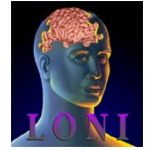


Semantic clustering and hippocampal atrophy in Mild Cognitive Impairment and Alzheimer's disease

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Background: Individuals with memory difficulties can use strategies to help them encode, store and recall information. One such strategy is semantic clustering – the ability to organize information into their superordinate categories. We examined the associations between recall and semantic clustering with hippocampal radial distance.

Methods: Eight subjects with mild cognitive impairment (MCI) and 14 with Alzheimer's disease (AD) completed the California Verbal Learning Test (CVLT) and T1-weighted 3D MPRAGE scans. Semantic clustering, the ratio of words from the same category recalled in clusters, was calculated for the learning, short delay and long delay trials to study the effect of strategy use.

Table 1. Demographic data [mean (SD)]

Variable	MCI (N=8)	AD (N=14)	p-value
Age, yr	71.3 (4.1)	76.0 (6.5)	0.050
Gender, M:F	4:4	5:9	0.512
Education, yr	13.6 (1.7)	15.4 (3.2)	0.096
MMSE	27.6 (2.4)	23.4 (3.2)	0.002

Scans were registered with a 9-parameter transformation to the ICBM53 template and bias-field corrected for spatial and intensity normalization. An expert tracer (AEG) manually delineated the hippocampi on each scan. The hippocampal traces were then converted to parametric mesh models by redigitizing and reslicing to create contours with 150 uniformly spaced slices with 100 uniformly spaced points per slice.

Figure 1. Hippocampal radial distance analysis

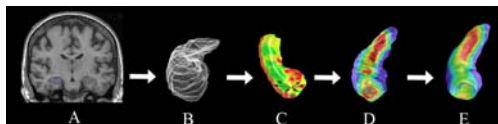


Figure 2. Significance maps relating hippocampal radial distance to neuropsychological measures

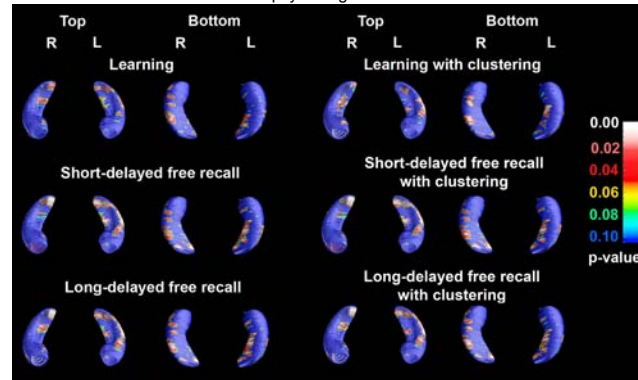
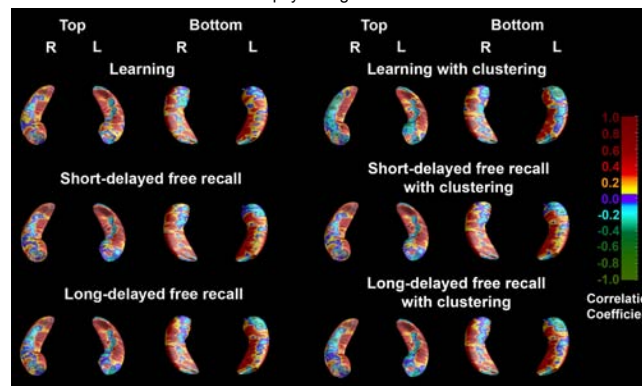


Figure 3. Correlation maps relating hippocampal radial distance to neuropsychological measures



The mesh model is split into top and bottom components and a centroid curve (medial core) is derived to calculate the distance from the core to the surface point. The measured distance is then mapped onto the corresponding surface point for point-wise analysis (Figure 1). We used linear regression models to examine the associations between semantic clustering and hippocampal radial distance with a permutation threshold of $p < 0.01$. Significance (Figure 2) and correlation (Figure 3) maps were created.

Results: We found trend-level association between semantic clustering at learning and the left hippocampus ($p_{\text{corrected}} = 0.08$) but no significant associations with initial learning without clustering. Short-delayed free recall and semantic clustering at the short-delayed free recall demonstrated a positive association with hippocampal radial distance on the left ($p_{\text{corrected}} = 0.025$ and $p_{\text{corrected}} = 0.037$, resp.). In addition to significant left-sided associations, long-delayed free recall and semantic clustering at the long-delayed free recall showed trend-level associations on the right (left $p_{\text{corrected}} = 0.024$ and $p_{\text{corrected}} = 0.039$, resp; right $p_{\text{corrected}} = 0.066$ and $p_{\text{corrected}} = 0.08$). Regionally the effects were most pronounced in the CA1 hippocampal subregion.

Conclusions: Our data indicate that impaired verbal recall and memory strategy use are associated with left-sided hippocampal atrophy, especially in the CA1 subregion. Overall, these findings suggest that in MCI and AD, neurodegenerative changes in the left hippocampus impacts strategy use, which can impact recall performance itself.

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