Amyloid beta in Alzheimer's disease

Amyloid beta (Aβ) deposition is one of the main hallmarks of Alzheimer's disease.

A study of Rahayel et al., assessed the associations between cortical and subcortical 11 C-Pittsburgh Compound B (PiB) retention, namely, in the hippocampus, amygdala, putamen, caudate, pallidum, and thalamus, and subcortical morphology in cognitively normal individuals. They recruited 104 cognitive normal individuals who underwent extensive neuropsychological assessment, PiB-positron emission tomography (PET) scan, and 3-T magnetic resonance imaging (MRI) acquisition of T1-weighted images. Global, cortical, and subcortical regional PiB retention values were derived from each scan and subcortical morphology analyses were performed to investigate vertex-wise local surface and global volumes, including the hippocampal subfields volumes. They found that subcortical regional Aβ was associated with the surface of the hippocampus, thalamus, and pallidum, with changes being due to volume and shape. Hippocampal Aβ was marginally associated with volume of the whole hippocampus as well as with the CA1 subfield, subiculum, and molecular layer. Participants showing higher subcortical Aβ also showed worse cognitive performance and smaller hippocampal volumes. In contrast, global and cortical PiB uptake did not associate with any subcortical metrics. This study shows that subcortical Aβ is associated with subcortical surface morphology in cognitively normal individuals. This study highlights the importance of quantifying subcortical regional PiB retention values in these individuals [1)].

Amyloid beta (Aβ or Abeta) denotes peptides of 36–43 amino acids that are crucially involved in Alzheimer disease as the main component of the amyloid plaques found in the brains of Alzheimer patients. The peptides result from the amyloid precursor protein (APP), which is being cut by certain enzymes to yield Aβ. Aβ molecules can aggregate to form flexible soluble oligomers which may exist in several forms. It is now believed that certain misfolded oligomers (known as “seeds”) can induce other Aβ molecules to also take the misfolded oligomeric form, leading to a chain reaction akin to a prion infection. The seeds or the resulting amyloid plaques are toxic to nerve cells. The other protein implicated in Alzheimer's disease, tau protein, also forms such prion-like misfolded oligomers, and there is some evidence that misfolded Aβ can induce tau to misfold.

The amyloid hypothesis of Alzheimer's disease (AD) maintains that the accumulation of the amyloid beta protein (Abeta) is a critical event in disease pathogenesis. A great deal of both academic and commercial research has focused on the mechanisms by which Abeta is generated. However, investigations into the mechanisms underlying Abeta clearance have blossomed over the last several years [2)].

The findings of Moriya et al. suggest that the shunting procedure can delay intracerebral deposition of Aβ in patients with idiopathic normal pressure hydrocephalus (iNPH) [3)].

Novel Alzheimer disease -associated risk genes have no significant effect on Aβ accumulation in the brain of iNPH patients. However, APOE4 affects the Aβ deposition in the brain of iNPH and AD patients in a similar manner [4)].

1)

Rahayel S, Bocti C, Sévigny Dupont P, Joannette M, Lavallée MM, Nikelski J, Chertkow H, Joubert S.

Subcortical amyloid load is associated with shape and volume in cognitively normal individuals. Hum Brain Mapp. 2019 May 30. doi: 10.1002/hbm.24680. [Epub ahead of print] PubMed PMID: 31148327.
2)

Tanzi RE, Moir RD, Wagner SL. Clearance of Alzheimer's Abeta peptide: the many roads to perdition. Neuron. 2004 Sep 2;43(5):605-8. Review. PubMed PMID: 15339642.
3)

Moriya M, Miyajima M, Nakajima M, Ogino I, Arai H. Impact of cerebrospinal fluid shunting for idiopathic normal pressure hydrocephalus on the amyloid cascade. PLoS One. 2015 Mar 30;10(3):e0119973. doi: 10.1371/journal.pone.0119973. eCollection 2015. PubMed PMID: 25821958; PubMed Central PMCID: PMC4379026.
4)

Laiterä T, Paananen J, Helisalmi S, Sarajärvi T, Huovinen J, Laitinen M, Rauramaa T, Alafuzoff I, Remes AM, Soininen H, Haapasalo A, Jääskeläinen JE, Leinonen V, Hiltunen M. Effects of Alzheimer's Disease-Associated Risk Loci on Amyloid-β Accumulation in the Brain of Idiopathic Normal Pressure Hydrocephalus Patients. J Alzheimers Dis. 2016 Oct 11. [Epub ahead of print] PubMed PMID: 27802227.