

The parkinsonism dementia complex of Guam and flying foxes

The identification of the high prevalence of parkinsonism dementia complex (PDC) and amyotrophic lateral sclerosis (ALS) on the Western Pacific island of Guam in the 1950s and 1960s raised hopes that the cause of these diseases could be identified on these island(s), and that this discovery would help to explain neurodegenerative diseases such as Parkinson's disease (PD), Alzheimer's disease (AD) and ALS in other parts of the world.¹ While the cause of ALS and PDC on Guam remains elusive, genes responsible for autosomal dominant forms of PD, ALS and AD have been discovered. Contrary to widespread neurological belief, PDC and ALS on Guam are unlikely to be due to cycad ingestion in tortilla flour. The excitatory amino acid beta-methylamino L-alanine (BMAA) is present in cycads, and experimentally does lead to an acute neurological syndrome in exposed animals.² Similarly, the motor neuron disease lathyrism relates to beta-N-oxalylamino-L-alanine (BOAA) exposure in humans following ingestion of chickling peas. Unlike lathyrism, PDC does not have a clear temporal relationship to cycad ingestion and it has been estimated that one would have to eat several kg of cycad every day to lead to a comparable exposure to that used in the animal models.³

Exotic geographical locations require exotic medical hypotheses, and Cox and Sacks propose, in the March 26 issue of *Neurology* and in this issue of *Advances in Clinical Neuroscience and Rehabilitation*, that ingestion of a type of Guamanian bat known as flying foxes leads to ALS and PDC by the process of "biomagnification".⁴ These bats were apparently frequently eaten on Guam at social and ceremonial gatherings and some species were hunted to extinction by the mid 1970s. The decline of flying foxes in Guam closely parallels the decline in the incidence of ALS, and the villages that had the highest incidence of PDC and ALS, Umatac and Inarajan, are reported to have had the highest consumption of bat meat. This theory invokes substantial BMAA accumulation in bat tissue, which would result in a sufficient excitatory amino acid load to cause chronic neurotoxicity in humans. It is interesting to speculate how another mammalian species could be resistant to a toxin that is lethal in humans. This could relate to the relative lifespans of bats and humans, and cumulative toxicity in human consumers of bat meat. Alternatively, there are known to be species differences in the propensity to develop tau containing neurofibrillary tangles – humans and ungulates such as sheep develop neurofibrillary tangles whereas monkeys do not, and this may relate to species differences in alternative splicing of the tau gene.⁵ A neuropathological examination of wild pigs on Guam, which avidly eat cycads in the wild, has not revealed neurofibrillary tangle

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formation (Dr. J. Steele, personal communication).

Some type of traditional Chamorro custom may account for PDC and ALS and explain the declining prevalence of these diseases, and the intriguing hypothesis put forward by Cox and Sacks adds to a number of proposed explanations. However, up to this point detailed anthropological enquiry in areas of Guam affected by these diseases has not identified any differences in lifestyle between areas of high and low prevalence (Dr. V. Keck and Dr. J. Steele, personal communication).⁶ The decline in the prevalence of these diseases could also be interpreted in genetic terms with increased social mobility and out breeding leading to a decline in recessive or co-dependant genetic factors. The clustering of these diseases in some families in Southern Guam has been confirmed in a recent long term follow up case control study confirming the excess of cases in first degree relatives of affected individuals as compared with spouses and Chamorro controls.⁷ In the meantime, an analysis of excitatory amino acids in bat meat on Guam will be shortly underway. Whether an environmental cause, genetic factor or combination of these was primarily responsible for these mysterious diseases, it seems likely that the further away the epidemic becomes, the harder it will be to come to any firm conclusions.



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