Keywords: Spiroplasma; Alzheimer's disease; Parkinson's disease; Prion; Alpha-synuclein; Creutzfeldt-Jakob disease; Bio lm

Introduction

e neurodegenerative diseases include Alzheimer's (AD), Parkinson's (PD), frontotemporal dementia (FTD), posttraumatic stress disorders (PTSD), including dementia pugilistica, and chronic traumatic encephalopathy (CTE) seen in athletes, and soldiers a er episodes of traumatic brain injury. All of these diseases present with dementia and show accumulation within the brain of misfolded disease-speci c amyloid proteins. e deposition of misfolded amyloid proteins is also a manifestation of Creutzfeldt-Jakob disease, a transmissible spongiform encephalopathy (TSE) in humans with a signi cant animal disease reservoir including scrapie in sheep, chronic wasting disease (CWD) in deer, and bovine spongiform encephalopathy (BSE) or 'mad cow disease' in cattle. All transmissible spongiform encephalopathies show accumulation of 'prion' amyloid deposits considered to be novel self-propagating proteins [1]. e pathogenic mechanism in TSEs involves accumulation of misfolded or unfolded proteins that trigger the 'unfolded protein response' (UPR), which is a protective cellular mechanism whereby protein translation is shut down and chaperone proteins are recruited [2]. e unfolded protein response and autophagy are important cellular homeostatic mechanisms that a ect cell survival or lead to cell death in the TSEs [2,3]. e toxicity of the prion amyloid proteins builds up with continued stimulation of the UPR and leads to neuro-degeneration and synapse loss [3].

Presumably the same phenomenon is operative in AD and PD, although the neuronal damage is not as severe as seen in TSEs. is comparison brings up the idea that alhs neve16036is

seeding by the foreign protein [16]. ere is continuous production of prion amyloid in experimental prion infection *in vitro*, even a er the infectious particles are eliminated [17]. e interpretation is that an environmental infectious agent initiates the process, and may no longer be present in late stages of the disease. Consideration must be given to the much dissimilarity between AD and the TSEs, exempli ed by recognition that the precursor and propagated proteins di er in TSE and AD, as well as clinical manifestations and pathological ndings [18]. Populations receiving growth hormone have been susceptible to TSE, but not to AD or PD [19] suggesting that there are major di erences in the pathogenesis of each disease. Furthermore, there are basic problems with the prion concept in TSEs, which raises the issue regarding the signi cance of association of enteric bacteria with AD.

Problems with the Prion Concept

in979(S)12(E, 042) s d pt E

Citation: Bastian FO (2014) Cross-Roads in Research on Neurodegenerative Diseases. J Alzheimers Dis Parkinsonism 4: 141. doi: 10.4172/2161-0460.1000141

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