Case study on Alzheimer's disease looks at progression before and after death

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A case study from the Swedish medical university Karolinska Institutet sheds light on the pathological course of Alzheimer's disease. The brain of the first Alzheimer's patient to display amyloids demonstrable with a PET scanner has been studied both during progression of the disease and after death.

One pathological characteristic of Alzheimer's disease is the accumulation in the brain of beta-amyloid proteins to form amyloid plaques. However, it is not known how early the plaques forms in the brain, whether they are the primary cause of the disease or what pathogenic role is played by other changes in the brain.

The very first PET scan in the world of amyloid plaque in a living patient with the amyloid-binding compound 11C-PIB was performed in 2002 by Professor Agneta Nordberg at Karolinska Institutet on a 56-year old Alzheimer's patient. The researchers then monitored the patient as the disease progressed with regular PET scans and memory tests. After the patient died, the team carried out pathological and neurochemical analyses of the brain tissue.

The combined result analyses, which are now published in the renowned neurological journal *Brain*, give a detailed picture of how Alzheimer's disease develops. For example, the results show that high concentrations of amyloid plaques were discovered at an early stage of the disease when the patient suffered slight memory loss. The levels remained unchanged during the course of the disease, in contrast to the increasingly declining

energy metabolism in the brain, which was also measured using PET as the patient's memory gradually deteriorated.

One formerly unknown connection that was discovered in the study is that the greater accumulation of plaque is accompanied by a reduction in the number of neuronal nicotinic receptors in the brain. These receptors are central to memory function, and this new finding demonstrates that the receptors are affected early on in the disease development. Further, inflammatory changes were measured in brain regions with low levels of plaques which suggest that the neuroinflammation related to Alzheimer's disease might have a different cause and evolve at different stage of the disease compared to that of amyloid accumulation. Studies on this are currently being carried out on living patients using PET technology.

Today, over 1,000 patients around the world have undergone PET scans for measuring amyloid concentrations in the brain. PIB-PET was recently recommended as the earliest clinical diagnostic biomarker for discovering Alzheimer's disease, following the diagnostic guidelines laid out by the American Alzheimers Association. However, if clinicians are to gain further insight into the importance of these PET examinations, a follow up of the results obtained from conducted PET studies should be performed in the brain tissue of deceased patients.

"If we combine different examinations, we will be able to affirm that complex changes take place at the same time in the brain during the development of Alzheimer's disease", says Professor Nordberg. "Our study shows that new, modern imaging technology known as molecular imaging makes it possible to discover the disease at an early stage. This opens up new opportunities for early diagnosis and for understanding the causes of the disease and identifying patients who can be expected to respond well to future Alzheimer's therapy."

More information: Ahmadul Kadir, et al. PET imaging and clinical

progression in relation to molecular pathology in first PIB PET AD Patient
BRAIN, online 14 December 2010. brain.oxfordjournals.org/