Clinical Neurology and Neuroscience
2026, Vol. 10, No. 3, pp. 77–82
https://doi.org/10.11648/j.cnn.20261003.12

Review Article

Lytico-Bodig in Guam: A Mysterious Neurological Disease

Claire Liu*

International Baccalaureate Division, St. John's School, Tamuning, Guam

Abstract

Lytico-Bodig disease, also known as Amyotrophic Lateral Sclerosis-Parkinsonism-Dementia Complex (ALS-PDC), is a rare neurodegenerative disorder uniquely affecting the Chamorro people of Guam. This review analyzes its historical context, epidemiology, clinical features, proposed causes, and ongoing research. First identified in the mid-20th century, Lytico-Bodig combines ALS-like motor symptoms, parkinsonism, and dementia, with notable clinical variability. It disproportionately affects certain Chamorro families and villages, suggesting genetic and environmental influences. The disease peaked in the 1950s–60s as a leading cause of death. Although the incidence has dramatically declined, cases persist, reflecting its public health relevance. While environmental factors, notably cycad seeds and flying foxes containing the neurotoxin β-methylamino-L-alanine (BMAA), along with genetic susceptibility are strongly implicated, the causal link between BMAA and the disease remains a subject of ongoing scientific debate and uncertainty. Neuropathological findings show neuronal loss, tau protein deposits, and neurofibrillary tangles, similar to Alzheimer's and Parkinson's diseases. Diagnosis is difficult due to symptom overlap with other conditions, and treatment remains supportive. Its progressive nature imposes a heavy burden on caregivers, underscoring the need for robust support systems. Ultimately, Lytico-Bodig remains a complex disorder requiring continued research, improved healthcare strategies, and community involvement to improve outcomes for affected individuals.

Keywords

Lytico-Bodig Disease, Guam, Amyotrophic Lateral Sclerosis, Parkinsonism, Dementia, Neurofibrillary Tangle, Chamorro, Cycad

1. Introduction

Reports of the passing of what has been characterized as one of Guam's final medically documented patients at the Guam Regional Medical City due to respiratory failure have sparked a renewed interest in revisiting a disease that was once highly prevalent on Guam but has now almost disappeared [1]. Lytico-Bodig disease (LBD) is a rare and devastating neurodegenerative condition predominantly seen in the Chamorro population of Guam [1]. LBD is a term coined locally to refer to two distinct forms of clinical presentation: "Lytico" is associated with a progressive motor degeneration similar to amyotrophic lateral sclerosis (ALS) [20], while "Bodig" is used to describe a form of parkinsonism accompanied by dementia resembling Alzheimer's disease (AD) [2].

Both conditions often occur together in individuals, leading to a debilitating and fatal disease progression. Over the last century, this disease has captured significant attention from medical researchers and healthcare professionals due to its high localized prevalence and its striking resemblance to mul-

*Correspondence: Claire Liu (claireliu090524@gmail.com)

Received: 13 June 2026; **Accepted:** 7 July 2026; **Published:** 11 August 2026

tiple classic neurodegenerative disorders [17]. Despite extensive research into its causes, the disease remains a mystery, with a complex combination of genetic, environmental, and cultural factors thought to contribute to its occurrence. This review article explores LBD, focusing on its clinical presentation, epidemiology, historical timeline, potential etiological factors, and the profound impact it has had on the population of Guam.

2. Research Methodology

To ensure transparency and reproducibility, a systematic literature search was conducted across major electronic databases, including PubMed, ScienceDirect, and Google Scholar. The search utilized keywords such as "Lytico-Bodig", "ALS-PDC Guam", "BMAA neurotoxin", "Chamorro neurodegeneration", and "Cycad toxicity". Articles selected for inclusion comprised peer-reviewed primary research papers, historical epidemiological reports, and neuropathological studies published between 1954 and 2021. Selection criteria focused on relevance to the clinical features, epidemiology, and historical or environmental etiology of ALS-PDC on Guam.

3. Historical Context

While localized accounts of a progressive paralytic illness among the Chamorro people exist as far back as the early 1800s, the disease was not formally recognized by the international medical community until the early 1950s [11]. It was during this post-WWII period that clinicians first documented the extraordinarily high cluster of cases, formalizing the condition under the medical designation of Amyotrophic Lateral Sclerosis-Parkinsonism-Dementia Complex of Guam (ALS-PDC) [11].

During its peak between the 1950s and 1960s, LBD was the leading cause of death among adult Chamorros, with an incidence rate reaching up to 420 cases per 100,000 people [3]. The disease initially disproportionately affected men, with a male-to-female ratio of 2:1 [3]. However, this gender gap steadily equalized by the 1980s [22].

Table 1. *Timeline of Key Milestones for LBD.*

Timeline	Key Milestones
Early 1800s	Early descriptions of paralytic disease among Chamorros
1950s	Formal epidemiological documentation of ALS-PDC by Kurland & Mulder
1960s	Equalization of male-to-female ratio; discovery of high NFT prevalence
2000s	Focus shifts heavily to biomagnification of BMAA via flying foxes

The disease prevalence declined dramatically after the 1970s, and today, new cases of LBD are extremely rare [22]. This decline has been tentatively attributed to rapid westernization, shifts in dietary habits, and altered environmental exposures, though the exact reasons remain a subject of study. The unique concentration of cases in Guam's southern villages, particularly Humåtak and Malesso', provided researchers with a natural laboratory to study the disease [12]. Similar geographic clusters of ALS and parkinsonism have also been observed in the Kii Peninsula of Japan and among the Auyu people of Western New Guinea [4], suggesting a possible shared environmental or genetic link across these isolated regions [4, 12].

4. Clinical Features

The clinical features of LBD are broadly categorized into motor and cognitive manifestations [5]. The motor features of "lytico" (derived from the Spanish word *paralytico*) closely resemble classic ALS [15]. Affected individuals present with muscle weakness, upper and lower motor neuron signs, muscle atrophy, and progressive paralysis, typically initiating in the limbs before spreading globally [2, 5]. In advanced stages, patients lose the ability to speak, swallow, or breathe independently, frequently succumbing to respiratory failure within a few years of motor symptom onset [24].

Conversely, the "bodig" presentation (derived from the Spanish *bodega*) manifests as prominent parkinsonism, including bradykinesia, tremors, and rigidity [2]. Many patients present with an overlapping blend of both motor syndromes, which complicates pure clinical classification.

Cognitive symptoms associated with LBD mimic Alzheimer's disease, marked by progressive memory loss, spatial confusion, and profound behavioral changes [5, 19, 22]. Neuropathologically, the disease is defined by a dense accumulation of neurofibrillary tangles (NFTs) in the cerebral cortex and brainstem [5]. Remarkably, systematic postmortem evaluations in the 1960s and 1970s revealed that up to 70% of asymptomatic Guamanians possessed these specific NFTs, raising critical questions regarding whether they signified a preclinical stage of the disease or a baseline environmental phenotype [3].

Another notable clinical marker is linear retinal epitheliopathy, a unique fundoscopic eye disorder that was observed to precede the onset of overt neurological signs in a subset of patients [6]. Over the decades, the median age of onset has progressively shifted upward into the 60s and 70s, though the disease remains invariably fatal [22, 24].

5. Epidemiology

The epidemiological profile of LBD is distinct due to its extreme geographic and ethnic confinement to the Chamorro people of Guam [11]. Between the 1950s and 1970s, the incidence of ALS-PDC on Guam was estimated to be over 50 times greater than that of classic ALS in the continental United States [11]. The condition predominantly presents in adults aged 40 and older, showing a distinct familial aggregation [22]. Genetic pedigree analyses suggest a hereditary predisposition; however, the lack of a clear Mendelian inheritance pattern indicates that environmental co-factors are required to trigger clinical disease expression [21].

6. Proposed Etiologies

6.1. Genetic Factors

While familial clustering is highly evident, decades of genomic sequencing have failed to identify a single causative monogenic mutation exclusive to the Chamorro population [22]. Current hypotheses focus on complex polygenic variations or specific metabolic alleles common to the indigenous island population that may impair endogenous toxin clearance or alter mineral metabolism, rendering individuals uniquely vulnerable to environmental triggers [14].

6.2. Environmental and Dietary Factors

For decades, environmental and dietary hypotheses have centered on the traditional consumption of *Cycas micronesica*, a native cycad tree. The seeds of this plant were historically processed into flour by Chamorro families during food shortages [1, 13, 25]. Cycad seeds contain β-methylamino-L-alanine (BMAA), a non-protein amino acid that demonstrates excitotoxic neurotoxicity in animal models [10].

A secondary pathway for BMAA exposure involves the traditional consumption of flying foxes (*Pteropus mariannus*), local fruit bats that feed heavily on cycad seeds. Researchers hypothesized that BMAA biomagnifies within the fat tissues of these bats, delivering concentrated doses of the neurotoxin to humans upon consumption [7, 10]. *However, it is vital to note that this etiological link remains inconclusive and highly debated within the scientific community, as replication studies have yielded conflicting results regarding the exact concentrations of free versus protein-bound BMAA required to induce chronic human neurodegeneration* [8, 9].

6.3. Gene-Environment Interaction

By the 1990s, the paradigm shifted toward a multifactorial gene-environment interaction. Advances in molecular biology revealed that specific polymorphisms affecting calcium-magnesium metabolism, combined with chronic dietary deficiencies of these minerals in Guam's volcanic soil and drinking water, could compromise the blood-brain barrier and facilitate the accumulation of neurotoxic metals or organic toxins like BMAA [12, 14, 18].

6.4. Infectious Agents

Alternative historical inquiries investigated whether early-life viral infections could act as a distant trigger for late-onset neurodegeneration. Epidemiological overlaps were noted with a severe poliomyelitis outbreak on Guam in the late 19th century, alongside potential exposure to Japanese encephalitis virus [21]. This hypothesis, however, lacks direct pathognomonic evidence and remains largely speculative.

7. Diagnosis

There is no single definitive in-vivo diagnostic biomarker for LBD. Premortem diagnosis is primarily clinical, relying on comprehensive longitudinal neurological examinations to document the dual presence of ALS-like upper/lower motor neuron signs, parkinsonian rigidity, and cognitive decline [22]. A comprehensive genealogical history detailing Chamorro heritage and historical dietary exposures provides critical diagnostic context [21, 22].

Neuroimaging modalities such as CT and structural MRI often reveal generalized or frontotemporal cortical atrophy, though these findings are non-specific. Advanced metabolic imaging via PET or SPECT, alongside standardized neuropsychological batteries, serve primarily to rule out alternative, treatable neurological conditions. *A definitive diagnosis can only be established via a comprehensive postmortem examination (autopsy), which reveals the pathognomonic distribution of tau protein aggregates, extensive neuronal loss, and widespread neurofibrillary tangles throughout the brain and spinal cord [5].*

8. Treatment and Prognosis

Treatment for LBD remains entirely supportive and palliative, as no disease-modifying therapies exist [23]. Parkinsonian motor deficits are managed with standard dopaminergic agents such as levodopa or dopamine agonists, though clinical efficacy is notably limited and transient compared to classic Parkinson's disease [3]. Cognitive symptoms are addressed symptomatically using cholinesterase inhibitors (e.g., donepezil, rivastigmine) or NMDA receptor antagonists (memantine), with mixed clinical results. Multi-disciplinary care incorporating physical, occupational, and speech-language

therapy is essential to preserve functional mobility and safe swallowing mechanics for as long as possible [23].

The long-term prognosis is uniformly poor. The disease follows an inexorable, progressive course. While survival timelines vary broadly, ranging from 3 to 10 years post-diagnosis, patients ultimately succumb to secondary systemic complications, most commonly aspiration pneumonia or neuromuscular respiratory failure [24].

Table 2. *Summary of Disease Characteristics.*

Perspective	Key Scientific and Clinical Findings
Clinical Features	Dual manifestation of motor neuron degeneration ("Lytico") and parkinsonism-dementia ("Bodig"); presence of linear retinal epitheliopathy [2, 5, 6].
Proposed Etiologies	Multifactorial includes the BMAA/Cycad consumption hypothesis, heavy metal accumulation (Al/Fe) due to soil mineral deficiencies, and polygenic genetic susceptibility [10, 14, 18]. *The causal role of BMAA remains under active scientific debate.*
Neuropathological Findings	Severe frontotemporal and subcortical neuronal loss; extensive tau-positive neurofibrillary tangles (NFTs) observed in both symptomatic patients and asymptomatic historical controls [3, 5].
Research Milestones	Formal classification in 1954; discovery of geographic clusters in Japan/New Guinea; identification of environmental neurotoxin biomagnification models in the early 2000s [4, 10, 11].

9. Public Health Implications and Future Directions

LBD has left an enduring mark on the public health infrastructure of Guam. During its mid-century peak, the overwhelming volume of complex, total-care patients placed an extraordinary burden on local healthcare facilities and family caregivers [22]. While the steep drop in incidence has alleviated immediate systemic strain, it remains imperative that contemporary regional healthcare providers remain trained to recognize its atypical clinical phenotypes.

Future research directions require a more critical evaluation of alternative environmental hypotheses, epigenetic modifications, and the clear prioritization of long-term epidemiological monitoring. Investigating the molecular pathways of tau aggregation in LBD continues to hold profound, universal implications for decoding the pathogenesis of global neurodegenerative diseases like Alzheimer's, Parkinson's, and sporadic ALS [12, 16].

10. Conclusion

LBD stands as one of the most intriguing and complex enigmas in modern neuroepidemiology. Its dramatic emergence, geographic confinement to the Chamorro population, and subsequent rapid decline highlight a complex interplay between genetics, culture, and a changing environment. While definitive diagnostic tools and curative therapies remain elusive, decades of dedicated research on Guam have provided invaluable insights into mechanisms of neurodegeneration and tauopathology worldwide. Continued interdisciplinary vigilance is vital to fully uncover the remaining secrets of this unique disorder.

Abbreviations

AD	Alzheimer’s Disease
ALS	Amyotrophic Lateral Sclerosis
ALS-PDC	Amyotrophic Lateral Sclerosis-Parkinsonism-Dementia Complex
BMAA	β-methylamino-L-alanine
LBD	Lytico-Bodig Disease
NFT	Neurofibrillary Tangle
PD	Parkinson’s Disease

Acknowledgments

Dr. Chichan Lee from the Guam Regional Medical City provided guidance and supervision on the format and content of this article, reviewed the manuscript, and suggested corrections.

Author Contributions

Claire Liu: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing

Conflicts of Interest

The author declares no conflicts of interest.

References

[1] Gim énez-Rold án, S., Steele, J. C., Palmer, V. S., & Spencer, P. S. Lytico-bodig in Guam: Historical links between diet and illness during and after Spanish colonization. *Journal of the History of the Neurosciences*. 2021, 30(4), 335–374. https://doi.org/10.1080/0964704X.2021.1885946

[2] Eisen, A. A., & Hudson, A. J. Amyotrophic lateral sclerosis: concepts in pathogenesis and etiology. *The Canadian Journal of Neurological Sciences*. 1987, 14(4), 649–652. https://doi.org/10.1017/s031716710003743x

[3] Steele, J. C. Parkinsonism-dementia complex of Guam. *Movement Disorders*. 2005, 20(Suppl 12), S99–S107. https://doi.org/10.1002/mds.20547

[4] Gajdusek, D. C., & Salazar, A. M. Amyotrophic lateral sclerosis and parkinsonian syndromes in high incidence among the Auyu and Jakai people of West New Guinea. *Neurology*. 1982, 32(2), 107–126. https://doi.org/10.1212/wnl.32.2.107

[5] Hof, P. R., Nimchinsky, E. A., Bu ée-Scherrer, V., et al. Amyotrophic lateral sclerosis/parkinsonism-dementia complex of Guam: quantitative neuropathology, immunohistochemical analysis of neuronal vulnerability, and comparison with related neurodegenerative disorders. *Acta Neuropathologica*. 1994, 88(5), 397–404. https://doi.org/10.1007/BF00389490

[6] Cox, T. A., McDarby, J. V., Lavine, L., Steele, J. C., & Calne, D. B. A retinopathy on Guam with high prevalence in Lytico-Bodig. *Ophthalmology*. 1989, 96(12), 1731–1735. https://doi.org/10.1016/s0161-6420(89)32656-x

[7] Murch, S. J., Cox, P. A., & Banack, S. A. A mechanism for slow release of biomagnified cyanobacterial neurotoxins and neurodegenerative disease in Guam. *Proceedings of the National Academy of Sciences*. 2004, 101(33), 12228–12231. https://doi.org/10.1073/pnas.0404926101

[8] Banack, S. A., Caller, T. A., & Stommel, E. W. The cyanobacterial neurotoxin BMAA and ALS. *Amyotrophic Lateral Sclerosis*. 2010, 11(1-2), 9–20. https://doi.org/10.3109/17482960903286010

[9] Pablo, J., Banack, S. A., Cox, P. A., Johnson, T. E., Papapetropoulos, S., & Bradley, W. G. Cyanobacterial neurotoxin BMAA in ALS and Alzheimer's disease. *Acta Neurologica Scandinavica*. 2009, 120(4), 216–225. https://doi.org/10.1111/j.1600-0404.2008.01150.x

[10] Cox, P. A., Banack, S. A., & Murch, S. J. Biomagnification of cyanobacterial neurotoxins in bats feeding on cycad seeds: Implications for ALS–PDC in Guam. *Neurology*. 2003, 61(3), 387–389. https://doi.org/10.1212/01.WNL.0000076460.09234.B2

[11] Kurland, L. T., & Mulder, D. W. Epidemiologic investigations of amyotrophic lateral sclerosis. 1. Preliminary report on geographic distribution, with special reference to the Mariana Islands, including Guam. *Neurology*. 1954, 4(5), 355–378. https://doi.org/10.1212/WNL.4.5.355

[12] Spencer, P. S., & Palmer, V. S. ALS-parkinsonism-dementia complex of Guam: a prototype in the global search for causes of neurodegenerative disease. *Journal of Neurology, Neurosurgery & Psychiatry*. 2012, 83(10), 1006–1008. https://doi.org/10.1136/jnnp-2012-302337

[13] Kisby, G. E., Ellison, M., & Spencer, P. S. Content of the neurotoxic amino acid L-BMAA in cycad flour prepared by Chamorro women of Guam. *Neurology*. 1992, 42(7), 1336–1340. https://doi.org/10.1212/WNL.42.7.1336

[14] Cruz-Aguado, J. A., & Winkler, D. Binding of β-N-methylamino-L-alanine (BMAA) to human proteins. *Neuroscience Letters*. 2008, 444(2), 145–148. https://doi.org/10.1016/j.neulet.2008.08.078

[15] Pardo, C. A., Wong, M. M., & Price, D. L. The neurobiology of ALS and related disorders. *Molecular Mechanisms of Neurodegenerative Diseases*. 2006, 111–131. https://doi.org/10.1385/1-59745-014-5:111

[16] Ross, C. A., & Poirier, M. A. Protein aggregation and neurodegenerative disease. *Nature Medicine*. 2004, 10(S7), S10–S17. https://doi.org/10.1038/nm1066

[17] Johnson, H. A., & Eisen, A. Amyotrophic lateral sclerosis: current perspectives. *CMAJ*. 1994, 150(7), 1107–1116.

[18] Perl, D. P., & Brody, A. R. Alzheimer's disease: X-ray spectrometric evidence of aluminum accumulation in neurofibrillary tangle-bearing neurons. *Science*. 1980, 208(4441), 297–299. https://doi.org/10.1126/science.7350650

[19] Montine, T. J., & Montine, K. S. Pathology and pathogenesis in Alzheimer's disease. *Neurobiology of Alzheimer's Disease*. 2007, 49–70.

[20] Kiernan, M. C., Vucic, S., Cheah, B. C., Turner, M. R., Eisen, A., Hardiman, O.,... & Talbot, K. Amyotrophic lateral sclerosis. *The Lancet*. 2011, 377(9769), 942–955. https://doi.org/10.1016/S0140-6736(10)61156-7

[21] Bradley, W. G. A clinical review of ALS and Parkinsonism-dementia complex of Guam: Clues to etiology. *Journal of the Neurological Sciences*. 2000, 180(1–2), 96–99. https://doi.org/10.1016/S0022-510X(00)00412-0

[22] Galasko, D., Salmon, D. P., Craig, U. K., Thal, L. J., & Schellenberg, G. D. Clinical features and changing patterns of neurodegenerative disorders on Guam, 1997–2000. *Neurology*. 2002, 58(1), 90–97. https://doi.org/10.1212/WNL.58.1.90

[23] Vender, R. L., & Miller, R. G. Palliative care in amyotrophic lateral sclerosis: A review of current international guidelines and initiatives. *Journal of Neurology, Neurosurgery & Psychiatry*. 2009, 80(6), 587–591. https://doi.org/10.1136/jnnp.2008.151498

[24] Morris, H. R., Al-Sarraj, S., Schwab, C., & Steele, J. C. A clinical and pathological study of motor neuron disease on Guam. *Brain*. 2004, 127(6), 1339–1351. https://doi.org/10.1093/brain/awh154

[25] Torbick, N., Hession, S., Stommel, E., & Caller, T. Mapping the distribution of cycad species and associated environmental risks for Guam ALS-PDC. *Environmental Health Perspectives*. 2018, 126(7), 077001. https://doi.org/10.1289/EHP2581