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## Learning What You Know:

### How Prior Knowledge Impairs New Associative Learning in Early AD

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### Abstract

While associative memory impairment is a core feature of prodromal Alzheimer's Disease (AD), whether prior knowledge affects associative learning is largely overlooked. Stimuli repetition yields suppression or enhancement of the BOLD signal, allowing the functional mapping of brain networks. We addressed the role of prior knowledge in associative encoding by manipulating repetition and familiarity of the memoranda in a subsequent memory fMRI study design.

17 patients with prodromal AD (AD-MCI) and 19 Controls learned face-scene associations presented twice in the scanner. Pre-experimental knowledge trials (PEK) involved famous faces while in Experimental Knowledge trials (EK), unknown faces familiarized before scanning were used. Study events were sorted as associative hits, associative misses or misses after a recognition test outside the scanner. We computed the Repetition X Prior knowledge interaction contrast to test whether the encoding networks differed along with prior knowledge, then looked for subsequent associative memory effects in the resulting clusters. PEK and EK yielded similar associative memory performance in AD-MCI, while PEK increased associative memory by 28% in Controls. Repetition effects were modulated by Prior knowledge in Controls, but AD-MCI showed aberrant repetition effects. Subsequent memory effects were observed only in Controls for PEK in the right subhippocampal structures. By contrast, in both groups, EK triggered a subsequent memory effect in the right hippocampus. Provided that tau pathology starts within anterior subhippocampal regions in early AD, our findings that subhippocampal, not hippocampal, involvement underlies the inability of the patients to benefit from PEK open innovative clinical and research perspectives.

**Keywords:** Associative memory; Prior Knowledge; Alzheimer's disease; Recognition memory; fMRI