NeuroImage 103 (2014) 139–151

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

The Reference Ability Neural Network Study: Motivation, design, and initial feasibility analyses

Yaakov Stern [a,*,1], Christian Habeck [a,1], Jason Steffener [a], Daniel Barulli [a], Yunglin Gazes [a], Qolamreza Razlighi [a], Danielle Shaked [a], Timothy Salthouse [b]

[a] Cognitive Neuroscience Division, Department of Neurology and Taub Institute for Research on Alzheimer's Disease and The Aging Brain, Columbia University College of Physicians and Surgeons, 630 W 168th St, P&S Box 16, New York, NY 10032, USA

[b] Department of Psychology, University of Virginia, 102 Gilmer Hall, PO Box 400400, Charlottesville, VA 22904, USA

ARTICLE INFO

Article history:
Accepted 13 September 2014
Available online 20 September 2014

Keywords:
Cognitive aging
fMRI
Convergent/discriminant validity

ABSTRACT

We introduce and describe the Reference Ability Neural Network Study and provide initial feasibility data. Based on analyses of large test batteries administered to individuals ranging from young to old, four latent variables, or reference abilities (RAs) that capture the majority of the variance in age-related cognitive change have been identified: episodic memory, fluid reasoning, perceptual speed, and vocabulary. We aim to determine whether spatial fMRI networks can be derived that are uniquely associated with the performance of each reference ability. We plan to image 375 healthy adults (50 per decade from age 20 to 50; 75 per decade from age 50 to 80) while performing a set of 12 cognitive tasks. Data on 174 participants are reported here. Three tasks were grouped a priori into each of the four reference ability domains.

We first assessed to what extent both cognitive task scores and activation patterns readily show convergent and discriminant validity, i.e. increased similarity between tasks within the same domain and decreased similarity between tasks between domains, respectively. Block-based time-series analysis of each individual task was conducted for each participant via general linear modeling. We partialled activation common to all tasks out of the imaging data. For both test scores and activation topographies, we then calculated correlations for each of 66 possible pairings of tasks, and compared the magnitude of correlation of tasks within reference ability domains to that of tasks between domains. For the behavioral data, globally there were significantly stronger inter-task correlations within than between domains. When examining individual abilities, 3 of the domains also met these criteria but memory reached only borderline significance. Overall there was greater topographic similarity within reference abilities than between them ($p < 0.0001$), but when examined individually, statistical significance was reached only for episodic memory and perceptual speed.

We then turned to a multivariate technique, linear indicator regression analysis, to derive four unique linear combinations of Principal Components (PC) of imaging data that were associated with each RA. We investigated the ability of the identified PCs to predict the reference domain associated with the activation of individual subjects for individual tasks. Median accuracy rates for associating component task activation with a particular reference ability were quite good: memory: 82%; reasoning: 8%; speed: 84%; vocabulary: 77%.

These results demonstrate that even using basic GLM analysis, the topography of activation of tasks within a domain is more similar than tasks between domains. The follow-up regression analyses suggest that all tasks with each RA rely on a common network, unique to that RA. Our ultimate goal is to better characterize these RA neural networks and then study how their expression changes across the age span. Our hope is that by focusing on these networks associated with key features of cognitive aging, as opposed to task-related activation associated with individual tasks, we will be able to advance our knowledge regarding the key brain changes that underlie cognitive aging.

Introduction

There is a divergence of methods in the study of cognitive aging, with different approaches pursued by researchers within cognitive neuroimaging and cognitive psychologists interested in the structure of cognition. In an attempt to understand the neural underpinnings of age-related differences within a specific cognitive domain, neuroimaging researchers

* Corresponding author.
E-mail addresses: ys11@columbia.edu (Y. Stern), ch629@columbia.edu (C. Habeck), js2746@columbia.edu (J. Steffener), djb2168@columbia.edu (D. Barulli), yl2107@columbia.edu (Y. Gazes), qr2108@columbia.edu (Q. Razlighi), ds3203@columbia.edu (D. Shaked), ts4v@virginia.edu (T. Salthouse).

[1] Shared first authorship. These authors contributed equally to the manuscript.

http://dx.doi.org/10.1016/j.neuroimage.2014.09.029
1053-8119/

typically evaluate age differences in neural activation associated with the performance of a selected task that purportedly taps that domain. In contrast, cognitive psychologists have repeatedly demonstrated the advantages of parsimoniously representing batteries of diverse cognitive tests by sets of latent variables that each summarize performance across multiple tests. For example, based on analyses of large test batteries administered to individuals ranging from young to old, Salthouse and colleagues have consistently identified latent variables, or reference abilities (RAs) that capture the majority of the variance in age-related cognitive change across four domains: episodic memory, fluid reasoning, perceptual speed, and vocabulary (Salthouse, 2005, 2009; Salthouse et al., 2008). Based on these findings, Salthouse et al. have argued that a productive and efficient approach to cognitive aging research is to try to understand how aging impacts performance of this small set of RAs, rather than on specific tasks (Salthouse and Ferrer-Caja, 2003). Similarly, we suggest that a more productive approach to cognitive neuroimaging research in aging is to shift the emphasis from evaluating age-related differences in brain activation during performance on an individual task to studying a set of task-independent neural networks postulated to underlie the reference abilities for the four cognitive domains. This would allow us to more reliably explore the neural basis of aging's influence on key cognitive abilities.

In this report we introduce the Reference Ability Neural Network (RANN) Study. The RANN Study is designed to identify networks of brain activity uniquely associated with performance across adulthood of each of the four reference abilities described above. Using analytic approaches that parallel those used to derive latent variables from cognitive, psychometric data, we aim to determine whether spatial fMRI networks can be derived that serve as the neural substrate for the latent cognitive structure of the reference abilities as derived from behavioral data. The desired structure of relationships between reference abilities and their neural substrates is shown in Fig. 1.

Just as a reference ability can be considered to represent the common cognitive ability underlying disparate tasks, "reference ability neural networks" (RANNs) are hypothesized to represent the common neural network that underlies the performance of each of the RAs. As in the analysis of the psychometric data, we expect the RANNs to demonstrate both convergent validity (for tasks within each cognitive domain) as well as discriminant validity (i.e. limited expression during performance of tasks in other cognitive domains). Ideally these RANNs would consist of a unique network of brain areas that are activated for each RA. Further, it would be compelling if the degree of expression or activation of a RANN was correlated with performance on the constituent tasks in that RA. Successful identification of these RANNs has the potential of contributing to a paradigm shift in research on the neural bases of age differences in cognition by emphasizing the broad and replicable aspects common to several tasks rather than the possibly idiosyncratic features of individual tasks.

The RAs that we are studying were identified in studies of several thousand individuals across the adult lifespan who have been administered extensive batteries of cognitive tasks (Salthouse, 2009). They have been modeled as latent constructs defined in terms of the common variance in four different sets of cognitive tasks representing: 1) episodic memory, 2) fluid reasoning, 3) perceptual speed, and 4) vocabulary. Although performance on the tasks that make up these RAs, and thus the levels of the abilities, differ across age, the latent constructs have been found to remain invariant across the adult lifespan. Further, although the modeled RAs are derived from performance of a limited set of tasks, these latent constructs have been found to account for the age-related performance differences on numerous other cognitive tasks (Salthouse, 2009; Salthouse and Davis, 2006; Salthouse et al., 2008). In the RANN study, we selected 12 tasks, three from each domain, that have reliably been associated with that RA. In turn, we hope to identify four RANNs, one for each cognitive ability. Once the RANNs are identified, we can investigate whether they too remain invariant over age despite different levels of performance. We can then explore the common and unique effects associated with chronological age on each of the RANNs. We also intend to examine

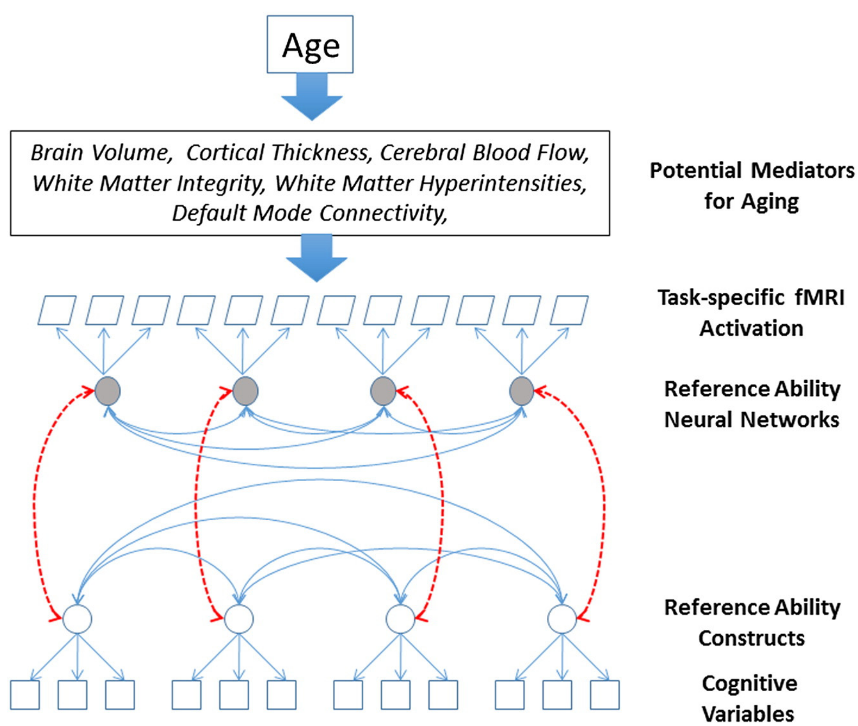

Fig. 1. Schematic sketch of brain-behavioral framework for the Reference Ability Neural Networks study: quantities given in rectangular or trapezoidal shapes are recorded in the study, while round shapes indicate both reference abilities and reference ability neural networks. The figure illustrates that not only are meaningful latent constructs expected on the basis of common patterns of fMRI activation across tasks representing the cognitive ability, but that those constructs are hypothesized to be related to the corresponding constructs defined on the basis of the correlations among behavioral performance in those same tasks. The upper boxes indicate that we expect that the effect of age on cognitive performance might be mediated by specific measures of brain aging. Further, brain changes may influence expression of the reference ability neural networks, yielding observed age-related cognitive changes.