

# Virologist hunts cryptic virus that may be responsible for a society-shattering disease in Central Africa

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A child with nodding syndrome.

In the Democratic Republic of Congo, they call it "epupuluga": a cluster of symptoms that affects children between the ages of 5 and 15. The children slip into epileptic seizures for several minutes, and then come out of the seizures with no memory of what's happened.

Next, they nod their heads repeatedly—and almost unconsciously—sometimes for 10 to 15 minutes. These episodes occur several times per day. The children stop growing and developing. They stop going to school. Their families miss work to take care of them.

Eventually, they die, either by falling on top of fire or drowning during a seizure, or from the disease itself.

In Western medicine, the disease is known as nodding syndrome. Even among other rare, mysterious maladies, it's poorly understood and understudied. The World Health Organization (WHO), which operates a series of programs targeting neglected tropical diseases, lacks any kind of formal program for nodding syndrome.

There have been reports that the disease is triggered by certain foods, or by exposure to cold. Many villagers think its roots are supernatural.

"What causes nodding syndrome is not really known," explained John Mokili. "When it doesn't have a cause, it's easy to believe the child has been affected by witchcraft."

The San Diego State University virologist is on a mission to identify the origins of this mystifying disease. He and his colleagues believe that a virus might be responsible for nodding syndrome, and the hunt is on to find it using state-of-the-art genomic sequencing techniques developed at SDSU.

## **Congolese native**

The work hits close to home for Mokili. He is a native of the DRC. He studied biology at the National Pedagogy University in Kinshasa, the nation's capital, before earning his master's degree in medical microbiology at London University's School of Hygiene and Tropical Medicine and a doctorate in virology at the University of Edinburgh in 1998.

Mokili has been on the forefront of some recent, major discoveries in his field. Last year, he and fellow researchers in SDSU's Viromics

Information Institute, along with their international partners, discovered a novel virus lurking in the intestines of between half and three-quarters of the world population. They made the discovery using a new computational technique that makes it easier to identify stretches of genetic code that could harbor viruses.

Mokili hopes to use this same technique to determine whether nodding syndrome is caused by a virus. In order to do these tests, he would need to gather a lot of genetic data from the people and environment—the metagenome—where the disease runs rampant.

"No one has done a thorough viral investigation of this population," Mokili said.

In March, Mokili was invited to join an international coalition of clinicians, epidemiologists, and entomologists banding together to look more closely at nodding syndrome, which has been found in several Central African countries including the DRC, South Sudan and Uganda. Nobody knows how many people have come down with nodding syndrome, but the WHO estimates that the number in the thousands.

Last year, Mokili and several colleagues made two trips to the DRC to collect samples. They primarily visited three villages: Dingila, Liguga and Titule. Many of the homes there are accessible only by Land Cruisers and motorbikes over winding, bumpy dirt roads. What they found in these villages was heartbreaking.

"In Dingila, every third house we visited had nodding syndrome," Mokili said. "In some places, they were saying it made malaria seem like nothing."

Nodding syndrome devastates whole communities. Mokili's team encountered a 21-year-old woman who looked 13. She had two more

siblings with the disease. When children come down with nodding syndrome, their families stop going to work to care for them. With so many of the village's children are dying, it strains the available workforce for both the present and future.

## **Amassing the metagenome**

Collecting data in such an environment isn't easy. For one thing, since nobody knows what causes the disease, it was unclear whether the researchers themselves were at risk for exposure.

Also, villagers in this region can be suspicious of Westerners with supposedly good intentions. At one point, the DRC was a wealthy, stable country. It's flush with natural resources, mostly in the form of rare and valuable minerals. It had one of the best health care systems in Central Africa, Mokili explained. But over time, through political upheaval and mismanagement, the infrastructure degraded. Today its citizens are among the poorest on the planet.

"The Congo has lots of resources," Mokili said. "It could have been one of the richest countries in the world, but it's being destroyed by what it has. It's been exploited inside and out."

Mokili's familiarity with the country and its people was essential to the researchers' mission. He spoke the villagers' language. He knew many of the country's government officials, medical workers and scientists. With his help, the research team was able to collect genetic samples from about 140 children, half with nodding syndrome and half without.

They also collected more than 700 samples of a tiny culprit who might be spreading the disease: the black fly.

The flies swarm in thick clouds around the region's rivers, and the

villagers bathe in these rivers almost every day. Mokili thinks it's possible these flies carry a heretofore unknown virus that's responsible for nodding syndrome. Outsiders tend not to come down with nodding syndrome after short visits, he added, so there may be some cumulative property of the disease which requires multiple exposures before it becomes deadly.

## Virus hunting

Back in his lab at SDSU, Mokili is currently generating data, and will work with computer science professor Rob Edwards to analyze the metagenomic data the team collected. They are looking for sequences of DNA and RNA only present in the samples from people with nodding syndrome. If they can identify such sequences, they might be looking at the genetic structure of the virus behind nodding syndrome.

It will be a difficult search, however, as there are likely many other viruses that can confound the data.

Still, Mokili is hopeful.

"If we know the cause of the disease, it will lead to new research," he said. "If we discover the virus causing nodding [syndrome](#), we can start thinking about vaccine development. That's the best way of preventing children from acquiring this [disease](#) in the first place. But the bottleneck right now is knowing the cause."

Provided by San Diego State University

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