

The Plight of the Lucluc  
Examining the Deadly Mystery of Nodding Syndrome

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### **Abstract**

Nodding syndrome (NS) is an emerging epidemic neurological disease that is shrouded in mystery. It is currently only found in the post-conflict regions of South Sudan, northern Uganda, and Tanzania. NS occurs in children from the ages of five to fifteen and is characterized by a loss of motor control in the neck muscles. Seizure episodes can range in intensity from atonic to tonic-clonic, and the onset of the first episode generally marks the beginning of a decline in the child's physical and mental health. NS is a progressive disease that generally results in physical wasting, stunted growth, behavioral difficulties, and a decline in cognitive and motor skills. The underlying cause of the disease has yet to be soundly established, but several closely correlated factors have been discovered and effective treatment methods are currently being developed. Children with NS are also susceptible to detrimental social factors such as negative perception and stigmatization. Additionally, socioeconomic conditions greatly influence the ability of healthcare workers to identify and treat the disease.

## The Plight of the Lucluc

### Examining the Deadly Mystery of Nodding Syndrome

If you have ever been fortunate enough to visit the West African country of Uganda, you know firsthand how beautiful it is. You have seen its lush and fruitful greenery, its beautifully jagged mountains, and its expansive and sprawling lowlands. It is a place reminiscent of Eden; and many of the locals will claim that life did indeed begin at the source of the Nile, which lies in the heart of Uganda. Yet, in the northern region of the country, in the midst of all the beauty, lies a troubling mystery that is disrupting and destroying the lives of many African children and their families. This mystery is the epileptic disorder known as nodding syndrome (NS).

In the early 1960s, this novel epileptic disorder was discovered in the sub-Saharan region of West Africa. Seizure victims were observed to lose motor control in the muscles of the neck prior to the onset of an episode (1). Initially this disorder was not independently studied or separated into a distinct clinical classification, as identical symptoms were rarely documented for almost half of a century. The early 1990s, then, saw an alarming reemergence of this peculiar disease in the conflict-torn areas of South Sudan and northern Uganda, with isolated cases occurring in Tanzania. Currently, NS is classified as a distinct neurological condition and has recently been labeled as an epidemic by the Center for Disease Control and the World Health Organization (2). As of today, the exact pathological cause of the disease is still unknown, and much remains to be learned about the mechanisms of the disease. There is also no known cure at this juncture, but several promising treatment methods are being investigated. The purpose of this thesis is to explore the available literature dealing with NS and to examine the

characteristics, possible causes, current treatments, and social effects of this mysterious disease.

### **History and Prevalence**

A type of seizure disorder characterized by the repetitive nodding of the head was first described in 1965 among the Wapogoro tribe in the Tanzanian highlands (3). A similar seizure disorder, with the onset of an episode characterized by a loss of motor control in the neck muscles leading to repetitive falling of the head toward the chest, was then described in 1983 (2). However, due to the rarity of the condition, unclear clinical records, and unreliable diagnoses this “head-nodding” disease did not receive its own classification until 1991 when it reappeared in South Sudan (4). Even with its own classification, NS was still such a rarely documented condition that it was not until it began to reach epidemic proportions in the late 2000’s that the world began to really take notice of the disease. In August 2012, the World Health Organization reached a consensus among the international scientific community for a case definition of NS (5). This definitive characterization of NS has greatly encouraged research into the mystery of NS by providing a much-needed measure of consistency when diagnosing patients suspected of suffering from NS.

NS is currently considered to be an epileptic disorder of epidemic proportions by the World Health Organization (2). Unfortunately, accurate data detailing the exact number of cases has yet to be acquired. Combined data sets gained through journalistic efforts, evaluations by government and health officials, and independent medical studies place the number of cases of NS in the northern Ugandan districts of Kitgum, Pader, and Lamwo and the Equatoria States of South Sudan to be anywhere from 3,000 – 8,000

cases (2). Data on NS occurrence in South Sudan is even less precise, and rough estimates as to the disease's prevalence in that region are highly inaccurate due to a lack of government infrastructure and public health systems from which to obtain records. To date, most studies into NS have focused on case studies or cohort studies using small samples of NS patients. No single study has yet been completed that accurately characterizes the full extent of the disease's prevalence in sub-Saharan Africa. However, it is likely that the actual number of children with NS is far greater than the current records and estimates show. Given NS's incidence in remote rural areas, there are likely large numbers of children who have yet to be identified and diagnosed. Currently, registration programs are being implemented in affected districts of Uganda to more accurately identify the spread of the disease, even in more remote regions, by keeping unified records of NS cases (6). Hopefully, this will provide an impetus for similar programs to be established in South Sudan so that the extent of the issue may be better understood.

### **Characterization**

NS is named for its most distinguishable characteristic, an atonic seizure resulting in loss of neck muscle control that seems to cause the child experiencing the seizure to nod his or her head uncontrollably. However there is much more to the characterization of this disease than just this single physical manifestation. NS is classified as a form of childhood epilepsy and has currently only been observed in subtropical regions of sub-Saharan Africa. The highest prevalence of the disease has been found in the Equatorial regions of South Sudan and the northern districts of Uganda. A few instances of the disease have been reported in Tanzania, though the epicenter of the disease has

consistently proven to be the aforementioned contiguous regions of Uganda and South Sudan. NS is classified as a childhood epilepsy because it has generally been observed to occur in children 5 to 15 years of age; however children as young as 3 and as old as 18 have been reported to contract the disease (See Figure 1).

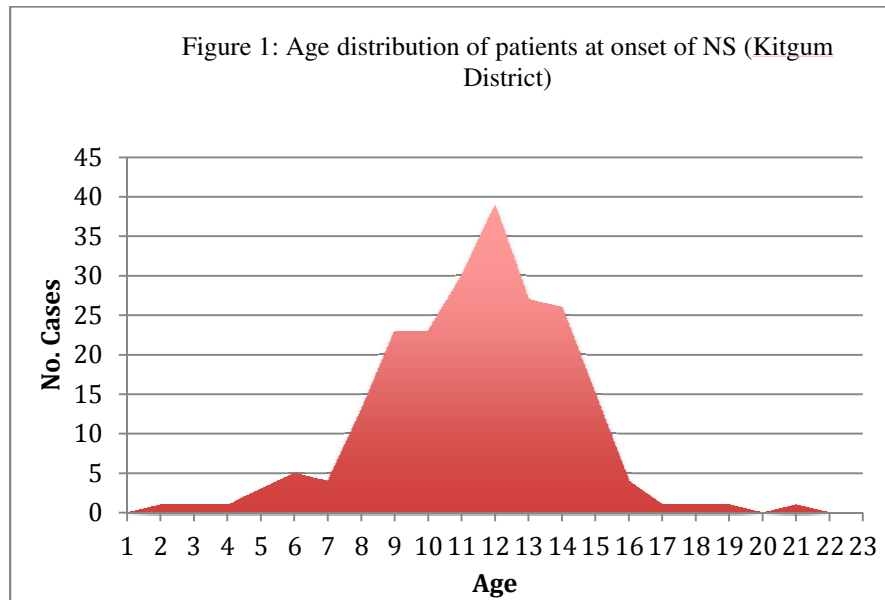


Figure 1: This graphic represents the age distribution of children with NS according to a large cohort study completed in the Kitgum district of Uganda by Foltz and colleagues. It should be noted that this is merely one district in one of the areas affected by NS and therefore is not a comprehensive evaluation of the age distribution of the disease. However this study is currently the largest cohort study compiled to date and therefore provides the best possible view of NS's relationship to age. Modified from Foltz and Dowell. (Dowell et al., pg. 1377. 2013;Foltz et al., pg. 6. 2013)

As previously stated, the hallmark of NS is the onset of an epileptic event resulting in the loss of motor control in the neck. The first occurrence of this type of atonic seizure is generally recognized by clinicians to mark the onset of the disease. The frequency of these nodding episodes can vary from a few times a week to several times a day. A general trend of increased frequency over time has been noted in several studies. Nodding episodes are classified as “head nodding” or “head nodding plus,” depending on the particular characteristics of the episode. The “head nodding” classification indicates a

seizure with only the manifestation of features of NS, while a “head nodding plus” classification is used to describe a seizure possessing characteristics of NS, as well as characteristics of potentially several other epileptic type disorders (7). Episodes garnering a “plus” designation occur in long-suffering NS patients and are commonly observed to consist of head nodding followed by generalized tonic-clonic seizures, which are separately classified from the characteristic atonic seizures regularly observed in NS due to the stiffening of muscle tone and spasticity of movement experienced by the patient (8). This demonstrates the progressive nature of NS if left unchecked. This progression is one of the most alarming features of the disease, and greatly contributes to the negative attritive effects of the illness.

As the disease progresses, children with NS show marked physical, functional, sexual, and cognitive decline. In some cases, nutritional and psychiatric deficits have also been noted in patients. A study was completed in 2013 by Richard Idro and colleagues detailing many of these developmental deficits in children with NS. According to their results, 73% of the NS patients they examined showed definite signs of physical wasting, with 41% showing marked signs of physical stunting. Patients exhibiting signs of wasting were shown to have had NS symptoms for three years or more, while severe wasting was associated with patients exhibiting symptoms for more than 7 years (8).

Using the findings and observations of this study, Idro then proposed temporal stages of progression in NS. Stage 1 is called the prodromal period and includes the earliest symptoms of the disease, such as self-reported dizziness, increasing inattention, and lethargy. Stage 2 was found to occur approximately six weeks after Stage 1 and is characterized by the onset of head nodding episodes. Stage 3 does not occur in all NS



patients, and is characterized by the development of additional types of seizures. Among the cohort studied by Idro, Stage 3 was found to occur one to three years after the onset of the initial symptoms. Stage 4 was found to develop four to eight years after the onset of nodding episodes. This stage is marked by deterioration and decline in speech, motor, and cognitive functions, as well as a discernable regression in the child's psychiatric behavior. Stage 5 is the final stage of the development of NS and is characterized by severe disability and wasting. Children in this stage exhibit severe physical wasting, mental apathy, severely limited communication ability, and poor appetites (9). It should be noted that not all children with NS experience all of these stages of progression.

Recent treatment methods have been mildly successful in halting much of the progression of the disease; nevertheless these stages serve to show the types of devastation that this disease can wreak upon its victims if it is left unchecked. The mental and physical decline brought on by NS is an especially destructive aspect of this disease, as a majority of NS patients are at crucial stages in their development, and thus, because of the disease, will never fully develop physically or mentally.

### **Possible Causes**

The most frustrating aspect of NS is also the very thing that makes it so fascinating; unfortunately the exact etiology of the disease is still very much a mystery. Like most epileptic disorders, the extreme complexity of the neurological system makes pathological studies difficult. However, much progress is being made towards a more complete understanding of the disease. Currently there are several plausible theories as to the causation of the disease. Exposure to opportunistic parasites, specifically the filarial worm *Onchocerca volvulus*, dietary deficiencies and toxicity, and psychosocial factors

have all been shown to correlate very closely with NS; genetic factors and family pedigrees have been examined in several studies but have yet to show any positive link or correlation. Common etiologies and pathologies found in other types of epileptic disorders have also been examined with extremely limited success. However, the several factors that have been found to positively correlate with NS have been used to formulate leading theories for the disease's causation. It should be reiterated that these theories are currently based only on correlational data and can therefore remain only as well-supported theories until scientific discovery provides repeatable causal links.

### **I. Onchocerciasis**

For the past decade, the favorite etiological theory of many publications detailing and characterizing NS has been in some way linked to Onchocerciasis. Onchocerciasis, also known as "river blindness," is a type of widespread parasitic infection that is commonly found in developing regions of the world. It is estimated that nearly thirty-seven million people in South America, sub-Saharan Africa, and tropical Asia are currently infected with the disease. (10). It is also the second leading cause of infection-related blindness in the world (11). The disease is named after the filarial nematode *Onchocerca volvulus*, which is responsible for the disease's manifestation and pathology in humans. This particular parasitic worm is vector-borne and is carried by the common black fly of the Simulian genus (11). These black flies are common inhabitants of tropical areas and commonly breed in moving bodies of water, such as the rivers and streams of rural, agricultural areas. They pose a significant health risk to the villages and communities that greatly rely on these waters for survival. The parasite is transmitted to the host in its microfilariae form via the bite of the black fly. Once inside the human host, the

microfilariae invade the skin and migrate throughout it into other bodily locations, where they begin to grow and eventually produce the clinical manifestations of Onchocercal infection (10). Symptoms of infection are generally characterized by severe itching, skin lesions and disfiguration, sub-dermal nodules, and visual impairment leading to blindness (12). These symptoms are caused by the induction of an inflammatory response in the tissue where the parasite is present. The blindness that results from this disease is specifically caused by inflammatory damage to infected tissue in and around the cornea (10).

Onchocercal infection has often been implicated as a possible factor in the etiology of NS. The reason for this implication is the consistently high correlation rates between children with NS and onchocerciasis exposure. A study published by Scott F. Dowell and colleagues provides one of the best characterizations of risk factors involved in NS currently available. According to the finding published in this study, which examined hundreds of NS patients in northern Uganda and Southern Sudan, ninety-three percent of Sudanese patients and ninety-five percent of Ugandan patients tested positive for *O. volvulus* (2).

Currently, the leading hypothesis for this causal link between NS and *O. volvulus* is that the black flies populating the NS-endemic areas transmit a novel pathogen that may result in NS or other types of epileptic disorders (13). This theory is based on a recent paradigm shift in the understanding of Onchocerciasis infection. It has long been understood that a large majority of filarial nematodes, such as *O. volvulus*, possess a symbiotic relationship with an intracytoplasmic bacteria called *Wolbachia* (14). *O. volvulus* has been shown to rely on *Wolbachia* to achieve normal embryo

development, as well as to provide a continuing support system to aid the survival of the adult nematode in the host (15). *Wolbachia* have been shown to possess great genetic variability.

At present, the high level of genetic deviation within the family has produced six distinct taxonomic groupings of the bacteria, with subdivisions having been established among each super group (16). One of the most common results of this genetic variation is the recombination of various surface proteins, which then explains the wide variety of physical traits and characteristics displayed by the organism (17). This is also a very significant factor in the relation of *Wolbachia* to Onchocerciasis, and ultimately to NS, because it is these surface proteins, serving as antigenic recognition sites for the immune system, which are partially responsible for the inflammatory immune response elicited against *O. volvulus* infection (15). Therefore, it is theoretically plausible that genetic differences in *Wolbachia* strains found in *O. volvulus* near NS-endemic regions could provoke a novel immune response that could possibly reveal a link between Onchocerciasis in those regions and the onset of NS. It has also been theorized by Robert Colebunders that perhaps a novel bacterial symbiont similar in function to *Wolbachia* is also spread via blackfly vector (18). Yet, at this current juncture, there has been no research into this line of hypothesizing.

It should again be realized that *O. volvulus* involvement in the causation of NS is still merely hypothesis. The theory poses one glaring shortcoming: that Onchocerciasis infection is not localized to the regions affected by NS. As previously stated, it is a very widespread disease experienced in several different geographic locations. However, NS is endemic to only one region of the world, and has yet to be observed in any other regions

where Onchocercal infections are prevalent. Additionally, no direct clinical evidence has yet to provide a causal link showing how this filarial infection of *O. volvulus* would bring on the symptoms of NS. On the other hand, and in defense of the Onchocercal theory, recent research and observation has noted a marked decline in new diagnoses of NS coinciding with widespread vector control methods being implemented by the Ugandan government in northern Uganda to curtail the spread of black fly vector and its corresponding parasitic infection (13). With all this being said, Onchocerciasis is still a very intriguing possible explanation of the mystery of NS.

## **II. Dietary Deficiencies**

Another theory behind the etiology of NS is the possibility of dietary deficiencies leading to the onset of the syndrome. An overwhelming majority of the children living with NS live well below international poverty lines, and therefore are rarely able to obtain the nutrients necessary for a balanced diet (4). One of the most promising dietary links to NS has been the recent characterization of pyridoxine (vitamin B6) deficiency in children with NS. Studies completed by the Center for Disease Control in Sudan and by Foltz and colleagues in northern Uganda showed ninety percent of patients examined with NS to also possess marked pyridoxine deficiencies (2, 19). This is a very important correlation as pyridoxine deficiency has been shown to be a factor in another type of epileptic disorder affecting pediatric patients, pyridoxine-dependent epilepsy (PDE). PDE is a rare genetic disorder that affects children from the ages of several months to three years. PDE is caused by a mutation in the ALDH7A1 gene, which results in the malformation of a dehydrogenase enzyme responsible for the breakdown of the amino acid lysine in the brain. It is readily and effectively treated through the usage of daily

administrations of pyridoxine supplements (20). While the genetic aspect of the disease makes PDE clinically variable from NS, and therefore not a perfect link between the two, the model of PDE provides an example of the disruption of a metabolic pathway involving pyridoxine leading to neurological disruption.

Various other dietary factors have been loosely linked to NS. Ingestion of toxic substances has often been cited as a possible cause of the disease. However, correlational data has yet to produce substantial evidence to back this particular hypothesis. Currently, the most plausible link to nutritional toxicity as a factor in NS is the common consumption of the staple crop cassava. Cassava is a root commonly grown and consumed in sub-Saharan Africa because of its resistance to famine, plant disease, and pests. While this hardy quality makes it a very beneficial crop, especially in areas of poverty and drought, it can be deadly if not properly prepared. Undercooked or bitter cassava has been shown to lead to cyanide production in the body (21). The production of this neurotoxin has been shown to be a causative factor in several neurological disorders found in NS endemic regions. This provides a very relevant precedence for dietary factors leading to neurologic disorders, specifically in that part of the world, and it could prove to be a useful model in formulating further hypotheses regarding causative factors of NS.

### **III. Violence**

Perhaps the most intriguing and complex theory as to the causation of NS lies in the ostensible correlation of a localized epidemic with the extreme violence and civil war of the region's recent history. Northern Uganda is still in the process of recovering from years of war and civil unrest between Ugandan government forces and Joseph Kony's

Lord's Resistance Army (LRA). This conflict lasted, roughly, from 1986 to 2008, which closely coincides with NS's rise to prominence from the late 1990's to the present day (22). Sudan has also been in an almost constant state of turmoil, due to religious and cultural conflicts, as well as various civil wars and government upheaval, since the 1950's (23). Because of these conflicts, both of these regions have experienced extreme violence in which citizens experienced widespread physical and psychological abuses were major factors. Many of the stories that have come from survivors of these conflicts are almost too terrible to fathom. Reports of violent wartime death, murder, rape, cannibalism, abduction, slavery, and other such terrible atrocities have all surfaced from these war-torn regions.

Because of the traumatic nature of these atrocities and the severe psychological stress brought about by living under such conditions, many of the inhabitants of these regions and the peoples displaced by these conflicts have experienced some sort of psychological damage. A study by Bayard Roberts and colleagues published in 2008 is one of the largest and most revealing studies into the psychological collateral damage that these particular regions experienced. For the study, Roberts visited internally displaced persons (IDP) camps in the conflict-plagued regions of Gulu and Amuru in northern Uganda. Cross-sectional cluster surveys were completed on over twelve hundred displaced persons using a questionnaire developed by Harvard University to test for post-traumatic stress disorder (PTSD) and another questionnaire developed by Johns Hopkins to determine stages of depression. The results of the survey showed that 54% of the IDP camp residents met the established criteria to be diagnosed with PTSD, and 67% of surveyed individuals also met the symptomatic criteria linked to depression (24). This

study serves to provide tangible evidence of widespread psychological effects that have yet to be fully quantified. Roberts and colleagues also completed an identical study in South Sudan using the same questionnaire and survey methods to determine mental health status among refugees. The results of this study showed 36% of individuals surveyed met symptomatic criteria for PTSD and 50% met criteria for depression (25). While these tests are merely a small sample of the hundreds of thousands of people affected by the violence, they do provide insight into the psychological state of the populations in these regions. Therefore, because NS is endemic to these areas of high violence, it is not out of the realm of possibility that NS may have some sort of psychological link that has yet to be fully understood.

The correlation of NS with wartime violence is further supported by the temporal association of violent conflict and number of deaths with new diagnoses of NS (See Table 1 and Figure 2). This relationship has been best characterized by a statistical analysis completed by Jesa Landis and colleagues in 2014 that shows the delayed onset of NS following violent activities in the Kitgum district of Uganda (See Figure 2). According to the data produced in this study, cases of NS first appeared in 1998, following several highly violent LRA massacres. NS diagnoses then increased again, and reached a peak in 2004 following several years of intense conflict and high mortality rates. Another peak of NS diagnosis was then reached in 2008. This also followed the upward trend of increased prevalence of NS following times of high violence. The data also shows a decline in new diagnoses of the disease following prolonged periods of peace, which would be expected if the disease were proven to be related to psychological duress (26). The correlational connection between NS and violence was also detailed in



aforementioned studies by Dowell and Foltz. According to the findings of these studies a majority (71% in the Foltz study and 54% in the Dowell study) of patients examined with NS had been directly exposed to firsthand military violence. While both of these studies were completed under the presuppositions of a previously held hypothesis that munitions exposure may play a role in NS development, they still serve to provide data linking wartime violence to NS (2, 19). Together, the data and evidence collected in these studies serve to provide a very good case for a psychological factor in the onset of NS.

Table 1: Annual Incidence of Violence, Fatalities, and Novel Diagnosis of NS in Uganda

Year	Violent Occurrences	Fatalities	New Cases of NS
*1997	22	128	0
*1998	57	143	3
1999	13	31	2
2000	19	70	5
2001	8	0	4
*2002	42	115	25
*2003	53	167	38
2004	33	87	42
2005	21	55	36
2006	8	45	52
2007	2	0	70
2008	1	10	82
2009	0	0	62
2010	0	0	46
2011	1	0	0

Table 1: This data provides the means to observe the correlation of violent events and fatalities with new diagnoses of NS in Uganda. The data was accumulated from Armed Conflict Location & Event Data with assistance from the Uganda Ministry of Health. Asterisks are used to signify dates of particularly violent occurrences. 1997-1998 saw a large number of deaths and marked violence due to the regular occurrence of LRA abductions and massacres throughout the northern districts. 2002-2003 was the peak of violent conflict between the LRA and Uganda national forces, also known as Operation Iron Fist (26). Modified from Raleigh and Landis (27)(26 pg 3).

Figure 2: Correlational relationship of violence and fatalities with the onset of new NS cases

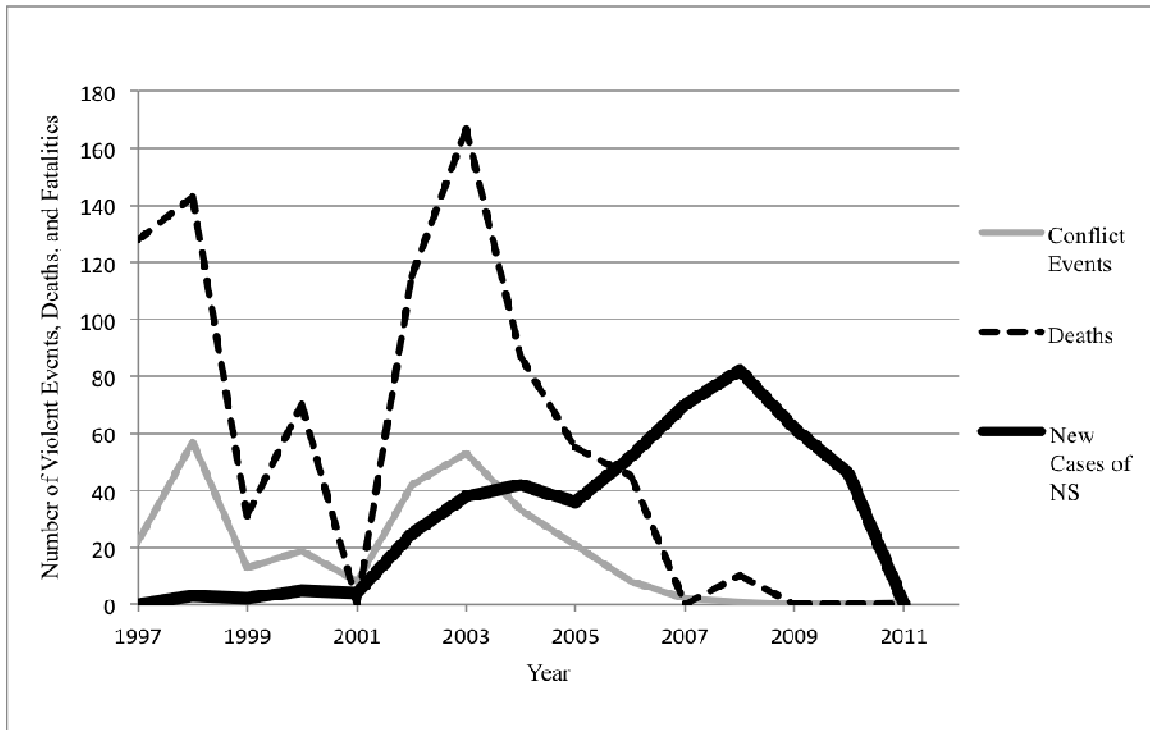


Figure 2: This Figure shows the correlational and temporal relationship of violence and fatalities with the increased occurrence of NS. The data used to compile this chart was obtained from the information found in Table 1. It should be noted that the incidence of NS markedly increases following a time of high violence. Conversely, new incidence of the disease declines rapidly during times of peace. Modified from Landis (26, pg. 3).

### Treatment Options

Because the exact etiology of NS has not yet been discovered, it is not possible to detail one single efficacious treatment plan for all patients with the disease. At this juncture, clinicians and physicians are forced to combat the disease using asymptomatic treatment methods that can vary depending on the specific needs of a particular patient. Idro and colleagues in association with Makerere Medical School in Uganda first proposed detailed treatment guidelines designed to encompass the many physical and mental aspects of NS. These methods include anti-epileptic drugs, ivermectin treatments to combat filarial infection, dietary supplementation, and physical and cognitive

therapeutic techniques. No one solution has been found to be completely effective, however, several multi-faceted treatment approaches have recently proven very successful in clinical trials.

The socioeconomic climate in which NS is prevalent also brings forth its own unique trials in regards to attempts at combatting the disease. Because a large number of individuals with NS subsist at or well below poverty lines, and because of structural instability found in communities experiencing NS due to civil unrest, treatment is often impossible outside of government programs or non-government organization aid. Additionally, NS is a fairly new, emerging disease with relatively little research and study having been published on the subject. While it has received some media attention, it is still mostly unheard of in most public circles. This provides a unique challenge for many healthcare workers dealing with the problem of NS, as funding and resources needed to advance treatment methods and purchase medical supplies necessary for current NS treatment methods are difficult to procure.

### **I. Anti-Epileptic Drugs**

Anti-epileptic drugs have been used to manage the onset of seizures in NS patients, but unfortunately, their success has been limited and consistency of results has yet to be achieved. The characteristics of NS make it a difficult target for drug treatment. An efficacious drug is necessary first and foremost, but because of economic factors, the pediatric demographic of affected patients, and the disease's unique characteristics, the drug also must be inexpensive, safe, and possess the ability to combat multiple seizure types. Currently, phenobarbitone, phenytoin, and carbamazepine are the three anti-epileptics most often used in clinical treatment of NS. However, only limited success has

been obtained. In clinical trials completed by Andrea Winkler and colleagues in 2013 and in 2014, the efficacy of these various anti-epileptics was examined. In these studies, the results greatly varied, so a definite conclusion regarding the most effective drug treatment method was not reached. However, all three of the aforementioned drugs were utilized, and were found to markedly reduce seizure frequency. It was also found in the 2013 study that around 40% of patients treated with either phenobarbitone or carbamazepine ceased seizure activity all together (28, 29). The limitation of these particular studies is the small sample size that was examined, however their results do point to the possibility of an effective method of NS control through the use of antiepileptic drugs. Sodium valproate has also been suggested as another possible drug treatment because of its wide range of efficacy and activity against behavioral difficulties, but it has yet to be tested in clinical trials. In summary, while several drug treatment methods have been examined, with a few showing some promise, a truly efficacious anti-epileptic drug against NS has yet to be found.

## **II. Vector Control**

Because of the close correlation of NS with Onchocerciasis, it is believed that elimination of the *O. volvulus* carrying black fly vector could potentially also eliminate the onset of NS. The theory behind this is that if the only way for onchocerciasis to be spread is through its black fly vector, then the disease's spread will be stopped if the vector is eliminated. In 1997, the African Program for Onchocerciasis Control decided upon a community-directed ivermectin treatment program to eliminate the spread of the disease. This program made ivermectin directly available to communities affected by the filarial disease. However, because of the violence and instability experienced in the

northern regions of Uganda and in South Sudan this treatment often could not be delivered. Since emerging from these conflicts, both of these regions have been able to benefit from the communal distribution of ivermectin. In 2012, the Ugandan Ministry of Health began to implement widespread environmental treatments, using boats and planes to spread the organophosphate Temephos into local river systems. While a causal link has yet to be established, these vector control measures have coincided with a drastic drop in the onset of new cases of NS in Uganda (13). At this juncture, there is no data detailing the effect of vector control methods in Sudan, but given the results obtained in Uganda, it is suggested that similar protocols be followed in that particular region as well. It should also be noted that this protocol is merely a preventative measure. If vector control does indeed prohibit the spread of NS, it still does nothing for those thousands of children that have already contracted the disease.

### **III. Multi-faceted Approaches**

Because of a greater understanding of NS, clinicians are now able to utilize multifaceted approaches to more effectively treat the full range of NS symptoms. In an exciting study completed at the end of 2014 by Idro and colleagues, a multi-faceted approach, consisting of both mental and physical care, was used to treat a group of NS patients. Sodium valproate was used to combat the onset of seizure. Dietary considerations were taken into account, and the patients were provided with nutritional supplements consisting of proteins and essential vitamins and minerals. Patients with emotional and behavioral problems were brought into counseling and provided with mental health services. Many of these patients were then subjected to physical therapy and cognitive stimulation. This approach proved to be successful as several of the

patients were found to have achieved seizure freedom after seven months of therapy. Adding to this success, over 70% of patients in Idro's study achieved remission of seizures (30). This study provides great impetus for further development of this treatment method, as a more holistic approach may yet provide the key to stopping NS.

### **Social Aspects**

One of the most devastating effects of NS is not found in its physiological damage or in any of its destructive cognitive impairments, but in the negative stigma and harmful stereotyping that have become as much a part of the disease as its pathological manifestations. This stigma is far-reaching and goes beyond the views of those on the outside observing the disease and extends to the families and even the physicians and nurses who are ultimately tasked with caring for the children suffering with the disease. This stigma and stereotyping is a very complicated issue that stems from a mixture of cultural and religious ideologies and a lack of fundamental education on the subject.

Mental and epileptic diseases have long been plagued with misconception. The ancient Babylonians recorded in stone tablets accounts of epileptic disorders, which they claimed were brought about by supernatural forces of evil (31). The Greek historian Herodotus posited that the wicked deeds committed by the Persian King Cambyses II brought about his judgment in the form of epileptic and mental disorders (32). In the Islamic kingdoms of modern day Saudi Arabia and Turkey, possession by a Jinn was thought to bring about epileptic seizures (33). Hippocrates was one of the first ancient thinkers to discredit entirely the notion of supernatural forces, as he hypothesized that most mental disorders, including epilepsy, were brought about by an excess of the bodily humor phlegm circulating in the blood, which would in turn cause a buildup of phlegm in

the brain (34). Even though the world medical profession has come a long way since the time of antiquity, much of the negative stigma attached to epileptic disorders is still very prevalent in societies and cultures throughout the world today. Given the mysterious and disruptive nature of NS, this negative stigma is far too often placed squarely upon many of the children with this disease.

In comparison with similar studies based in the United States and other developed nations, there is very little qualitative and quantitative data, which addresses the issue of social stigma toward those with epilepsy. However, several studies have been published demonstrating the negative views held by many in sub-Saharan Africa towards those with epileptic disorders and NS specifically. These studies serve to highlight the social harm that these pervasive beliefs continue to bring upon people, families, and communities affected with these types of ailments.

In sub-Saharan Africa, a region that constitutes the epicenter of NS, several misinformed and errant views have led to the formation of many different, and often harmful, belief systems pertaining the origins and causations of such epileptic disorders. Many in this area of the world attribute the frightening onset of a seizure disorder to supernatural means, with evil spirits, curses, and sorcery most often cited as the causative agent (35). This is generally due to deep-rooted traditional religious beliefs that still very much hold to animistic and spiritual ideology. This usually results in spiritual help being sought by the afflicted patient well before any actual medical assistance. To give a loose idea as to the widespread incidence of these practices, a study done by Gretchen Birbeck of UCLA posited that over 70% of the people of Zambia (a country neighboring the NS locus) would seek traditional help regarding epileptic disorders. This number was also

expected to greatly increase in more rural areas where even lower levels of education generally exist. Furthermore, of persons with epilepsy encountered during Birbeck's study, less than four percent reported that they had sought modern medical help for their seizure disorder (36). This is problematic as many of the practices of traditional healers or medicine men are often detrimental to the health of a patient and can oftentimes lead to further complications. For example, in the case of children suffering from febrile seizures, typically brought about by malarial infection, children who were first taken to traditional healers possessed much higher levels of parasitemia and generally required much longer hospital stays and more treatment than children that were first taken to medical professionals (35). Unfortunately, this supernatural attribution and stigmatization does not begin and end with the common layperson, but it also extends to those more educated as well.

Several studies have been published regarding stigmatization and its effects on the presuppositions of healthcare workers and primary caregivers who are directly tasked with assisting children suffering with the disease. In one study by Mutamba and colleagues, one hundred health professionals from the three districts in Uganda most affected by NS were asked a series of interview questions designed to reveal underlying bias. Those participating in this study included doctors, nurses, clinical officers, and laboratory technicians. Of the one hundred individuals polled, over sixty-five percent believed that the disease was linked to evil spirits. Eighty-percent believed that NS is incurable and there is ultimately nothing that can be done for those with the disease. Other alarming responses surfaced throughout the interview that further betrayed underlying negative bias against children with the disease. One registered nurse



communicated her opinion that, "...children with this disease are useless, they cannot do anything for themselves." Another community health officer expressed his view that "these children are a burden to the community, parents cannot work because of them..." (37). This negative perception is very problematic because it is so pervasive amongst those tasked with trying to alleviate this condition. These negative perceptions and unfounded beliefs may then have a direct negative effect upon the quality of patient care. What is more, those in the health care community are looked to as examples of proper response toward many diseases. If these professionals' response is based in fear and ignorance, the response of the general public will in many ways mirror it.

Another recent study, published in early 2015 by Kristine Buchman, reveals much of the same stigmatization among those close to children with NS, such as parents, close relatives, teachers, and religious leaders. Buchman's study used an interview method similar to Mutamba's, in which questioning was used to better understand the experience of caring for a child with the disease. This line of questioning resulted in many negative responses similar to those elicited in the Mutamba study, but also shed some light into other fears and misconceptions surrounding children with the disease. It was revealed that many of the subjects in the study were afraid to directly assist the child with NS in the event of an episode because they feared that the disease was contagious. One teacher reported that, "The only thing for us we can do, normally when a child falls this side maybe when the wind is blowing the other side, we make children move away from where the wind is going. Because we might be thinking it's going to infect them through air." A brother of a child with NS also related his fear of the unknown nature of the disease, saying, "You know when these childrens [*sic*] are having this nodding attack you

can see the saliva coming out from their mouth, and the belief is that maybe that saliva contains something that actually contains the germs that cause epilepsy” (38).

According to the many other interviews conducted by Buchman, these misconceptions are not just isolated ideas, but widely held beliefs among communities that have been exposed to the disease. There were many reported cases of children being excluded from group play with peers, as well as many instances of name-calling, and derogatory references directed at children with the disease. In northern Uganda these children are often referred to as “lucluc” which loosely translates to “head-nodder” (39). An earlier study by Buchmann, conducted using the same interview based methods, found that this derision and exclusion did not begin and end with other children and playmates, but could also extend into the adult realm and affect more serious matters such as exclusion from school admission and community activities (40).

This stigmatization does not only affect the child with the disease, but also greatly affects their families. Most caregivers in the 2015 Buchmann study reported a dramatic reduction in the amount of visitors they received at their homes, and that any visitors would adamantly refuse to eat, drink, or stay the night (38). According to the earlier Buchmann study, this community-wide isolation comes from the traditional African way of thinking that, in regards to disease, the question is generally “who is responsible for my sickness?” not “what is responsible for my sickness?” (40). This widespread community-based stigmatization makes life very difficult for families with children with NS, and in many cases, according to both Mutamba and Buchmann, it can lead to caregivers hiding their children away instead of seeking the proper professional help (37, 38). This may then mean that many children with NS will never receive the care that they

so desperately need as long as these harmful and extremely negative stigmas are allowed to dominate these particular communities.

### **Conclusion**

At the beginning of this paper it was stated that this thesis represented a review of literature serving to examine the mystery of NS. While this may be the direct purpose of the paper, it is in no way the exclusive purpose. For the overall subject is not a mysterious disease, but about assisting the thousands of children affected by that mysterious disease. It is highly probable that before reading this paper you had never heard of NS, for this is the case for many on the western side of the Atlantic. Sadly, many of those affected by NS lack the voice with which to plead their case. Children with this disease are almost always outcasts from their community and have no platform from which to be heard. Therefore, because of a worldwide ignorance to their condition, thousands of children are forced to slowly waste away, mentally and physically, beneath the crushing weight of their mysterious disease. These children need a voice with which to cry out and be heard. They need advocacy among those with the power and pull to initiate change and provide aid. However, this advocacy cannot be achieved without knowledge of the issue. The world must first be made aware of these nodding children before it can act on their behalf. Because with awareness comes hope and the potential for a spark to be lit that will lead to a flame that clearly illuminates the plight of the lucluc.

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