

Nodding syndrome: origins and natural history of a longstanding epileptic disorder in sub-Saharan Africa

Spencer PS¹, Palmer VS², Jilek-Aall L³

1. Department of Neurology, School of Medicine; Senior Scientist, Center for Research on Occupational and Environmental Toxicology, and Director, Global Health Center, Oregon Health & Science University, 3181 S.W. Sam Jackson Park Road, L356, Portland, Oregon 97239, USA
2. Global Health Center, Oregon Health & Science University, 3181 S.W. Sam Jackson Park Road, L356, Portland, Oregon 97239, USA
3. Clinical Professor Emerita, University of British Columbia, 571 English Bluff Road, Delta, B.C. Canada V4M 2M9

Abstract

Background: Repetitive involuntary head nodding was first reported in the 1960s in the Wapogoro tribe of Tanzania.

Objectives: We describe the natural history of head nodding in the Wapogoro tribe, with special reference to the earliest reported dates of onset.

Methods: We analyzed clinical data from 150 historical patients seen between 1960 and 1971.

Results: Head nodding with or without *grand mal* convulsions was present in 33/150 (~20%) cases, was mostly familial and equally distributed by gender. Age at onset of head nodding ranged from 2-22 years (mean: ~10 years) in the period 1934-1962. Head nodding preceded onset of *grand mal* convulsions by up to 12 months, and motor and psychomotor deficits indicative of brain damage developed with time. Fourteen of the 33 cases died at 13-39 years of age (mean: ~20 years) while nineteen aged 16-28 years (mean: ~16 years) were still alive.

Conclusion: Historical accounts of head nodding (*amesinziya kichwa*, Swahili) among the Wapogoro tribe fit the August 2012 World Health Organization (WHO) case definition of probable Nodding Syndrome. Reported to have existed in this population for at least 80 years, Nodding Syndrome is a progressive seizure disorder that leads to generalized convulsions (*kejafa*), brain damage and death.

Key words: Tanzania, *amesinziya kichwa*, primary generalized epilepsy, seizure disorder, parkinsonism

African Health Sciences 2013; 13(2): 176 - 182 <http://dx.doi.org/10.4314/ahs.v13i2.1>

Introduction

Nodding Syndrome is a generalized seizure disorder that appeared *de novo* in 1991 in Western Equatoria, South Sudan, and some years later in northern Uganda.^{1,2} The affected populations were at high risk for infectious disease because of inactive vaccination and drug prophylaxis programs, severe shortages of food and medicine, prolonged civil disturbance, and repeated displacement from their homes. A case-control study carried out in 2002 in then-southern Sudan found a positive case association with two parasitic nematodes (*Onchocerca volvulus*, *Mansonella perstans*) and an inverse association with childhood measles infection. Among non-infectious environmental exposures, food contamination with fungal neurotoxins could not be excluded^{2,3}. Others have suggested without evidence an etiologic role for heavy metals, pesticides, or

warfare chemicals.

Clues as to the origin, cause and natural history of Nodding Syndrome may be gained from studies of a Tanzanian focus of epilepsy⁴, where, in the 1960s, one of us (L. J-A.) observed repetitive head nodding (*amesinziya kichwa*, Swahili) among members of the rural Wapogoro community of the Mahenge highlands of Tanganyika (now the United Republic of Tanzania),⁵ where malnutrition, infectious disease (notably onchocerciasis) and *grand mal* convulsions (*kejafa*, Swahili) are highly prevalent⁵⁻⁷. While the clinical features, treatment and course of epilepsy among patients seen at the Mahenge Epilepsy Clinic have been extensively documented elsewhere, including a 30-year follow-up in 1992 of the available caseload⁸, there has been no systematic examination of clinical notes from the early years (1959 onwards). The objective of this study is to illuminate the traceable origins, clinical course and outcome of *amesinziya kichwa* among the Wapogoro. Based on the analysis of data extracted from clinical notes of 150 patients seen by L. J-A between 1960 and 1971, we conclude that *amesinziya kichwa*, and hence Nodding Syndrome, has been present in this community for at least 80 years. This conclusion should be helpful in distinguishing between etiologic hypotheses for the recent epidemics of Nodding Syndrome in northern Uganda and South Sudan.

*Corresponding author:

Prof. Peter S. Spencer *PhD, FANA, FRCPath*
Global Health Center, L356
Oregon Health & Science University
Portland, Oregon 97239
USA
T: 001-503-209-0986
Email: spencer@ohsu.edu

Methods

In the 1960s, as today, the Wapogoro tribe lived in the Mahenge mountains, a remote area of central Tanganyika. While the history of these people is unclear, they appear to have lived with other tribes on the lowland Ulanga plain until 1750, when the chief began to move his clansmen to the mountains. Some time later (*circa* 1850), the Wapagoros were reported to have fled to the Mahenge mountains to avoid conflict with the Ngoni, an aggressive tribe that had moved into the Ulanga plain. The Wapagoro settled in small villages spread out in isolated regions in the mountains.^{9,10}

In 1959, L. J-A established an outpatient clinic for the Wapogoro tribe at the Kwiwo Mission in Mahenge. Staffed by a single registered nurse, the mission station provided medical care for people who came for treatment from mountain villages and for the homeless and handicapped. Conditions in the clinic were primitive (no electricity and running water), and medical equipment was confined to a stethoscope, reflex hammer, thermometer and simple microscope. Several adult patients presented with severe burn wounds acquired by falling into a fire during a convulsive attack (*kejafafa*). Since the community feared *kejafafa* and considered the disorder to arise from an evil spirit that could be passed from one person to another, *kejafafa* victims were shunned and rescued from fire by only the closest of relatives. While traditional medical healers provided treatment for burns, the community considered *kejafafa* untreatable until L.J-A began to dispense phenobarbital, which successfully reduced or eliminated *grand mal* seizures.⁸

We analyzed the unnamed standardized case records of ~180 patients with *kejafafa* seen by L.J-A at the Mahenge clinic between 1960 and 1971, with follow-up for up to 10 years. At initial presentation, each patient was given a simple physical, neurological and psychological examination, the nutritional state assessed by observation, a blood sample taken to determine hemoglobin status, and treatment (including iron, phenobarbital) initiated as required. Patients were followed periodically by the nurse (monthly where possible) and antiepileptic therapy adjusted as directed by L.J-A. Histories given by the patient in Swahili were simultaneously translated to and recorded in English and later summarized by L.J-A on a standard record sheet.

Thirty of the 180 cases were omitted for lack or paucity of recorded data. Data for 150 cases included: (a) family and patient history, the latter including sex, age, and year of onset; age at first observation, follow-up duration, and age at death; history of birth trauma, antecedent illnesses or febrile convulsions; frequency, type, laterality, and description of attacks, including aura, head nodding, and state of consciousness; (b) physical examination for nutritional state, liver and spleen size, and skin burns, (c) neurological examination of cranial and peripheral nerves; for pyramidal, extrapyramidal, or cerebellar signs; and for higher cortical function (intelligence, psychological function), and (d) laboratory examination of blood for %

hemoglobin (Hgb), where 80% Hgb was taken as within normal limits (wnl), <60% Hgb as evidence of anemia, and <40% Hgb as indicating the need for iron supplementation.

Results

Head nodding with or without (n=4) *grand mal* seizures was reported in 33/150 cases (16 females and 17 males) (table 1), while the balance at the time of their clinic visit had mostly primary generalized seizures (convulsion group) without head nodding. The latter were born between 1911 and 1960, and the head-nodding group between 1924 and 1955. The earliest report (1934) of head nodding involved a 10-year-old female who died at age 39. While almost all head-nodding cases (~95%) were children of epilepsy-free parents, most had familial associations with *kejafafa* and/or *amesinziya kichwa* either via affected siblings or through either parent. One case in the convulsion group had a sibling with head nodding, as well as paternal relatives who suffered from convulsions. The age of onset of seizures for the convulsion group ranged from 2 months to 36 years, while those cases with head nodding ranged from 2-22 years (mean: ~10 years). Nineteen of the 33 nodding cases were aged 16-28 years (mean: ~16 years) and 14 had died at 13-39 years of age (mean: ~20 years) as indicated in table 1. Most patients died at home and no autopsies were performed, of 26 cases in which a cause of death was noted, 9 had an unknown cause, 7 died in *status epilepticus*, and individual cases died in states associated with "bad headaches and frequent seizures", "neglect and epilepsy", "most probably from epilepsy", "complete mental derangement", marasmus with and without leprosy, "high fever" (probably malaria), "pneumonia", "after 2 days of unconsciousness" and "or fell into fire". Unlike the *kejafafa* group, where drowning of adults was not infrequently reported,⁸ children with *amesinziya kichwa* were guarded and restricted to their homes.

In the head-nodding group, drowsiness, narcolepsy or head nodding frequently preceded onset of *grand mal* convulsions (when present) by up to 12 months. When recorded, onset of head nodding occurred while eating and/or at night, with nodding occurring before, between, or following *grand mal* seizures. Some patients reported experiencing an aura (n=12). Physical examination of head-nodding cases typically revealed a thin, neglected child, often small and underdeveloped for age, and in either a poor (n=18), good (n=14) or unrecorded (n=1) nutritional state (table 2). Burn scars and tongue scars were present in some. Anemia was evident in all but 3 cases, and liver and spleen examination was usually unremarkable. Neurological signs included extremity hyperreflexia (n=9) and areflexia (n=4) usually involving all extremities, but pathological reflexes (e.g. extensor plantar) pathognomonic of pyramidal-tract dysfunction were absent.

Table 1: Head nodding cases: gender, lifespan, onset year and age, familiarity, nutritional status, exam age, follow-up and notable history

Case	Sex No	DoB DoD	Onset year (age) and familial link	Age at observation/ follow-up period	History of notable events/observations
1	F	1924-63	1934 (10) S	37/2	Drowsy from birth, pre-school febrile convulsions
2	F	1936-63	1942 (6) P,M,S	25/2	Head nodding when eating
3	M	1934-	1943 (9) P,S	27/10	Nodding for 1 month before convulsions
4	M	1943-65	1952 (9) P	18/4	Head nodding at age 5
5	M	1948-68	1953 (5) M	13/7	Febrile convulsions as infant
6	F	1946-66	1953 (7) M,1/2S	15/5	Nodding for 1 year before convulsions
7	F	1951-	1953 (2) S	12/NS	Nodding on eating, no convulsions
8	F	1944-61	1954 (10) M	17/2mo	Febrile convulsions as child. Nods to right side first
9	M	1933-	1955 (22) M,S	28/10	Head nodding between convulsions
10	F	1943-	1955 (12) P,1/2S	18/NS	History of febrile convulsions
11	F	1948-65	1955 (7) M	13/4	Nodding for 1 year before convulsions
12	M	1941-	1956 (15) ?S	20/3	Convulsions every day usually at night
13	M	1943-	1957 (14) S	18/10	Hyperactive before once-monthly convulsion
14	M	1946-	1957 (11) P,M	15/10	Malaria, febrile convulsions, and severe head injury at age 9. Nodding began 10 days post-injury
15	F	1943-	1957 (14) M	18/7	Malaria and febrile convulsions as infant
16	F	1945-	1958 (13) P,M	15/1	Physical appearance of a 7-year old
17	F	1945-	1958 (13) S	16/10	Head nodding on eating
18	F	1948-	1958 (10) GM	13/NS	Febrile convulsions to age 4
19	M	1949-	1958 (9)	15/NS	Narcolepsy for half-year prior to convulsions
20	M	1951-	1958 (7) P,S	10/10	Once/twice-monthly daily head nodding followed by convulsions and then head nodding for hours
21	M	1952-	1959 (7) P	9/10	History of febrile convulsions. Nodding at age 2
22	F	1949-63	1960 (11) M,S	12/2	History of febrile convulsions. Died with marasmus
23	F	1953-	1960 (7) half-S	8/10	Convulsions 3-4 monthly; some months free of attack
24	M	1953-70	1960 (7) S	7/10	No <i>grand mal</i> attacks. Died with marasmus
25	M	1954-71	1960 (6) S	7/10	Emaciated
26	M	1947-76	1960 (13) S	14/5	Monthly convulsions follow "sensation of wind" on face
27	M	1946-	1960 (14) S	15/10	Childhood infection of head region. Neglected
28	F	1950-	1960 (10) P	11/NS	Febrile convulsions in infancy
29	M	1953-70	1961 (8) P	8/9	Semi-conscious during head nodding, daily for ~3 years; <i>grand mal</i> seizures only in later years
30	F	1956-71	1961 (5) F	6/9	Nodding began a few months before progressively more frequent convulsions; died in <i>status epilepticus</i>
31	F	1955-	1962 (7) P,M,S	8/1	Small, thin, with edematous face
32	M	NS	NS (14) P,S	20/8	Febrile convulsions at age 6; unconscious for days
33	M	NS	NS (7)	7/6	Head nodding on eating. No convulsions. Died age 13

DoB: Date of birth. *DoD*: Date of death. Familial case, paternally (*P*), maternally (*M*), grandmaternally (*GM*), siblings (*S*) or half-siblings (*1/2S*). *NS*: Not stated

Possible signs suggestive of extrapyramidal involvement were evident in one-third, including mask-like facies (n=9), monotonous grating voice (n=4), and/or hypersalivation (n=4). Intelligence was judged as bright (n=2), normal (n=14), low to dull (n=13), or moronic (n=4). Psychological

examination revealed normal (n=9) and abnormal states, including timid/restless/frightened/anxious (n=9), depressed/uninterested/absent-minded (n=8), psychomotor retardation (n=3), or near-mute/mute (n=3).

Table 2: Head Nodding cases: physical, neurological and psychological findings

Case No.	Sex	Age at onset Observation span	Nutritional state/stature/other	Hemoglobin/liver/spleen examination	Abnormal neurological and psychological findings
1	F	10/37-39	Poor/small, thin, gnome-like/dirty	40% Hgb/normal/normal	Monotonous grating voice. Depressed, timid, low intelligence
2	F	6/25-27	Good/NS/burn scars	55% Hgb/normal/not palpable	Areflexia in arms and legs. Timid, dull normal, close to mute
3	M	9/27-37	Good/small/burn scars	60% Hgb/normal/not palpable	Depressed and mentally confused after attacks
4	M	9/18-22	Good/NS/burns palpable	60% Hgb/normal/not palpable	Mask-like expression, and grating, not with monotonous voice
5	M	5/13-20	Good/NS	Hgb/normal/not palpable	None
6	F	7/15-20	Good/small stature/burn	50% Hgb/normal/not palpable	Areflexia in arms and legs. Mask-like expression, uncoordinated, clumsy gait. Depressed, mute, dull normal, confused at times
7	F	2/12-NS-	Poor/facial edema, wounds and infections	45% Hgb/normal/not palpable	Hyperreflexia, asymmetrical; no pathologic signs. Ataxic, staggering gait. Hyperactive, cries, whines, moronic
8	F	10/17-17	Good/NS/burns	50% Hgb/normal/not palpable	Mask-like expression, facial tics, hypersalivation, parkinsonism. Unsteady gait. Slow in articulation. Depressed dull, moronic
9	M	22/28-38-	Good/NS/tongue scars	70% vnormal/not palpable	Formication, left arm. Bright, suffers terrible nightmares
10	F	12/18-NS-	Poor/small neglected-looking	45% Hgb/normal/not palpable	Normal except for mental confusion after attack
11	F	7/13-17	Poor/NS/tongue scars	40% Hgb/normal/not palpable	Hypereflexia in arms and legs, mask-like facial expression, tumbling gait. Normal intelligence with psychomotor reduction
12	M	15/20-23-	Good/NS	Wnl/normal/not palpable	Mask-like facial expression, thin, monotonous voice, rigid movements, rambling speech. Anxious.
13	M	14/15-25-	NS/burn	55% Hgb/normal/not palpable	Wnl
14	M	11/15-25	Poor/small, dishevelled	50% Hgb/normal/palpable and enlarged.	Areflexia right arm, hyporeflexia right leg. Dull, nearly mute, does not understand questions
15	F	14/18-25-	Good/NS	45% Hgb/normal/palpable	Dull normal.
16	F	13/15-16-	Poor/small for age (looks age 7)	45% Hgb/normal/not palpable	Depressed, extremely timid, low-normal intelligence.
17	F	13/16-26	Poor/facial edema, swollen hands, thick dry skin/burns	50% Hgb/normal/palpable	Mask-like expression, hypersalivation with drooling, grating voice, clumsy movement. Psychomotor retardation. Depressed, dull, frightened, timid
18	F	10/13-NS	Poor/NS/tongue scar	45% Hgb/normal/enlarged	Timid, at times restless, wanders away from home
19	M	9/15-NS	Good/NS	60% Hgb/normal/not palpable	Hyperreflexia, symmetrical
20	M	7/10-20	Poor/small for age	45% Hgb/normal/palpable	Hyperreflexia in arms and legs, rigid facial expression, unsteady gait. Dull, frightened, non-responsive to questions
21	M	7/9-19	Poor/small, thin	50% Hgb/normal/palpable	Friendly, retarded (5-year-old level)
22	F	11/12-14	Poor/small for age/retarded	45% Hgb/normal/not palpable	Areflexia in all limbs, no abdominal reflexes, hypersalivation, tumbling gait, poor coordination. Low intelligence, timid, speaks in a whisper

Table 2: Head Nodding cases: physical, neurological and psychological findings

Case No.	Sex	Age at onset Observation span	Nutritional state/ stature/other	Hemoglobin/liver/ spleen examination	Abnormal neurological and psychological findings
23	F	7/8-18	Good/NS	70% Hgb/normal/ not palpable	None
24	M	7/7-17	Poor/small for age	40% Hgb/normal/ not palpable	Low normal intelligence, timid, anxious
25	M	6/7-17	Poor/very thin and small for age/burns	60% Hgb/normal/ enlarged	Depressed, timid, never speaks, low intelligence
26	M	13/14-19	Good/NS	50% Hgb/normal/ not palpable	None
27	M	14/15-25	Poor/neglected, dirty/tongue scar	55% Hgb/normal/ not palpable	Hyperreflexia, mask-like facial expression, tumbling gait, ataxia. Psychomotor retardation. Depressed, timid, moronic, cannot find words
28	F	10/11-NS	Good/NS	60% Hgb/normal /not palpable	Timid
29	M	8/8-17	Poor/weak, small and neglected	45% Hgb/normal/ palpable	Hyperreflexia in arms and legs, masked expression, unsteady gait. Depressed, uninterested, dull normal, increasingly moronic, slow, often absent-minded
30	F	5/6-15	Poor /very small for age	45% Hgb/normal/ not palpable	Hyperreflexia in arms and legs. Timid
31	F	7/8-9	Poor/small, thin, facial edema	NS/normal/not palpable	Hyperreflexia symmetrically. Dull, friendly, indifferent, timid
32	M	14/20-28	Good/NS	70% Hgb/normal/ not palpable	None
33	M	7/7-13	Poor/thin small	40% Hgb/normal/ not palpable	Timid, frightened

NS: Not stated. *Wnl*: Within normal limits

Case reports

Nodding Case #1

A female who, according to family members, was aged 10 at onset of *amesinziya kichwa* in 1934. She exhibited a dreamy state, diminished intelligence, and continuous head nodding for ~1 year prior to the onset of *grand mal* seizures. Her older brother died at age 15 from epilepsy. Parents were free of *keifafa* but both came from families with members who had epilepsy. The mother had an unremarkable pregnancy, birth trauma was absent but, at pre-school, the child often had febrile convulsions. On presentation at the clinic at the age of 37, the patient reported 2-3 episodes of convulsions daily for 3-5 days over periods of 2 weeks. Pre-convulsive auras were absent. Convulsions were preceded by a loud cry and falling. Semi-conscious between attacks, upon awakening she complained of headache, was confused and cried. The patient presented as a dirty, thin, timid, gnome-like adult female in a poor nutritional state. Physical examination revealed tachycardia and anemia (40% Hgb). Neurological

examination was unremarkable, with the exception of depression, very low intelligence and a monotonous grating voice. The patient was followed for 2 years when she died at age 39 with marasmus.

Nodding Case #7

A female born in 1951 developed *amesinziya kichwa* at age 2. Parents were free of *keifafa*. Four older brothers had died, of whom two had head nodding, as did a deceased elder sister. The child had no birth trauma, nor were preceding illnesses reported. At age 12, the child was brought to the clinic by her parents who described episodes of head nodding while eating during morning and evening meals when she appeared absent-minded, the head would fall forward progressively until striking the floor, whereupon the child would get up but, at times, fall to her knees. She experienced no *grand mal* seizures and no auras prior to head nodding.

Physical examination revealed a poor nutritional state with anemia (45% Hgb), edematous face, and multiple infected wounds on her body. She exhibited a staggering, ataxic gait and, on neurological examination, asymmetrical extremity hyperreflexia but no pathological reflexes. The child was hyperactive, cried and whined frequently, and was found to be in a moronic state indicative of severe cognitive impairment.

Nodding case #8

A female born in 1944 developed *amesinziya kichwa* at age 10 but was only examined in the clinic at age 17, 2 months before her death. Her parents were free of epilepsy, but there were numerous familial cases on the mother's side. The patient experienced no birth trauma, nor were childhood or antecedent illnesses reported, other than a single episode of febrile convulsions as a small child. During periods of head nodding, the head would nod to the right side. Her primary generalized convulsions occurred without aura or warning, whereupon she would fall to the ground with a cry, remain unconscious for about 20 minutes and, at times, remain in a fugue state thereafter. Her arms and legs had numerous small burns. She was in a good nutritional state but anemic (50% Hgb). Neurological and psychological examination revealed an unsteady gait, parkinsonian-like features (masked facies, with facial tics when speaking, very slow word articulation, and hypersalivation), depression, and cognitive deficits (dull, absent-mindedness, moronic).

Discussion

Head nodding among the Wapogoro fits the WHO case definition of probable Nodding Syndrome developed in August 2012 by international scientific consensus¹¹. Agreement was unanimous that clinical signs of this epileptic disorder were indistinguishable among affected populations of south Sudan, Uganda and Tanzania. Nodding of the head, staring and automatisms (chewing, verbal) have also been described in seizure-prone tribal groups in Liberia.^{12,13}

We document the earliest known cases of head nodding (*amesinziya kichwa*) in an epilepsy-prone population of Tanzania,⁵ with cases of head nodding reportedly dating from 1934. This period appears to pre-date the introduction to this population of manmade chemicals with neurotoxic potential, such as pesticides. Because Nodding Syndrome in the Wapogoro affected mostly undernourished, small-for-age children in a marginalized population at high

risk for epilepsy, onchocerciasis¹⁴ and seasonal food shortages, the search for etiology is logically focused on infectious disease and/or nutritional factors, the latter including naturally occurring chemical components in food. The association in some cases between head nodding and food/eating as a precipitating factor⁶ has been noted in another epilepsy-prone population with high prevalence of onchocerciasis,² and the possible role of certain plant and fungal neurotoxins in Nodding Syndrome has been discussed.³ Genetic factors in *kifafa* have been considered previously¹⁵ but parents of children with Nodding Syndrome were usually free of epilepsy, and familial association of disease can also arise from common exposures to etiologic agents. Febrile convulsions were an antecedent event for *amesinziya kichwa* in up to 20%.⁶

Patient histories of cases from Uganda and South Sudan suggest that Nodding Syndrome may begin with a prodromal period marked by drowsiness, absences, and staring, evolve into different schedules of repetitive head nodding and, with time, advance in most cases to *grand mal* seizures. The Wapogoro fear *amesinziya kichwa* in a child because it portends extant or impending convulsive *kifafa*. Affected subjects are often of small stature, poorly nourished, shy and neglected. Left untreated, children and young adults developed neurological signs indicative of psychomotor and motor-system involvement, including parkinsonism in some cases, signs of which have not been described in other foci of Nodding Syndrome. Recent studies^{6,7} utilizing magnetic resonance imaging have revealed subcortical frontal gliosis and/or hippocampal sclerosis/atrophy in a few Wapogoro cases of Nodding Syndrome with or without other types of seizures. In sum, the natural history of Nodding Syndrome is one of a progressive seizure disorder attended by evolving brain damage likely caused or amplified by repeated hypoxia/anoxia during the convulsive event.

Acknowledgments

This study utilized written summaries of medical records of unnamed patients seen by J. L-A. in the course of her clinical practice at the Kwiro Mission in Mahenge beginning in 1959. She performed her clinical duties at the request and with the knowledge, consent and support of the Catholic Diocese of Mahenge, and with the knowledge of the Prime Minister of Tanganyika, the Honorable Mr. Rashid Kawawa. The clinical records were not collected as

part of a research study, and data drawn from these records have been published previously in numerous peer-reviewed publications, including a 30-year follow-up study of 164 patients on long-term treatment with phenobarbital⁸.

This study was made possible with the collegial support of Sister Sieglinda, former head Sister of the Kwiwo Catholic Mission Outpatient Clinic in Mahenge. A Swiss-certified nurse with exceptional clinical knowledge, she led the Clinic for many years and was a friend, helper and assistant to L. J-A. When L. J-A was away from Mahenge, she looked after the treatment and care of the epilepsy patients while keeping track of their history and progress in meticulous notes that were communicated to L. J-A for comment and consultation. P.S.S. and V.S.P. are supported by a grant from the U.S. National Institute of Neurologic Disorders & Stroke 1 R01 NS079276. We thank Amelia Bartolini for analytical assistance and Dr. Diane Stadler for commenting on the manuscript.

References

1. Centers for Disease Control and Prevention. Nodding Syndrome – South Sudan, 2011. *Morb Mortal Wkly Rep* 2012; 61: 52-4.
2. Tumwine JK, Vandemaele L, Chungong S, Richer M, Anker M, Ayana Y, *et al.* Clinical and epidemiologic characteristics of nodding syndrome in Mundri County, southern Sudan. *Afr Hlth Sci* 2012; 12:242-8.
3. Spencer PS, Vandemaele K, Richer M, Palmer VS, Chungong S, Anker M *et al.* Nodding Syndrome in Mundri county, south Sudan. Environmental, nutritional and infectious factors. *Afr Hlth Sci* 2013; 13(2): 183-203.
4. Aall-Jilek L. Epilepsy in the Wapogoro tribe in Tanganyika. *Acta Psychiatr Scand* 1965; 41: 57-8.
5. Aall-Jilek L. Geisteskrankheiten und Epilepsie im tropischen Afrika. *Fortschr Neurol Psychiatr Grenzgeb* 1964; 32: 213-59.
6. Winkler AS, Friedrich K, König R, Meindi M, Unterberger I, Gotwald T. *et al.* The head nodding syndrome - Clinical classification and possible causes. *Epilepsia* 2008; 49: 2008-15.
7. Winkler AS, Friedrich K, Meindi M, Kidunda A, Nassri A, Jilek-Aall L, *et al.* Clinical characteristics of people with head nodding in southern Tanzania. *Trop Doct* 2010; 40:171-5.
8. Jilek-Aall L, Rwiza HT. Prognosis of epilepsy in a rural Africa community: A 30-year follow-up of 164 patients in an outpatient clinic in rural Tanzania. *Epilepsia* 1992; 33: 645-50.
9. Schoenake R.S. Die ideologischen Hintergründe im Gemeinschaftsleben der Pogoro. Vienna, Eigenverlag, 1965, 176p.
10. Lussy PK, Kunibert OFMCap, Die Waffen der Wapogoro. *Acta Tropica* 1947; 4: 135-45.
11. World Health Organization. Nodding Syndrome meeting, researchers agree on case definition and establish research agenda. WHO Regional Office for Africa. <http://www.afro.who.int/en/uganda/press-materials/item/4826-nodding-syndrome-meeting-researchers-agree-on-case-definition-and-establish-research-agenda.html>
12. Gerrits C. Conceptions and explanations of *sii*, epilepsy. A medical-anthropological study among the Bassa and Kpelle in Liberia. *Curare* 1983; 6: 33-40.
13. Van der Waals FW, Goudschmit J, Gajdusek DC. *See-ee*: Clinical characteristics of highly prevalent seizure disorder in the Gbawein and Wroughbarh Clan Region of Grand Bassa County, Liberia. *Neuroepidemiology* 2:35-44, 1983.
14. Jilek-Aall L. Neurofilariasis. In Chopra JS, Sawhney IMS, eds, *Neurology in Tropics*. New Delhi, Churchill Livingstone 1999; 259-71.
15. Jilek-Aall L, Jilek W, Miller JR. Clinical and genetic aspects of seizure disorders prevalent in an isolated African population. *Epilepsia* 1979; 20: 613-22.