

Memory performance is negatively correlated with resting CBF level in hippocampus in healthy elderly

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Introduction:

The medial temporal lobe (MTL) subserves episodic memory function, and is activated during episodic memory encoding and retrieval. Deficits in both episodic memory performance and fMRI activation have been observed in disorders affecting the MTL such as temporal lobe epilepsy and Alzheimer's disease. However, MTL function can be difficult to modulate experimentally [1]. It is also challenging to control for effects of memory performance on observed activation and to distinguish changes in task activation from changes in baseline function. Mounting evidence suggests that genotypic-phenotypic variations in behavior modulate resting brain function as measured by arterial spin labeled (ASL) perfusion MRI [2]. Here we correlated resting CBF with episodic memory performance in 31 healthy older adults to explore the utility of ASL MRI as a biomarker of memory performance phenotype.

MATERIALS and METHODS:

Thirty-one elderly subjects with no history of neurological or psychiatric disorders (mean age 69.6 years, range 54-85 years, 13 males) participated in this study after providing written consent according to the University of Pennsylvania Institutional Review Board.

Episodic memory was assessed using an associative recognition task. During the encoding stage, participants were presented with word pairs on the computer screen. For each pair, participants were instructed to form a mental image of the two objects and determine which was bigger. In the recognition stage, intact, rearranged, and novel pairs were presented. Participants were asked endorse items as 'old' only if presented exactly as previously studied (intact pairs). 'Recollection' and 'familiarity' scores were calculated in a standard manner [3].

ASL perfusion MRI scans were performed on all subjects using a pseudo-continuous ASL sequence (TR=4 sec, labeling duration = 1.5 sec, post-labeling delay=1.5 sec) on a Siemens 3.0T Trio whole-body MRI scanner equipped with a product eight-channel array coil. Interleaved images with and without labeling were acquired using a gradient EPI (echo-planar imaging) sequence with 8 mm slices and 4 mm in-plane resolution. During the resting scans, participants were asked to relax, keep their eyes open and stay awake. The data were analyzed in SPM5 with a multiple regression model, controlled for age, education years, gender and whole brain mean CBF values.

RESULTS:

A negative correlation was found between CBF and 'recollection' values in left hippocampus ($p < 0.001$, uncorrected). These results are illustrated in the figure below. A negative correlation between CBF and 'familiarity' values was smaller, but still present in an adjacent location ($p < 0.02$, uncorrected, not shown).

DISCUSSION:

Episodic memory performance for word pairs was inversely correlated with resting CBF in the left hippocampus in this cohort of healthy elderly subjects. This finding suggests that resting MTL perfusion can be used as a biomarker for phenotypic variations in CBF, and that reduced activation during episodic memory tasks may be attributable to increased baseline function rather than reduced task responses. For example, although reduced BOLD fMRI activation during episodic memory tasks has been observed in patients with Alzheimer's disease [4], recent data suggest that patients with Alzheimer's disease have increased MTL perfusion at rest [5]. Increased hippocampal perfusion in Alzheimer's disease has been attributed to either compensatory increase in MTL activity, or possibly to pathological inflammation. The present finding of an inverse correlation between hippocampal perfusion and memory function in healthy elderly participants suggests that the compensatory hypothesis is more likely.

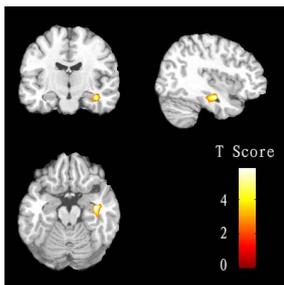


Fig. 1 Negative correlation was found in left hippocampus between CBF value and memory task performance ('recollection').

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