Neural Correlates to the Episodic Memory Continuum from Health to Alzheimer's Disease

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Purpose. Behaviorally, episodic memory in health and Alzheimer's Disease (AD) is thought to reflect a continuum. If so, neural correlates should exist which reflect this. This study was undertaken to look for neural correlates of episodic memory continuum in appropriate subjects.

Methods. Twelve patients with mild AD (61.7 ± 5.0 yo) and 24 healthy volunteers, divided into subgroups reflecting memory task performance (12 low performing (LP), 66.1 ± 6.3 yo, and 12 high performing (HP), 62.8 ± 7.0 yo) were scanned with fMRI using a block design episodic memory task described previously [1]. Briefly, the paradigm consisted of a learning phase, in which ten abstract patterns were presented and had to be memorized, and a free recall period, where memorized patterns had to be typed in by a dedicated keyboard. Both learning and retrieval were repeated 5 times. On a Siemens Magnetom Vision MR scanner at 1.5 T, 32 slices (3 mm + 0.6 mm gap) covering the whole brain were acquired using a single-shot EPI sequence with cartesian readout at 64x64 matrix, FoV 230 mm and TE/TA/FA 66/4000 ms / 90°.

Data processing and analysis was performed with SPM 99. For each participant neural activation was computed from the recall block with maximum individual recall performance. First, the contrast between retrieval and rest was calculated. Between-group analysis was analyzed by one-way ANOVA with three levels (AD, LP, HP) based on these individual contrast images. In voxels with significant group differences, linear trends were computed to find voxels with increasing sizes of the modeled effect across groups from AD (lowest) to HP (highest). Linear fits were thresholded at $p < 0.05$. For each participant sizes of modeled effects were averaged from each of the linearly increasing voxels constituting one specific cluster. After calculating mean and standard error of the mean for each group cluster t-values were computed. From these t-values correlation coefficients r were calculated that were inserted in the formula by Friedman [2] to give effect sizes d ($d = (2r)/(\sqrt{1-r^2})$). Thus, the calculated effect sizes represent the in groups calculated subjects' mean of the size of the modeled effect while integrating subject-related variance of its estimated size. They reflect the extent of different neural activation across groups as they ultimately refer to the size of the modeled effect, i.e. the height of the (contrast-weighted) beta values from the regression equation correlating the experimentally induced (i.e. modeled) variance with the observed variance of the voxel time series.

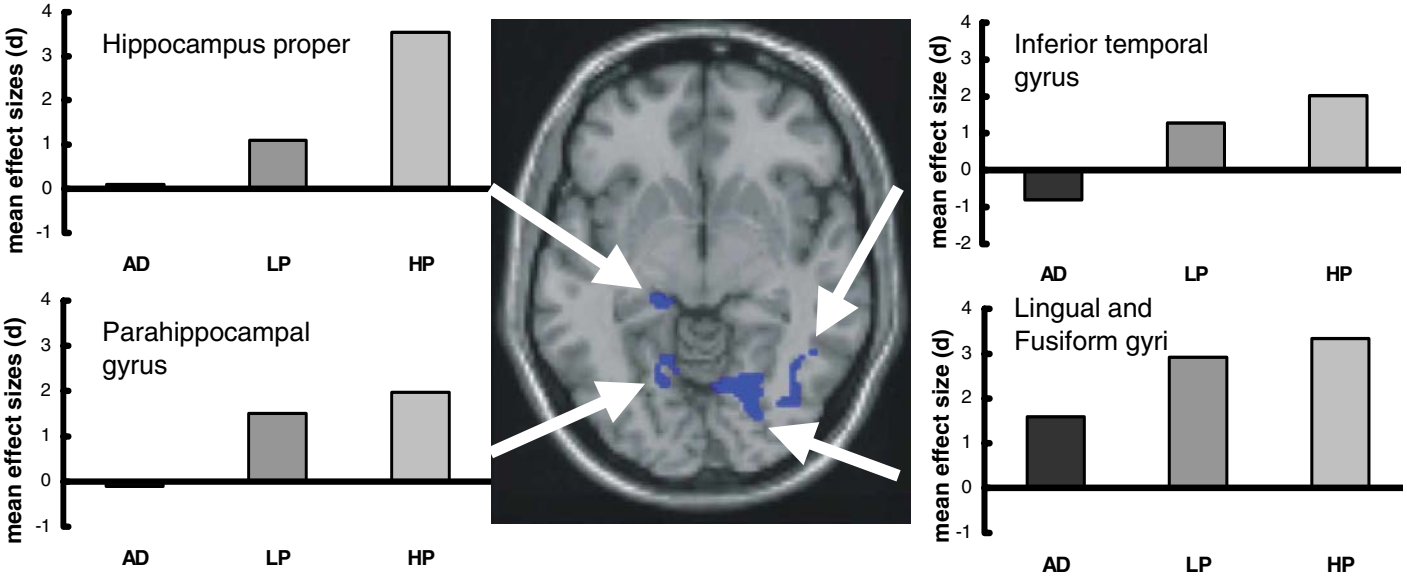

Fig. 1 Brain regions with increase in activation between groups (center) and mean effects of these areas.

Results. A significant group effect with increasing effect sizes from AD (lowest) to HP (highest) is observed exclusively in posterior medio-temporal regions (Figure 1), i.e. hippocampal formation, including the parahippocampal gyrus (56 voxels) and hippocampus proper (31 voxels), lingual and fusiform gyri on both hemispheres (117 voxels), as well as right middle and inferior temporal gyrus extending posteriorly into the middle occipital gyrus (74 voxels).

Discussion. Assessment of memory performance in old individuals fostered the conclusion that the risk of developing AD increases with decreased memory performance (3) . While the observation is established, its underlying biological substrate is not. Impairment of episodic memory is the earliest symptom of AD (4). Degeneration of cells in the hippocampal formation and surrounding cortex is the earliest cellular feature in AD (5). Integrity of hippocampal function is required for episodic memory performance (6). Bringing these lines of evidence together, the present study shows that the spectrum of episodic memory performance in health and disease can be mirrored on a neural substrate level in the extent of posterior medio-temporal recruitment relevant for episodic memory performance (7).

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