Neuroimaging technique shows potential of bapineuzumab treatment and might be useful in assessing other drugs for Alzhei

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A neuroimaging technique known as ^{11}C-PiB PET* shows that a new investigational drug, bapineuzumab,** reduces amyloid-β deposits in the brain by about 25% compared with placebo in patients who have mild-to-moderate Alzheimer's disease. As such, ^{11}C-PiB PET imaging might be useful for assessing which drugs work to prevent the build up of amyloid-β deposits in the brains of people living with Alzheimer's disease. These are the conclusions of an Article published Online First and in the April issue of The *Lancet Neurology*.

Evidence suggests that accumulation of amyloid-β plaques in the brain is central to the development of Alzheimer's disease, but until recently confirmation of the presence of these plaques was only possible at autopsy. A new technique has been developed that measures amyloid-β load by use of PET scans and the radiotracer ^{11}C-PiB, which binds to amyloid-β plaques and shows the amount and distribution of amyloid deposits in the brains of living people. Using this technique, research has shown that patients with Alzheimer's disease have about two times greater retention of ^{11}C-PiB in areas of the cerebral cortex that are targeted by amyloid deposits compared with healthy controls.

It has been suggested that bapineuzumab might bind to amyloid-β plaques and clear deposits from the brain to slow down disease progression in Alzheimer's disease. In this phase 2 study, Juha Rinne from the University of Turku in Finland and colleagues investigated

whether bapineuzumab could reduce amyloid-β load measured using ^{11}C-PiB PET imaging in cortical areas in patients with Alzheimer's disease.

28 patients with mild-to-moderate Alzheimer's disease were randomly assigned to receive one of three doses of bapineuzumab (0•5, 1•0, 2•0 mg/kg) or placebo by intravenous infusion every 13 weeks for up to six infusions. ^{11}C-PiB PET scans were done at the start of the study and at weeks 20, 45, and 78.

Findings showed that compared with the start of the study, treatment with bapineuzumab for 78 weeks led to a significant reduction in mean ^{11}C-PiB retention compared with placebo. The authors estimate that bapineuzumab treatment was associated with about a 25% reduction in amyloid-β load over 78 weeks compared with placebo. ^{11}C-PiB retention increased in the placebo group relative to the start of the study, whereas it decreased in the bapineuzumab group.

The difference in ^{11}C-PiB retention between the bapineuzumab and placebo groups was similar for each of the three doses, and the treatment difference increased over time, suggesting that greater differences in ^{11}C-PiB retention might be possible with extended treatment.

Bapineuzumab treatment was generally well tolerated and adverse events were mild to moderate. However, two patients in the 2•0mg/kg bapineuzumab group experienced transient cerebral vasogenic oedema (an accumulation of water in brain tissue).

These findings suggest that: "Monitoring of the effects of anti-amyloid β drugs on amyloid-β deposition might be possible with radiotracers that bind to amyloid β in patients with Alzheimer's disease or those at risk before the onset of clinical decline", say the authors.

They conclude: "This technique offers the opportunity to test more

directly the amyloid-β hypothesis by confirming the ability of a particular drug to reduce or prevent amyloid-β accumulation and to assess the effect this has on clinical outcomes."

In an accompanying Comment, Sam Gandy from Mount Sinai School of Medicine, New York, USA, says that these findings: "report something of a breakthrough by demonstrating the feasibility of eventually testing the so-called amyloid hypothesis of sporadic Alzheimer's disease in vivo." He points out that although it is too early to say that we have effective disease-modifying drugs, these new data about bapineuzumab: "Move us closer to the goal of understanding, treating, and, eventually preventing major neurodegenerative diseases such as Alzheimer's disease."

Notes:
*carbon-11-labelled Pittsburgh compound B
**a humanised monoclonal antibody targeted against amyloid β

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