Small or big, brain cells don’t like protein gunk that lead to diseases like Alzheimer’s, Parkinson’s and Huntington's

An interdisiciplinary study by scientists at Trinity College Dublin (TCD, Ireland) have answered a hotly debated question in the neurodegenerative diseases research area: “Which protein aggregate form is the primary pathogenic agent in neurodegenerative diseases – (i) the prefibrillar oligomeric species, or (ii) the mature amyloid fibrils?”

For many years, it has been known that protein aggregates were strongly correlated with various specific neurodegenerative diseases. For example, within the brains of patients, two different proteins (called beta-amyloid and tau) are found for Alzheimer’s disease, alpha-synuclein is found for Parkinson’s disease, huntingtin is found for Huntington’s disease, and prions are found for variant Creutzfeld Jakob disease (= the human analogue of mad cow disease). However, it was unclear which was the aggregated culprit largely responsible for the real cytotoxicity: the small oligomeric forms, or the long and tensile mature amyoid fibrils. Significant contention existed between the two schools of thought, with the 'oligomeric hypothesis’ gaining favour in recent years.
To solve this, Trinity College Dublin’s scientists decided to tackle the issue in ‘neutral territory’ by avoiding any disease-based context by artificially generating protein prefibrillar oligomers and mature fibrils from a protein that had no connection whatsoever with any known amyloid disease: the humble hen egg protein lysozyme Surprisingly, both the oligomers and fibrils generated from lysozyme demonstrated cell death in cell cultures as well as in animals, and especially it was shown through electrophysological experiments that the lysozyme aggregates could impact on potential memory processes, just like the neurodegenerative disease-related proteins.

In other words, just like all complex scientific problems, the answer is ‘depends”. One important lesson that does emerge appears to be that, more important than the identity of the protein involved, is the overall aggregated shape in endowing these particles to be harmful to the brain cells. Scientists all across the world, including TCD’s very own, are tirelessly working to develop drug candidates that will prevent such protein aggregation from happening, ultimately improving the quality of our lives.

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