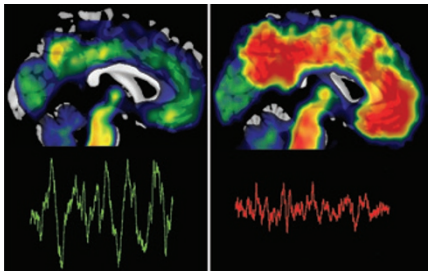
Nature Reviews Neurology **11**, 368 (2015); published online 9 June 2015; doi:10.1038/nrneurol.2015.102

SLEEP

Amyloid-β accumulation impairs memory by disrupting deep sleep—but could the vicious cycle be stopped?

New research has shown that excessive amyloid-β (Aβ) deposits can disrupt slow-wave oscillatory activity during deep sleep, which is required for memory consolidation. The finding implicates Aβ-associated sleep disruption as a mechanism for memory impairment, such as that seen in Alzheimer disease (AD). "Sleep could be a novel therapeutic target for fighting back against memory decline," say Matthew Walker, who led the study.



In individuals with low Aβ deposition (left), slow-wave activity (as seen on EEG) during sleep is intact. In individuals with high Aβ deposition (right), slow-wave activity is disrupted. Image courtesy of M. P. Walker.

Walker and colleagues used PET to measure Aβ accumulation in the brains of 26 older adults (aged 65–81 years). The study participants then memorized 120 word pairs, and slept overnight under EEG monitoring to quantify slow-wave activity.

The next morning, the participants' word pair recall performance was tested while their brain activity was scanned with functional MRI. The participants with the highest levels of Aβ deposits in the medial prefrontal cortex—a brain area known to generate slow-wave oscillations—showed the lowest slow-wave oscillations during sleep and, consequently, performed worst on the memory test.

A recent mouse study has suggested that sleep has an important role in clearance of toxic Aβ from the brain, indicating a bidirectional relationship. "We don't know yet which of these two factors—the deterioration of slow-wave sleep or the Aβ aggregation—initially begins the vicious cycle," says Walker.

The researchers plan to use the imaging and EEG measures to determine the longitudinal relationships between Aβ load, disrupted slow-wave activity and impaired memory consolidation.

Bryce Mander, the first author of the study, explains that enhancement of slow-wave activity during sleep can boost memory consolidation in young adults. Next, the investigators will examine potential ways to restore or enhance slow-wave sleep in older adults—and, potentially, in individuals with AD—to salvage learning and memory functions.

Hemi Malkki

Original article Mander, B. A. *et al.* β-amyloid disrupts human NREM slow waves and related hippocampus-dependent memory consolidation. *Nat. Neurosci.* doi:10.1038/nn.4035

Further reading Yu, Y.-E. *et al.* Sleep and Alzheimer disease pathology—a bidirectional relationship. *Nat. Rev. Neurol.* **10**, 115–119 (2014)