Amyloid formation drives brain tissue loss in animal studies

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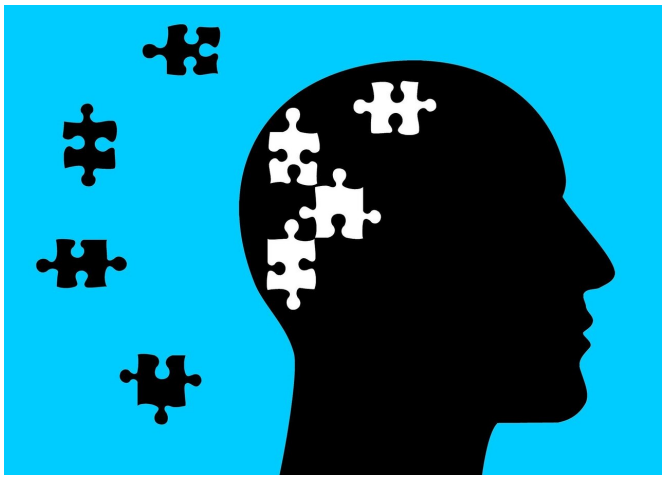

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Amyloid plaque formation directly causes brain tissue loss in animals, but a drug called lithium reduces the life-shortening effects of this loss, shows a study published today in *eLife*.

Patients with Alzheimer's disease experience progressive memory loss and loss of brain matter over time. This study provides new details about what happens in the brain in Alzheimer's disease and suggests a potential strategy to slow it.

Both the production of small protein fragments called Amyloid-ß and the assembly of these fragments into large clusters or plaques have been implicated in Alzheimer's disease. But teasing apart the role of Amyloid-ß versus the role of plaque formation has been difficult.

"There is currently a lack of tools that can directly control the formation of Amyloid-ß plaques in animals, which would allow scientists to examine the effects of plaque formation in Alzheimer's disease," explains lead author Lim Chu Hsien, a researcher at, and recent graduate of Yale-NUS College, Singapore, who is currently pursuing her medical degree at Duke-NUS Medical School, Singapore.

Using a technique called optogenetics, Lim and her colleagues were able to engineer Amyloid-ß fragments that would form plaques when exposed to light in the brains of fruit flies, tiny worms and zebrafish. The experiments showed that both the presence of Amyloid-ß and the formation of plaques were detrimental to the lifespan and health of these animals.

The team found that formation of the plaques caused both metabolic problems in the brain and physical damage that led to a loss of brain tissue. It also impaired the animals' sensory motor skills and behaviour.

Next, the researchers tested whether a drug called lithium that is used to treat some psychiatric disorders might mitigate the harm caused by light-induced plaque formation in fruit flies. They added lithium to the flies' food and found that this led to an extended lifespan in the insects.

"These data demonstrate the potential use of our optogenetics system for Alzheimer's disease drug testing," explains senior author Nicholas Tolwinski, Associate Professor of Science (Life Sciences) at Yale-NUS College, Singapore. "This light-driven plaque formation approach could be used in cells to enable mass screening of potential treatments. It might also help scientists study the effects of treatments on the different stages of Alzheimer's disease development."

More information: Chu Hsien Lim et al, Application of optogenetic Amyloid-? distinguishes between metabolic and physical damage in neurodegeneration, *eLife* (2020). DOI: 10.7554/eLife.52589

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