Abnormal proteins in the gut could contribute to the development of Alzheimer's disease

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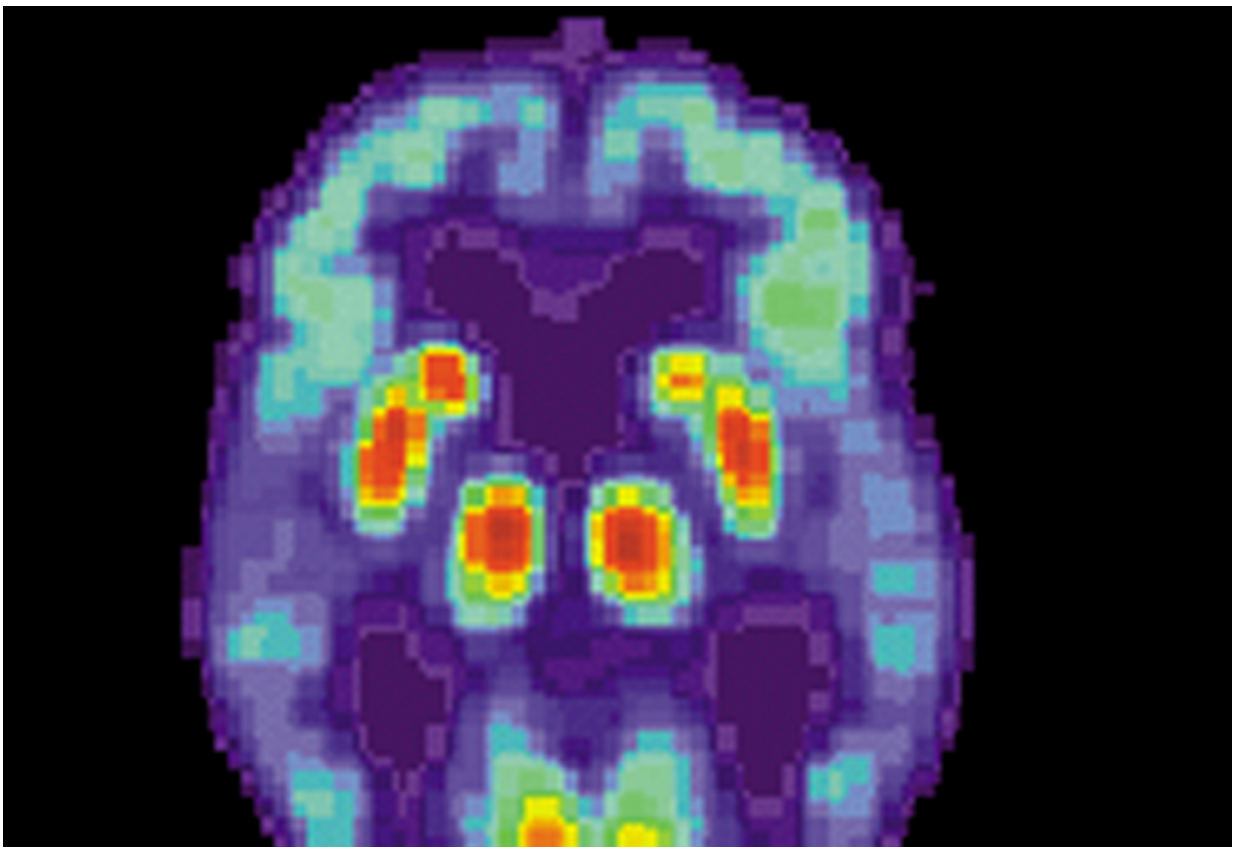

PET scan of a human brain with Alzheimer's disease. Credit: public domain

A new study published in the *Journal of Physiology* has shown that

misfolded protein build-up in the gut could contribute to the development of Alzheimer's-like symptoms in mice. This could suggest a new treatment approach for Alzheimer's disease that would target the gut before symptoms of cognitive deficits appear in patients.

As these proteins were found in the gut, which is a window to the world, this suggests environmental factors might be contributing to cognitive deficits seen in Alzheimer's disease and other conditions.

The misfolded protein, known to be involved in Alzheimer's disease, called beta amyloid, was injected into the guts of mice and travelled to the "gut-brain" (the nervous system in our gut), and also to the brain.

If some of the beta amyloid build up in the central nervous system (brain and spinal cord) is originating from the outside the brain (peripheral nervous system), reducing the amount that makes it to the brain, or trapping the protein in the periphery may delay the onset of Alzheimer's disease. This treatment would begin before any signs of dementia appear in the patient.

The researchers at The Chinese University of Hong Kong injected fluorescently-tagged beta-amyloid into the gut of mice. The proteins moved to the nervous system in our gut. The misfolded proteins were seen a year later in parts of the brain involved in cognitive deficits of Alzheimer's disease including the hippocampus, the part of our brain that affects our memory. These animals experienced cognitive impairments.

As this study was conducted in mice, it needs verification by looking for post-mortem changes in inflammation in the gut and brain of patients with Alzheimer's disease.

Development of drug treatments for Alzheimer's disease has been

unsuccessful so we instead need new approaches for preventing AD development. This could be a potential route for preventing the disease by targeting these misfolded proteins in the gut.

Commenting on the study, senior author John A Rudd said:

"This concept is similar to the transport of misfolded proteins from the gut such as those responsible for mad cow disease. If this is the case, a similar process may start in humans many years ahead of the manifestations of the classical hallmarks of AD including memory loss, and so prevention strategies would need to start earlier as well."

More information: Yayi Sun et al, Intra-gastrointestinal amyloid-β1-42 oligomers perturb enteric function and induce Alzheimer's disease pathology, *The Journal of Physiology* (2020). DOI: 10.1113/JP279919

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