2022

Disappearance of High Incidence Amyotrophic Lateral Sclerosis and Parkinsonism Dementia in the Western Pacific: Clues to their Etiology

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INTRODUCTION

- Amyotrophic Lateral Sclerosis (ALS) and Parkinsonism Dementia (PD) are two important neurodegenerative disorders that affect motor neurons of the brain and spinal cord leading to progressive weakness and atrophy of skeletal muscles (ALS) and loss of neurons in the brain leading to tremor, rigidity, slowness of movement and dementia (PD).[1]
- Since pre- WWII the incidence rates of ALS and PD in 3 foci in the Western Pacific (Figure 1) were 100 to 1000 times greater than incidence rates of ALS found on the mainland United States and elsewhere globally.[2]
- More recent surveillance of ALS and PD in the Kii Peninsula of Japan (sub-foci in Kozagawa and Hohara), in West New Guinea (West Papua), and on Guam in the Mariana Islands, have dramatically declined from their initial high incidence rates decades ago (Figure 2).[3-8]
- The initial thinking for the high incidence was that it might be due to genetic factors. However, the disappearance of the high incidence, within 30-40 years post WWII, along with changes in lifestyle practices, strongly suggest environmental factors in their cause and disappearance.[1]
- On Guam, non-genetically related spouses in the same household of patients had measured risk of developing ALS and PD, while offspring did not.[9]

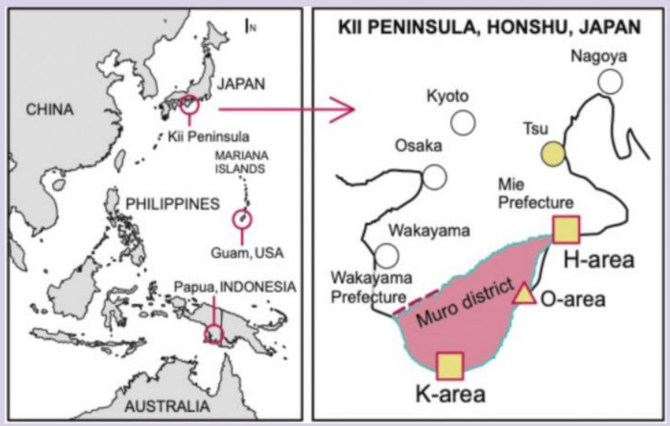

Figure 1: Map of the Western Pacific Foci (from Spencer et al., 2020)[2].

METHODS

- Cross-referencing of data and an analysis of recent scientific reports, helped establish the trends in incidence rates and the dramatic decline of ALS and PD in all three foci.
- We also reviewed and evaluated possible environmental causes and lifestyle changes that likely account for the disappearance of the high incidence of ALS and PD in these foci.

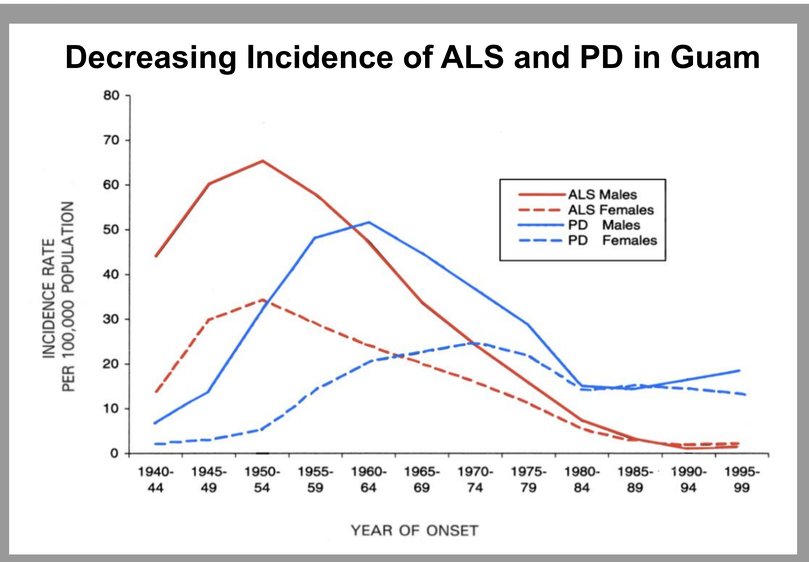

Figure 2: Decrease in average annual incidence rate of ALS and PD males and females per 100,000 population of Guamanian Chamorros per 5 year periods between 1950 to 1999 (Modified from Plato et al.,2003)[3]

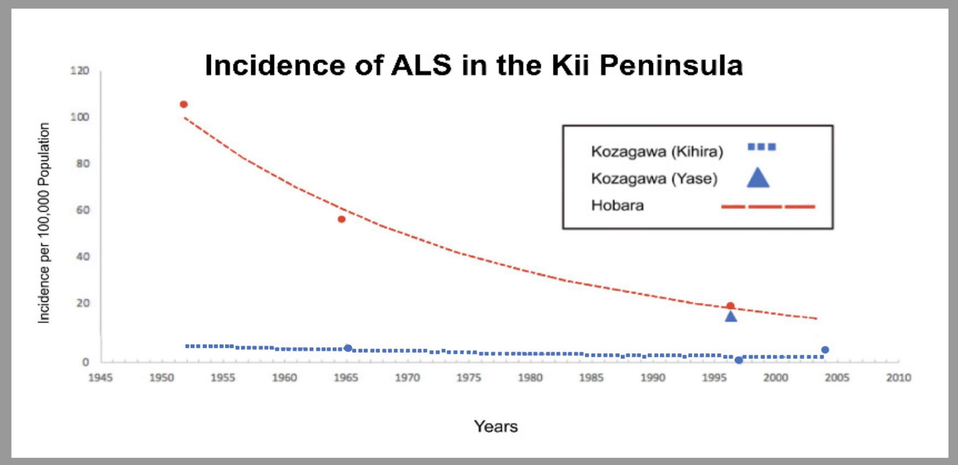

Figure 3: Decrease in the incidence of ALS in Kozagawa and Hobara, two sub foci within the Kii Peninsula of Japan between the years 1950 to 2010 (Data from Kihara et al., 1992; Yale et al.,1972 and Kuzuhara & Kokubo et al., 2012).[4,5,6]

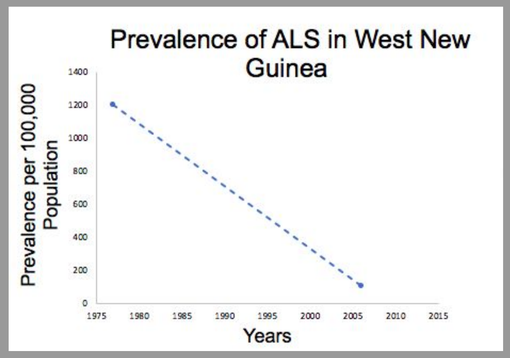

Figure 4: Decrease in the prevalence of ALS in West New Guinea from 1975-2012 (Data from Gajdusek & Salazar et al., 1982 and Okumiya et al., 2014). [7,8]

RESULTS & DISCUSSION

- In support of the disappearance of the high incidence of ALS and PD in these foci, the age at onset of clinical symptoms of patients has increased, along with changes in the male to female sex ratio from 2:1 to near unity today (Figure 2).
- A potential cause of ALS and PD includes consumption of Cycad seeds that were traditionally ground into flour to make tortillas. They contain the neurotoxin β-N-methylamino-L-alanine (BMAA) that has been previously implicated in these disorders.[10-12]
- A second potential cause is aluminum (Al^{+3} ions) in soil and drinking water that has been shown to be toxic to fish, plants, and trees (acid rain) and experimentally in animals producing neurodegenerative changes similar to ALS and PD.[10,11]
- Post WWII, these foci experienced changes in traditional cultural practices and rapid modernization, often relying on imported foods and other goods, rather than those found in the wild or produced in their local environment.[13]

CONCLUSION

- The rapid disappearance of the high incidence of ALS and PD in these 3 foci strongly suggest that environmental factors are partially or wholly involved in their etiology and that modernization and changing lifestyle practices of people living in these foci likely led to their subsequent decline.
- Future research should include a further assessment of these and other potential neurotoxins in the environment and the development of experimental animal models for suspected environmental agents as a cause of ALS and PD globally.

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