Personalized Psychiatry and Neurology

Letter

Amyloids and Neurodegeneration: More Complex Than It Seems

Anton A. Nizhnikov

Citation: Nizhnikov, A.A. Amyloids and Neurodegeneration: More Complex Than It Seems. *Personalized Psychiatry and Neurology* **2024**, *4 (2)*: 1-2.

Chief Editor: Nikolaj G. Neznanov, D Med Sci, Professor

Publisher's Note: V. M. Bekhterev NMRC PN stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Amyloids represent fibrillar protein aggregates with highly ordered spatial structure called "cross-β". These protein fibrils are widely known for their association with different diseases but also perform different biological functions in a wide variety of species including humans. At least 40 human proteins are demonstrated to form pathological amyloid deposits associated with the development of a set of diseases called amyloidoses. Among them, neurodegenerative amyloidoses are of great social importance, since they often occur in old age, reduce the quality of life, and prevent healthy longevity. For example, every third person over 85 suffers from Alzheimer's disease. A special example of transmissible neurodegenerative amyloidoses are prion diseases such as Creutzfeldt-Jakob disease caused by the amyloid form of the PrP protein, which can arise not only due to the spontaneous conversion of endogenous human PrP to its infectious amyloid state PrPSc, but can also be transmitted through food products and, potentially, from environmental sources.

Although the formation of amyloid deposits is a typical feature of amyloidoses, in some cases it is unclear whether these aggregates are the sole cause or rather a consequence of the development of a particular disease. For example, Alzheimer's disease has strong genetic component with heritability of 60% to 80% and dozens of associated genetic loci. Thus, age-related amyloidoses may be mediated by very complex molecular mechanisms. Moreover, several recent studies demonstrated that several amyloids can interact with each other affecting efficiency of their aggregation. In addition, the external environment represents a huge reservoir for different amyloids that may potentially affect amyloid formation in humans. For example, amyloids were found to be formed by plant seed storage proteins in seeds during germination. Thus, plant products represent the important source of such protein aggregates that are ingested with food [8]. The analysis of effects of plant amyloids unexpectedly demonstrated that they can decrease aggregation of some human pathological amyloids at least in vitro. Another important source of amyloids is present by human microbiome. Bacteria are known to produce diverse amyloids that are functional for them but can be associated with antibiotic resistance, biofilm

formation and development of several infections in humans. The role of microbiome in development of several neurodegenerative amyloidosis has become apparent in recent years. Several bacterial amyloids were shown to directly induce amyloid formation by presynaptic neuronal protein α-sinuclein whose aggregation contributes to development of Parkinson's disease.

Overall, based on recent data, we can suggest that the development of neurodegenerative amyloidoses is determined by very complex gene networks and molecular mechanisms, and the aggregation of amyloid proteins is only one step along this path. Moreover, complex interactions with external sources of amyloid fibrils, such as foods and bacterial amyloids, provide a probable link between neurodegeneration, diet, and the microbiome.

Professor, Acting Head of Department of Genetics and Biotechnology of
St. Petersburg State University,
St. Petersburg, Russia

Anton A. Nizhnikov,
Dr., Professor of Russian Academy of Science