ALZHEIMER DISEASE

Maternal history of Alzheimer disease correlates with amyloid-β deposition

A PET study using Pittsburgh compound B (PIB) has shown that among cognitively normal individuals, those with a family history of late-onset Alzheimer disease (LOAD) had higher levels of fibrillar amyloid-β (Aβ)—the main component of neuritic plaques—than did those with no familiy history of dementia. The research also revealed a parent-of-origin effect. "The major finding from our study is, in my opinion, that Aβ accumulation was more strongly related to having a LOAD-affected mother than having an affected father," says lead author Lisa Mosconi.

> "...Aβ accumulation was more strongly related to having a LOAD-affected mother..."

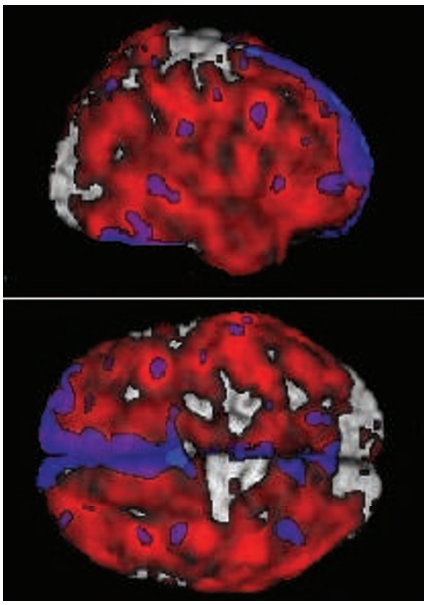
The deposition of Aβ in the brain seems to occur years before the onset of symptoms in AD. Genetic evidence suggests that rare early-onset forms of AD are caused by the mismetabolism of Aβ, but whether such a scenario occurs in LOAD remains unproven. Many cases of LOAD show familial aggregation, but the underlying genetics are currently unclear.

Mosconi and colleagues measured PIB retention—a marker of fibrillar Aβ levels—in 42 cognitively normal individuals aged 50–80 years. Of these individuals, 14 had a mother with LOAD, 14 had a father with LOAD, and 14 had no family history of dementia.

A maternal history of LOAD was found to be associated with higher levels and a more widespread distribution of PIB retention than was a paternal history of this condition. Moreover, individuals with a LOAD-affected father exhibited greater PIB retention than did people with no family history of dementia.

According to Mosconi, the results of the current study suggest the "involvement of still unknown maternal genes in LOAD." Indeed, these findings are consistent with the researchers' previous work showing that a maternal rather than a paternal history of LOAD was associated with AD-like metabolic deficits in normals brains.

The researchers aim to follow up the study's participants to try and understand why some individuals develop AD while others do not. As Mosconi highlights, this goal is important because Aβ deposition can be found in cognitively normal people who do not go on to develop AD.



Composite images showing areas of elevated fibrillar amyloid-β in cognitively normal individuals with a maternal (red) or a paternal (blue) history of late-onset Alzheimer disease. Images provided by Dr Lisa Mosconi.

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Original article Mosconi, L. *et al.* Increased fibrillar amyloid-β burden in normal individuals with a family history of late-onset Alzheimer's. *Proc. Natl Acad. Sci. USA* **107**, 5949–5954 (2010)