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Disconnection of working memory processes by cerebrovascular disease

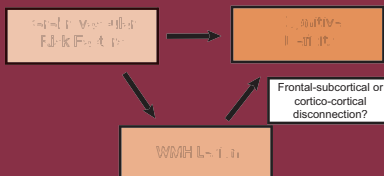
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Background

- Mild Cognitive Impairment (MCI) is characterized by episodic memory deficits beyond that expected for normal aging and is a heterogeneous syndrome with multiple etiologies, including cerebrovascular disease (CVD).
- Recent evidence shows that CVD as measured by MRI white matter hyperintensities (WMH) may indirectly affect episodic memory in MCI by disrupting working memory.

We propose that these working memory deficits are the direct result of white matter fiber tract disconnections. We hypothesized two potential systems: 1) Subcortical Frontal as described by Cummings or 2) Cortico-cortical containing parieto-occipital connections described by Goldman-Rakic.



Methods

Imaging:
We employed diffusion tensor imaging (DTI) to generate fractional anisotropy (FA) maps as a measure of white matter fiber tract conductivity.

Subjects:
Twelve MCI patients with varying degrees of WMH burden

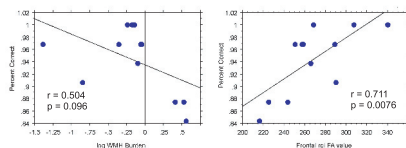
MCI	n	Age	Education	Gender (m/f)	MMSE
	12	75.9 (5.7)	15.9 (2.3)	4/8	26.1 (2.1)

Working memory tasks:
- verbal 4-item recognition
- 2-back

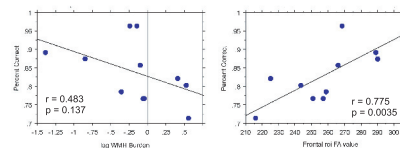
Data analysis:
Two different methods of analysis were employed including ROI-driven and inter-subject mapping.

Region of Interest Analysis

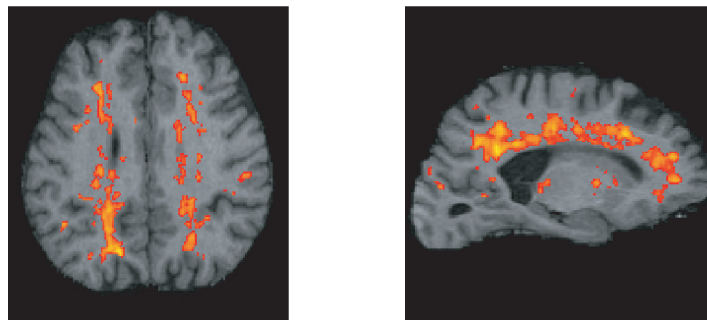
Superior longitudinal fasciculus ROI correlates strongly with 4-item working memory task



Frontal ROI correlates strongly with 2-back working memory task



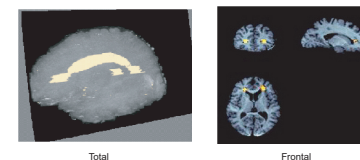
Inter-subject Mapping



Voxel regression images at a threshold for t significance less than 0.05 using the 4-item task.

Data Analysis

- Regions of Interest
Superior longitudinal fasciculus
-Total, Frontal, and Posterior



Results

- FA values in several regions of interest were more strongly correlated with performance on the working memory tasks than WMH volumes in the same region.

- There appears to be a different pattern of white matter tract disruption for the 4-item recognition task (maintenance) and the 2-back task (manipulation).

	Frontal roi		Posterior roi		Connection between Frontal and Posterior roi		Total Superior Longitudinal Fasciculus	
	R ²	P-value	R ²	P-value	R ²	P-value	R ²	P-value
4-item task	0.595	0.0076	0.396	0.0095	0.458	0.007	0.691	0.0029
2-back task	0.601	0.0028	0.161	0.240	0	0.969	0.2	0.1723

• Significant

Conclusions

1. CVD impairs cognitive function through disruption of white matter tracts.
2. Preliminary evidence suggests that multiple cognitive processes are affected and that these may involve disconnections of different and discrete white matter tracts. The maintenance task appears to be mediated by the superior longitudinal fasciculus, whereas the manipulations task appears to be mediated by more frontal regions.

References

- Cummings, J.L. 1993. Frontal-subcortical circuits and human behavior. Archives of Neurology: 50(8), 873-80.
- Goldman-Rakic, P. 1987. Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In Mountcastle, V. B. & Plum, F., eds. Handbook of Physiology, section 1, The nervous system, vol. 5, Higher functions of the brain, part 1. Bethesda: American Physiological Society. Pp. 375-417.