

Neurotoxins and the Effects on the Chamorro People of Guam

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Neurodegenerative disease has become a more popular field of biological research in the United States over the past decade, largely due in part to an aging population. However, in other parts of the world, the environment, rather than age, may play a larger role in the onset of neurodegenerative disease (Trojsi, Monsurro, & Tedeschi, 2015). The Chamorro people of Guam, an indigenous group living primarily on the Mariana Islands, have been studied to have among the highest rates of a certain type of neurodegenerative disease in the world: amyotrophic lateral sclerosis-Parkinsonism dementia complex, or ALS-PDC. ALS-PDC is a fairly aggressive disease, with the age of onset as early as 18 years old in Chamorro people. It first presents as ALS/Lou Gehrig's disease, causing weakness and eventually paralysis of the limbs. However, unlike ALS alone, symptoms of Parkinson's Disease and Alzheimer's also become present, typically not long after the ALS symptoms get to be their worst (Cox, Banack, & Murch, 2003). Up until the beginning of the century, not much was known about why these people had such high rates of this very progressive neurodegenerative disease. Some thought it was genetic, others environmental, and some even thought it was perhaps a newly discovered prion disease. It was not until the diets of Chamorro people were extensively studied that it became clear that their diets contained a fairly high amount of the neurotoxin beta-N-methylamino-L-alanine, BMAA. However, it appeared the Chamorro people shouldn't have been taking in enough of the toxin to cause such extensive damage. Another discovery was made, this time taking into account the food web of the Mariana Islands. A staple of the Chamorro diet is the flying fox (*Pteropus mariannus*), once a fairly common mammal on the islands. Militarization and urbanization of Guam, however, destroyed much of the flying foxes' habitats. This caused the Chamorro people to hunt more readily for flying foxes. The problem with this is that flying foxes exclusively eat seeds of the cycad tree, and these seeds contain BMAA. While the Chamorro people also consume cycad seeds (*Cycas micronesica*), they primarily grind them up and make them into flour; the grinding up of the seeds decreases the potency of the BMAA (Banack, Murch, & Cox, 2005). The relationships between BMAA, ALS-PDC, and the Chamorro people has been studied over the past decade, but less research has been done on the exact role of the flying fox and how militarization and urbanization also tie in to the overall problems of the Chamorro people.

The Chamorro people of Guam have inhabited the Mariana Islands since at least 3,500 years ago (Vilar, et al., 2012). A culture of its own, these people have traditions dating back centuries. These traditions, however, may have a negative impact on Chamorro people. When it was found that BMAA was biomagnified within the tissues of flying foxes – that is, BMAA accumulated in the tissues and increased in concentration – the Chamorro people were informed of the dangers. They continued (and still continue) to consume flying foxes, boiling them in coconut milk and eating them whole (Cox, Banack, & Murch, 2003). Militarization, urbanization, and the population of flying foxes were all a factor in the rate of ALS-PDC among Chamorro people in the early 21st century and in many cases, there is overlap.

When Guam was militarized in the 20th century, many problems began to arise in relation to flying foxes almost immediately. Areas of forest were cut down and firearms were more readily available, decreasing their habit and increasing the amount of hunting done on the animals, specifically by Chamorro people. From 1950 to the mid 1970s, the rate of ALS-PDC dramatically increased, correlating with the increased consumption of flying foxes. However, the foxes were hunted to near-extinction and after that, the ALS-PDC rate declined in the Chamorro people (Monson, Banack, & Cox, 2003). But why exactly did the rate spike with the increased consumption of flying foxes? Chamorro people were also taking in BMAA from the cycad flour they consumed almost daily. Why was there such a drastic correlation between ALS-PDC and the population of flying foxes? To understand how BMAA is more toxic within the tissues of the flying fox, it is important to first have an understanding of the toxin itself. BMAA is produced by nearly all taxa of cyanobacteria, including cyanobacteria that lives in the cycad tree (Cox, et al., 2005). When ground up and made into flour, the

grinding and washing processes significantly decrease the concentration of BMAA, hence why consuming the flour daily does not have a significant effect on the rate of ALS-PDC in Chamorro people. The issue is that the toxin is biomagnified, gaining toxicity as it is consumed through higher trophic levels (Cox, Banack, & Murch, 2003). BMAA was found to accumulate throughout nearly all the tissues of the flying foxes – skin, brain, liver, kidneys, etc. Since Chamorro people consume flying foxes whole, they took in all the BMAA within the flying foxes they consumed (Banack, Murch, & Cox, 2005). Once consumed by the Chamorro, BMAA accumulates in their tissues as well, killing certain motor neurons and bringing about the symptoms of ALS. BMAA can also cross the blood-brain barrier in the body as well and causes proteins to misfold and aggregate in the brain, leading to more damage and neurodegeneration (Cox, et al., 2015). The reason the flying foxes fail to exhibit signs of any kind of neurodegeneration is still disputed, however Dr. Cox and Dr. Sacks hypothesize that the BMAA is localized in their fat stores and not directly having an impact on their tissues like in humans.

As flying foxes continued to be hunted and lose their habitats, the rate of ALS-PDC continued to slowly decline. Another cause for the decline in ALS-PDC among the Chamorro people of the Mariana Islands was that many of them left the island for the United States. Even in the United States though, the Chamorros who left the islands still sometimes exhibited ALS-PDC, though at much lower rates than their still-native counterparts (Monson, Banack, & Cox, 2003). With the younger generation of Chamorro people becoming more informed on the negative consequences of consuming flying foxes, efforts are being made to end consumption (Trojsi, Monsurro, & Tedeschi, 2015) and efforts are being made to try to reverse the damaging effects of ALS-PDC. One of the leading efforts is by Dr. Cox and his use of L-serine, an amino acid. It has been shown to reduce the amounts of aggregated misfolded proteins (Cox, et al. 2015), therefore suggesting that an increase in consumption of L-serine may significantly help with the toxic effects of BMAA.

While the occurrence of ALS-PDC in the United States is uncommon, studying it among the Chamorro people has offered insight to not only neurodegenerative diseases as a whole, but also to relationships within tropical forests. A seemingly small relationship, such as cyanobacteria and the cycad seed, have profound impacts on the surrounding ecosystem – providing food to some organisms and causing sometimes fatal diseases in others. The study of ALS-PDC also shed light on the biological mechanisms of neurotoxins such as BMAA and how they play different roles at different trophic levels (Cox, Banack, & Murch, 2003). It would be interesting to study how different neurotoxins within tropical forests play different roles within their given ecosystems, and if certain animals have adaptations to overcome the toxicity or transform it into something beneficial. Clearly this is not the case with BMAA and ALS-PDC in Chamorro people, but with as diverse and dynamic as tropical forests are, it would not be surprising to discover a number of organisms that adapt to the microscopic dangers of their environments.

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