

## Is hippocampal atrophy in healthy elderly individuals with subjective cognitive decline related to amyloid deposition?

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**Background:** Healthy elderly individuals with subjective cognitive decline (SCD) have an increased risk to develop Alzheimer's disease (AD). There is evidence for AD-type pathology in SCD including reduced brain volume and hippocampal atrophy. According to the amyloid cascade hypothesis, amyloid deposition is responsible for the AD-type neurodegeneration. The objective of the present study was to investigate the brain atrophy profile in SCD individuals and to assess the influence of amyloid deposition. **Methods:** A total of 54 elderly without objective cognitive deficits were included in the study, of which 15 were recruited from a memory clinic (SCD group), and 39 age-, education-, sex-, and MMSE-matched were elderly from the general population (control group). All individuals underwent neuropsychological assessment, structural-MRI and amyloid Florbetapir-PET. Between-group voxel-wise comparisons were done on neuroimaging data ( $p < .005$ , uncorrected). **Results:** Significant gray matter atrophy in the hippocampal region was found in the SCD group compared to controls. There was no significant difference in the proportion of amyloid-positive individuals between the two groups. To directly test the influence of amyloid deposition on hippocampal atrophy, group comparison analyses of gray matter volume were recomputed i) removing the 2 amyloid-positive SCD individuals, ii) adding amyloid deposition values (SUVR) as a covariate. In both conditions, the results remained unchanged, i.e SCD showed significant hippocampal atrophy. Moreover, this hippocampal atrophy correlated with episodic memory decline in the SCD, even after controlling for amyloid deposition. **Conclusions:** Our findings showed that healthy elderly individuals with SCD have significant brain atrophy in the hippocampal region, similar to that observed in AD, and that correlated with decreased episodic memory performance. Importantly, this memory-related hippocampal atrophy in individuals with increased risk for AD seems to be independent from the presence of amyloid deposition as measured with Florbetapir-PET. These results suggest that the AD-like atrophy in SCD is not (directly and/or only) due to amyloid deposition but may involve other neuropathological processes.