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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 (SSA). 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 (MMSE), Digit Span, Selective Reminding Test (SRT), Spatial Recall Test (SPART), Test Battery of Attentional Performance (TAP)) and a World Health Organization (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 (LMs) 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, visuoconstructive ability, and attentional performance were significantly reduced in PWE compared with healthy controls (ANCOVA and LM, $p < 0.05$). Quality of life of PWE was significantly lower in three domains (psychological, social, environmental) and in overall Qol compared with 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 Qol.

Epilepsy was found to be associated with cognitive impairment and reduced Qol. People with epilepsy due to NCC had similar cognitive impairment and Qol compared with 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.

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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.

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1. Introduction

1.1. Neurocysticercosis (NCC) and epilepsy: aspects of the burden of disease

Neurocysticercosis 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 comorbidity of epilepsy in this region [6]. Two case-control studies in SSA found significantly impaired cognitive functions of people with epilepsy (PWE) in comparison with 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, visuoconstructive ability, and memory skills are reported to be significantly more impaired in people with NCC compared with 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 (AEDs), 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 with 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 with 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]. Healthcare in this community is provided by the Mtandaza Rural Health Center (RHC) 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 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. in detail [5]. In short, 4443 people (above 5 years of age) in the Mtandaza RHC 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. People with epilepsy 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 Qol. 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 were a time gap of about 20 min.

The Digit Span from the Wechsler Memory Scale [27] was used to assess nonverbal 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

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