The heterogeneity of local regional correlation in hippocampus and caudate predicts behavioral performance in old adults

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ABSTRACT

Normal aging is associated with declines across a broad range of cognitive functions. However, the neural bases of cognitive aging are unclear. Recent studies have suggested that age-related decline in cognitive performance might reflect deficits in neural modulation that result from changes in synaptic signaling (Gajjar et al., 2011; Reeswagen et al., 2011). FMRI studies of cognitive aging have produced conflicting results. While some studies have reported reduced activations, others have suggested more typical, or even enhanced activation levels. For instance, FMRI studies of hippocampus have reported reduced blood oxygen level-dependent (BOLD) signals (e.g., Antoun et al., 2009), typical (e.g., Pesonen et al., 2011), and enhanced activations (e.g., Issler et al., 2010) in older adults, in contrast to younger adults. Such divergent results might be due at least in part to heterogeneity in variability of cognitive aging. FMRI is a technique that exploits individual differences in neural specificity to probe responses to a single stimulus. Therefore, the neural specificity of older adults can be quantitatively linked to local regional heterogeneity of correlations (Hcorr). This technique is based on analysis of voxel-wise correlations of fMRI activation patterns with an assumption that the sparsity of neural activations is related to neuronal selectivity: The highly selective neurons produce a sparse neural code, with each neuron responding to a very small set of stimuli. In contrast, less selective neurons respond to a greater number of stimuli, leading to greater overlap in responses among the neurons and less sparse representations. Thus, for a neural representation of objects or events, activation patterns should be sparser for a population with more sharply tuned neurons than more broadly tuned neurons. This then predicts that the sharply tuned population should have a higher degree of heterogeneity in neural correlations than the population with more broadly tuned neurons. Thus, when measured with fMRI, tuning specificity in a brain region should correlate with the degree of sparseness, which in turn should correlate with the heterogeneity of correlations in the region. Hcorr = standard error of correlations between voxels. Therefore, a lower local regional heterogeneity of correlations (Hcorr) in a brain region should be associated with lower behavioral performance.

RESULTS

I: Hcorr at hippocampal formation predicts episodic memory, but not working memory performance, and Hcorr at parahippocampal region does not predict episodic memory performance, suggesting that individual differences in episodic memory performance in older adults might be due to reduced neural specificity in the hippocampal formation, a critical region for episodic memory (Square et al., 2004; Eichenbaum et al., 2007; Bird & Burgess, 2009).

II: Hcorr at VWFA predicts verbal fluency, but not episodic memory, and Hcorr at R-VWFA (the right hemispherical symmetrical region) does not predict verbal fluency. Suggesting individual differences in verbal fluency in older adults are due to variations in neural specificity in VWFA, a critical region for neural representations of words (McChanlites et al., 2003; Glazer et al., 2009).

III: Hcorr at left caudate nucleus, in particular the body and tail regions, increased with training in the implicit sequence learning task, suggesting that the body/tail regions of left caudate nucleus might be involved in encoding and acquisition of the implicit sequence, in contrast to the head region. This is in line with previous studies that have found the body and tail regions, but not the head region of caudate nucleus are involved in the acquisition of implicit knowledge (Ashby & Spaniog, 2004; Seger & Cicci, 2009; Nomura et al., 2007).

DISCUSSION

In older adults, individual differences in episodic memory can be quantitatively predicted by neural specificity in hippocampal formation, but not in selected other brain regions, including the parahippocampal area.

In older adults, individual differences in verbal fluency can be predicted by neural specificity in VWFA, a region critical for neural representations of words, but not selected other regions, including R-VWFA, the right hemispherical symmetrical region.

At the group level, implicit sequence learning is associated with an increase in neural specificity in the left caudate nucleus, in particular the body and tail regions, which have been linked to implicit acquisition of knowledge, in contrast to head region, which has been linked to acquisition of explicit rule-based knowledge.

Individual differences in cognitive performance in older adults can be quantitatively linked to variations in neural specificity at corresponding brain regions.

CONCLUSIONS

Individual differences in cognitive performance in older adults can be quantitatively predicted by variations in neural specificity measured with the novel technique, local regional heterogeneity analysis, carried out on data from a conventional fMRI study. This method holds promise for investigating the neural bases of cognitive aging in new and previously collected data.

METHODS

Participants: Twelve older adults (9 female, age 67.5±3.2). Data from two participants were excluded due to excessive head movement (n=1) and missing neuropsychological tests (n=1).

Neuropsychological tests:

- EPIC Memory (total units from WMS Logical Memory)
- Working memory (trial digit in Digit Span)
- Writing memory (word digit in Digit Span)

Experimental design: FMRI data was collected from three runs while subjects were engaged in different tasks. The first task was a control task, the second task was an episodic memory task, and the third task was a verbal fluency task. In the control task, participants were asked to recall a list of words. In the episodic memory task, participants were asked to recall a list of words after a delay. In the verbal fluency task, participants were asked to generate as many words as possible that start with a particular letter. The tasks were presented in a random order. The time to complete each task was recorded.

Hcorr = standard error of correlations between voxels. Therefore, a lower local regional heterogeneity of correlations (Hcorr) in a brain region should be associated with lower behavioral performance.

CONCLUSIONS

Individual differences in cognitive performance in older adults can be quantitatively linked to variations in neural specificity at corresponding brain regions.

ACKNOWLEDGMENTS

Supported by R01AG038683, R37AG15450, and F31AG03469 from NIA/NIH

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