The effects of age on medial temporal lobe function

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BACKGROUND

The cognitive neuroscience of ageing suggests the occurrence of two general age-related changes in the brain; dedifferentiation and compensation. One class of findings have demonstrated that old adults display significantly less neural specialization for visual stimuli such as houses, faces, chairs, and pseudowords, compared to young adults (Park et al. 2004). Another class of findings suggests that increasing age leads to activation changes – typically activation *increases* – related to a preserved performance in older adults, e.g., in the prefrontal cortex (Cabeza et al. 2004). The age-related changes in the MTL region are less known, although recent studies imply that it may be a good model for the study of age-related changes in neural functions. We studied the effect of age on neural differentiation using a Region of Interest (ROI) fMRI analysis with an image acquisition optimized for the MTL region (Figure 1). The paradigm was designed to study the effects of content (processing of objects and positions) during different processing stages (preparation, encoding and rehearsal), as shown in Figure 2.

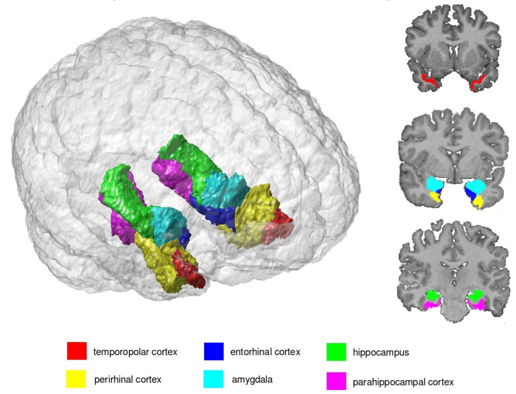


Figure 1 – The medial temporal lobe regions of interest

SUBJECTS

54 subjects (age range 18 to 81 years, 31 male, 46 right handed, 7 left handed, 1 ambidextrous) were tested with a comprehensive neuropsychological battery, a morphology scanning session, and a functional scanning session, including perfusion imaging. There were no effect of age on estimated IQ levels, as measured by the DART (t=1.10, p=.276) and WAIS vocabulary (t=-.08, p=.941).

MR SCANNING

Structural images, used for ROI drawing, included a 3D whole brain MPRAGE and a 3D whole-head T2-weighted sequence. A BOLD fMRI sequence optimized for the MTL region was applied, and consisted of a 1s instruction cue; a 3s preparation epoch; 6 stimuli presented serially 2s each for encoding; a 6s rehearsal epoch; and 6 stimuli presented serially 2.5s each for old/new recognition judgements (see Figure 2). EPI data analysis was performed in native space using SPM2, using realignment with no smoothing, and with nuisance regressors (Lund et al. 2006). A multivariate GLM was used and results were compared to results from an analysis of of the youngest sample of this cohort.

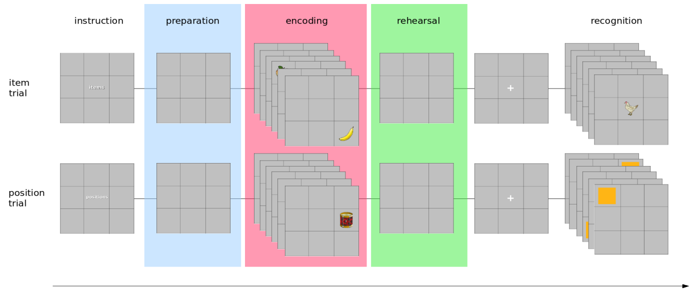


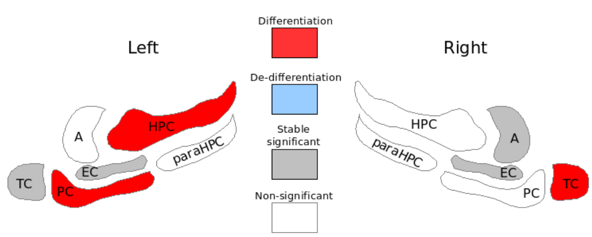
Figure 2 – The intentional encoding paradigm, showing object and position tasks on each line

RESULTS

We found no age-effect on reaction time for either object (t=.65, p=.522) or position (t=.02, p=.986) responses. Age was associated with a reduction in both performance scores (objects: t=-3.87, p<.001; positions: t=-3.34, p<.001).

At all processing stages, we found significant changes as well as preserved content effects in MTL regions. Interestingly, some regional changes were modulated by processing stage, and did thus not show a uniform pattern of dedifferentiation or compensation (see figures and tables below).

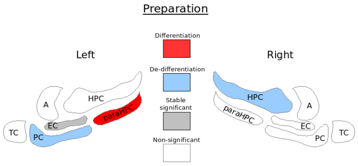
Encoding



Region	Young		Age effect	
	T	p	T	p
left TC	6.6	<.001		
right TC	5.5	<.001	2.56	0.01
left EC	6.64	<.001		
right EC	5.56	<.001		
left PC	4.7	<.001	2.53	0.02
left HP	5.77	<.001	2.17	0.04
right AM	4.67	<.001		

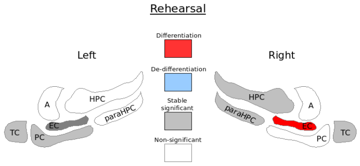
The results suggest that healthy ageing leads to a dynamic pattern of changes in the MTL region that are related to reduced function and compensatory mechanisms. However, as regional changes were not uniform across all processing stages, we suggest that these changes are modulated by extra-MTL input, e.g. a fronto-parietal attentional network, and that changes in this network may explain some of the changes observed here.

Preparation



Region	Young		Age effect	
	T	p	T	p
left EC	4.01	<.001		
left PC			-2.09	0.04
left parahpc.			2.52	0.02
right hp	2.84	0.01	-2.17	0.04

Rehearsal



Region	Young		Age effect	
	T	p	T	p
left TC	3.42	0		
right TC	5.99	<.001		
left EC	-4.06	<.001		
right EC			-2.15	0.04
left PC	2.89	0.01		
right paraHPC	2.16	0.04		
right HP	4.36	<.001		

None of the age-related changes were found to be related to performance in the old adult group. This suggests that the age-related changes observed are only generally related to changes in cognitive performance.

CONCLUSION

Age-related decline in episodic memory is related to dynamic and process-specific alterations in the MTL region. Age-related changes in neural activation were dependent on processing stage, suggesting that the effects of age on MTL activation is a mixture of loss of function (dedifferentiation) and top-down modulation (compensation). Further study of the relationship between high-resolution assessment of regional MTL activation and whole-brain activation during episodic memory formation is needed.

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Region Hovedstaden

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