Regional Homogeneity is Associated with Dopamine Synthesis Capacity and Maintained Cognitive Stability in Older Adults

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Introduction

- Alzheimer’s disease (AD) is associated with alterations in functional magnetic resonance imaging measures of regional homogeneity (ReHo)1
- AD-related reductions in ReHo are observed in posterior parietal regions including precuneus/posterior cingulate cortex, which are sites of amyloid plaque accumulation and are implicated in memory and executive function2.
- Dopamine-related genes have been shown to be related to precuneus ReHo and also executive function3.
- Stable or increasing dopamine synthesis capacity is observed in aging4,5 despite losses in dopamine receptors and may play a role in maintaining optimal cortical function.
- The influence of elevated dopamine synthesis capacity on precuneus/posterior cingulate cortex ReHo and successful maintenance of executive function in healthy aging is not known.

Aims:
1. To test whether reductions in ReHo are apparent in normal aging
2. To determine whether higher ReHo is a marker for preserved cognition using retrospective longitudinal neuropsychological testing
3. To examine the relation between ReHo and individual differences in dopamine synthesis capacity using [18F]fluoro-m-tyrosine PET

Methods

Participants
Cognitively normal older (n = 50, 60+ years old, mean age = 77.2, 28 f) and younger adults (n = 29, 20-35 years old, mean age = 24.8) were recruited through the Berkeley Aging Cohort Study.

Procedure
Subjedts underwent longitudinal (Older only) and cross-sectional neuropsychological testing (mean longitudinal span = 5.4 years). Subjects underwent cross-sectional [18F]fluorom-t-tyrosine ([18F]PET) and [18F]Pittsburgh compound B ([18F]FMR) (Older only) PET imaging, structural MRI and resting-state fMRI.

Cognitive Assessment
Composite scores were created for memory, cognitive stability and executive function. Memory tests were CVLT II Long Delay Free Recall, Logical Memory Total Recall, Visual Reproduction Recall Total, and when available Verbal Composite scores were created for memory, cognitive stability and cognitive flexibility. Memory tests were CVLT II Long Delay Free Recall, Logical Memory Total Recall, Visual Reproduction Recall Total, and when available Oral Verbal Paired Associates Score. Stability tests were Stroop and Digit Span Backwards. For subjects who had Listening Span Total Recall data available, we included this score in the composite. Flexibility tests were Trail Making: Trail B minus A, and Wisconsin Card Sorting Perseverative Responses. Longitudinal change in cognition for 2-11 testing sessions was calculated then averaged across tasks for each composite.

MRI
Functional and structural MRI were acquired, preprocessed, and denoised in native space as described in Adams et al. (2018)6. Native space 3DReHo was computed in AFNI (See Fig. 1 for detailed description of ReHo computation).

PET
Participants underwent [18F]PET and [18F]FMR PET scanning as previously described in Berry et al. (2016) for acquisition and preprocessing details. K1 images were generated, representing the [18F]PET accumulation in the brain relative to a cerebellum reference region. K1 signal was extracted from hand drawn midbrain regions of interest using a combination of methods described by Dong et al. (2012)7 and Murty et al. (2014).8 [18F]PET positive was defined as [18F]FMR Ki > 0.03.

Results

Precuneus ReHo is decreased in healthy cognitive aging

Higher Precuneus ReHo is associated with successful maintenance of Cognitive Stability in Older Adults

Higher Dopamine Synthesis Capacity is Associated with Higher Precuneus ReHo

Conclusions

- Higher, youth-like ReHo in precuneus is associated with preserved cognitive stability performance in aging
- Higher dopamine synthesis capacity is related to higher ReHo in older adults

Dopaminergic neuromodulation (direct or indirect) may represent a mechanism underlying successful maintenance of ReHo in aging

References