not be appropriate for the described sample. The participants of our study came from a rural area and both PWE and healthy controls, respectively, reported few schooling years (2.7 in average). The scores of healthy controls were not located within the spectrum considered as normal according to European and American standard values. Effects of schooling on neuropsychological test performance have been described before [38]. It is very likely that the participants were not used to these kinds of tests and the test conditions.

Although some tests were culturally adapted before administration and translated from English to the local language Chewa, misunderstandings cannot be ruled out. For example, during the administration of the MMSE, participants were asked to follow the instruction "take this paper in your right hand" but some individuals would take the paper with both hands because they considered it as impolite to take something with only one hand. According to Nell et al. [39], even the use of culturally adapted neuropsychological tests is difficult, because culture still has an impact on test performances. The constructs we intended to measure might not be transferable, which could have affected the construct validity. Therefore, we conclude that norms used in high income countries are not applicable and the healthy control group we used to compare with PWE in this study was essential to interpret neuropsychological results.

Our findings demonstrate that PWE both with and without NCC are significantly more impaired in Qol than healthy controls. This is consistent with previous findings on Qol of PWE in SSA [7; 12; 13] which indicate that lack of treatment and thus poor seizure control, as

well as stigmatization, social exclusion, unemployment, and low level of education are associated with low quality of life. The Qol of NCC patients in comparison to healthy controls was significantly reduced according to a study from Mexico [15]. 31% of these NCC patients also had epilepsy and NCC patients with epilepsy were more affected in the mental health domains than patients with NCC only.

PWE with NCC and PWE without NCC reported similar impairment in most domains of Qol in our study. Another study conducted in Latin America found similar levels of Qol in NCC patients (without epilepsy) and PWE (without NCC) and in Latin America [40]. This indicates that epilepsy as well as NCC is associated with Qol to a similar degree.

A number of limitations might have influenced the results obtained. Epilepsy cases were detected by a screening questionnaire and mainly severe epilepsy cases were included in the study. Accordingly, a possible recruitment bias towards more severe cases and probably higher impairment might have influenced the results [5]. Thus, generalization of our results may apply to severe cases of epilepsy only.

Furthermore, we did not distinguish between the different subtypes of epilepsy; neither did we stratify the patients according to seizure frequency, because this study was designed as a pilot study with a small number of participants. We do not know if these aspects differed between the groups PWE with NCC and PWE without NCC and how they might have influenced the results. As reported by Rodrigues et al. [10], the stage of NCC might account for the degree of cognitive impairment, indicating that cognitive impairment in the chronic calcified stage of NCC, in which epilepsy usually develops, is less severe than in an earlier stage. We did not investigate different stages of NCC in our study.

In addition, the sample size of PWE without NCC (n=19) was small. The comparison between PWE with NCC (n=28) and PWE without NCC may be affected by this limitation. It was not

possible to directly match the PWE with NCC with healthy controls because at the time of neuropsychological evaluation and Qol assessment the NCC status was not known. Because of the same reason PWE with and without NCC were not matched for age, gender and number of school years, but the named variables were used as covariates in the analysis.

5. Conclusion and suggestions for further research

Our findings are the first to show cognitive impairment and Qol reduction of PWE with and without NCC in Sub-Saharan Africa. This work contributes to assessing the burden of disease of NCC and epilepsy, which is necessary to allocate sufficient resources to prevent the disease.

Studies with an additional focus on NCC patients without epilepsy could bring light on the role of seizures on cognition and Qol in people with NCC. One important goal should be to investigate the impact of the number of cysts, localization of cysts, the stage of NCC and the age of onset of epilepsy.

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Disclosure of Conflicts of Interests

None of the authors has any conflict of interest to disclose.

Ethical Publication Statement

We confirm that we have read the Journal´s position issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Table 1.

Demographic data of people with epilepsy (PWE) and healthy controls (HC).

	PWE (n=47) Numbers and percentage or Means ± standard deviations	*PWE with NCC (n=28) Numbers and percentage or Means ± standard deviations*	*PWE without NCC (n=19) Numbers and percentage or Means ± standard deviations*	**HC (n=50)** Numbers and percentage or Means ± standard deviations
Sex				
Female:	23 (48.9%)	*12 (42.9%)*	*11 (57.9%)*	25 (50.0%)
Male:	24 (51.1%)	*16 (57.1%)*	*8 (42.1%)*	25 (50.0%)
Mean age:	32.9±15.5	*33.3±16.3*	*32.5±14.7*	33.1±14.8
Mean number of school years:	2.3±2.7	*2.7±2.9*	*1.7±2.3*	3.1±2.8
Marital status				
Unmarried:	18	*13*	*8*	9
Married:	21	*10*	*8*	24
Divorced:	5	*2*	*3*	8
Widowed:	2	*2*	*0*	3
Unknown:	*1*	*1*	*0*	*6*
Mean number of children:	3.2±2.4)	*3.4±2.7*	*2.9±2.2*	3.2±2.6

There were no statistically significant differences between PWE and HC as well as between PWE with NCC and PWE without NCC ($p>0.05$).

Table 2.

Results from the neuropsychological tests: Mean values, standard deviations and adjusted p-values from Analysis of Covariance (ANCOVA) and Linear models (LM) for people with epilepsy (PWE) versus healthy controls (HC) and PWE without Neurocysticercosis (NCC) versus PWE with NCC.

Variable	**PWE (n=47)** Means ± standard deviations	**HC (n=50)** Means ± standard deviations	**p-values ANCOVA** (co-variates: age, number of school years)	**p-values LM** (co-variates: age, sex, number of school years)	**PWE without NCC (n=19)** Means ± standard deviations	**PWE with NCC (n=28)** Means ± standard deviations	**p-values ANCOVA** (co-variates: age, number of school years)	**p-values LM** (co-variates: age, sex, number of school years)
Mini Mental State Examination	22.2 ± 5.1	24.9 ± 1.9	**P=0.01***	**p=0.00***	21.3 ± 5.2	22.8 ± 5.1	**p=0.83**	**p=0.04***
Digit Span	3.9 ± 2.7	5.3 ± 2.0	**p=0.02***	**p=0.00***	2.8 ± 2.3	4.5 ± 2.8	**p=0.24**	**p=0.01***
Selective Reminding Test: Long term storage	6.9 ± 3.3	8.2 ± 2.9	**p=0.04***	**p=0.01***	5.7 ± 3.3	7.6 ± 3.2	**p=0.24**	**p=0.23**
Selective Reminding Test: Consistent long term retrieval	2.8 ± 2.9	4.2 ± 2.6	**p=0.02***	**p=0.00***	1.9 ± 2.4	3.4 ± 3.2	**p=0.24**	**p=0.10**
Selective Reminding Test: Delayed Recall	6.0 ± 3.3	7.5 ± 2.3	**p=0.02***	**p=0.01***	5.5 ± 3.3	6.4 ± 3.2	**p=0.79**	**p=0.30**
Spatial recall test	11.5 ± 4.9	15.8 ± 4.3	**p<0.01***	**p=0.00***	10.9 ± 3.7	11.9 ± 5.6	**p=0.99**	**p=0.01***
Spatial recall test: Delayed recall	3.9 ± 1.8	5.1 ± 1.9	**p=0.01***	**p=0.01***	3.7 ± 1.5	3.9 ± 2.0	**p=0.83**	**p=0.72**
Tonic Alertness (TAP): Median of reaction time	588.5 ± 228.4ms	462.3 ± 185.1ms	**p=0.01***	**p=0.01***	625.0 ± 244.6 ms	563.8 ± 217.8 ms	**p=0.83**	**p=0.88**
Tonic Alertness (TAP): Standard deviation of reaction time	138.5 ± 64.5 ms	94.3 ± 63.8 ms	**p=0.01***	**p=0.02***	139.9 ± 57.8 ms	137.6 ± 69.7 ms	**p=0.99**	**p=0.28**

Phasic Alertness (TAP): Median of reaction time	538.3 ± 185.1 ms	426.8 ± 186.3ms	**p=0.01***	**p=0.03***	525.2 ± 179.4 ms	547.2 ± 191.6 ms	**p=0.83**	**p=0.39**
Phasic Alertness (TAP): Standard deviation of reaction time	139.8 ± 71.9ms	95.9 ± 58.7ms	**p<0.01***	**p=0.01***	143.6 ± 81.7 ms	137.3 ± 66.0 ms	**p=0.99**	**p=0.56**
Quality of life: physical	66.4 ± 14.1 ms	68.0 ± 14.1 ms	**p=0.66**	**p=0.01***	63.4 ± 14.5	68.4 ± 13.8	**p=0.63**	**p=0.01***
Quality of life: psychological	57.8 ± 17.9 ms	67.0 ± 12.9 ms	**p=0.02***	**p=0.01***	49.8 ± 11.5	63.2 ± 19.6	**p=0.24**	**p=0.07**
Quality of life: social	64.2 ± 27.7	79.5 ± 19.2	**p=0.01***	**p=0.01***	56.2 ± 27.4	69.6 ± 26.9	**p=0.39**	**p=0.12**
Quality of life: environmental	52.8 ± 15.54	61.4 ± 12.5	**p=0.01***	**p=0.01***	47.2 ± 12.2	56.6 ± 16.6	**p=0.24**	**p=0.07**
Quality of life: overall	54.4 ± 24.3	65.2 ± 20.3	**p=0.02***	**p=0.03***	58.1 ± 25.4	51.9 ± 23.7	**p=0.83**	**p=0.30**
Quality of life scale	62.3 ± 35.3 mm	69.1 ± 28.3 mm	**p=0.29**	**p=0.06**	51.3 ± 38.3 mm	69.7 ± 31.6 mm	**p=0.24**	**p=0.10**

Supplement material

Table S1.
Differences between Mini Mental State Examination (MMSE), Bangla adaptation of Mini Mental State Examination (BAMSE) and Zambia adaption of MMSE

	MMSE Scores max.: 30	**BAMSE** Scores max.: 30	**Zambia-adapted MMSE (version used in our study)** Scores max.: 28
Orientation to time	Season, month, time of day, day, date (5)	Season, month, time of day, day, date (5)	Season, month, time of day, day (5)
Orientation to place	Country, district, village/city, area/ street/neighbourhood, house/place. (5)	Country, district, house/place, area/street/neighbourhood (asked in reverse order) (5)	Country, district, house/place (3)
Three objects registration	Pot, bed, umbrella (3)	Mango, flower, fish (3)	Mango, flower, fish (3)
Calculation and Attention	Spell `HAJABARALA' backwards (5) OR Subtract 7 from 100, then 7 from that number, and so on, five times. (5)	Name the days of the week backwards (eg before Sunday comes Saturday, and before Saturday comes . . .?). (5) OR `A man has 20 taka for rickshaw fare. Every day, he spends 3 taka for rickshaw fare. After spending the first day's rickshaw fare, he will be left with 17 taka. How much money will be left after the next day's rickshaw fare, and the next day's fare ....' and so on, five times. (5)	Name the days of the week backwards (e.g. before Sunday comes Saturday, and before Saturday comes . . .?). (5)
Recall	Name the three objects learned earlier. (3)	Name the three objects learned earlier. (3)	Name the three objects learned earlier. (3)
Naming	Pencil and watch. (2)	Glass and spoon. (2)	Pencil and watch. (2)
Repetition	`Neither this nor that' (1)	`Neither this nor that' in Bangla (1)	'She doesn't lend him any money anymore', read out in the local language Chewa: 'Sini zakubwerekansondalama' (1)
Language/ comprehension	Read and follow command `Close your eyes'. (1)	The individual is asked to follow the interviewer who will raise his/her right hand. (1)	The individual is asked to follow the interviewer who will raise his/her right hand. (1)
Three-step task	The individual is asked to follow the interviewer's instruction: `Take the paper in your right hand. Fold the paper in half. Put the paper on the floor'. (3)	The individual is asked to follow the interviewer's instruction: `Take the paper in your right hand. Fold the paper in half. Put the paper on the floor'. (3)	The individual is asked to follow the interviewer's instruction: `Take the paper in your right hand. Fold the paper in half. Put the paper on the floor'. (3)
Sentence construction	The individual is asked to write a sentence. (1)	The individual is asked the question: `If you did not know my name how would you find out my name?' (1)	The individual is asked the question: `If you did not know my name how would you find out my name?' (1)
Copying a figure	The individual is asked to copy a figure of overlapping pentagons. (1)	The individual is asked to construct a figure with sticks following a laid out construction of overlapping pentagons. (1)	The individual is asked to construct a figure with sticks following a laid out construction of overlapping pentagons. (1)

In brackets: Possible scores

Table S2.

Differences between the original wordlist and the Zambia adaptation of Selective Reminding Test (SRT)

	SRT Original Wordlist	**Zambia-adapted Wordlist in local Chewa language and English (in brackets)**	
1	Christmas	Khisimisi	(Christmas)
2	Predator	*Mbewa*	*(Rodents)*
3	Policeman	Polisi	(Policeman)
4	Doll	*Chalich*	*(Church)*
5	Meet	Nyama	(Meet)
6	Mother	Amai	(Mother)
7	Gift	*Mpwando*	*(Party)*
8	Bird	Mbalame	(Bird)
9	Elephant	Njobvu	(Elephant)
10	Soup	Supu	(Soup)
11	Wool	*Cotoni*	*(Cotton)*
12	Animal	Chinyama	(Animal)

italic: changed words in the Zambia-adapted wordlist of SRT