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The Reference Ability Neural Network Study: Life-time stability of reference-ability neural networks derived from task maps of young adults

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A R T I C L E I N F O

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A B S T R A C T

Analyses of large test batteries administered to individuals ranging from young to old have consistently yielded a set of latent variables representing reference abilities (RAs) that capture the majority of the variance in age-related cognitive change: Episodic Memory, Fluid Reasoning, Perceptual Processing Speed, and Vocabulary. In a previous paper (Stern et al., 2014), we introduced the Reference Ability Neural Network Study, which administers 12 cognitive neuroimaging tasks (3 for each RA) to healthy adults age 20–80 in order to derive unique neural networks underlying these 4 RAs and investigate how these networks may be affected by aging.
We used a multivariate approach, linear indicator regression, to derive a unique covariance pattern or Reference Ability Neural Network (RANN) for each of the 4 RAs. The RANNs were derived from the neural task data of 64 younger adults of age 30 and below. We then prospectively applied the RANNs to fMRI data from the remaining sample of 227 adults of age 31 and above in order to classify each subject-task map into one of the 4 possible reference domains. Overall classification accuracy across subjects in the sample age 31 and above was 0.80 ± 0.18. Classification accuracy by RA domain was also good, but variable; memory: 0.72 ± 0.32; reasoning: 0.75 ± 0.35; speed: 0.79 ± 0.31; vocabulary: 0.94 ± 0.16. Classification accuracy was not associated with cross-sectional age, suggesting that these networks, and their specificity to the respective reference domain, might remain intact throughout the age range. Higher mean brain volume was correlated with increased overall classification accuracy; better overall performance on the tasks in the scanner was also associated with classification accuracy. For the RANN network scores, we observed for each RANN a higher score was associated with a higher corresponding classification accuracy for that reference ability. Despite the absence of behavioral performance information in the derivation of these networks, we also observed some brain–behavioral correlations, notably for the fluid-reasoning network whose network score correlated with performance on the memory and fluid-reasoning tasks. While age did not influence the expression of this RANN, the slope of the association between network score and fluid-reasoning performance was negatively associated with higher ages. These results provide support for the hypothesis that a set of specific, age-invariant neural networks underlies these four RAs, and that these networks maintain their cognitive specificity and level of intensity across age.
Activation common to all 12 tasks was identified as another activation pattern resulting from a mean-contrast Partial-Least-Squares technique. This common pattern did show associations with age and some subject demographics for some of the reference domains, lending support to the overall conclusion that aspects of neural processing that are specific to any cognitive reference ability stay constant across age, while aspects that are common to all reference abilities differ across age.

Introduction

Analyses of large test batteries administered to individuals ranging from young to old, have consistently yielded latent variables, or reference abilities (RAs) that capture the majority of the variance in age-related cognitive change. Salthouse et al. have identified 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, for cognitive neuroimaging research in aging the emphasis on age-related differences in a set of

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broad neural networks underlying the reference abilities for the four cognitive domains would be more productive than piecemeal approach focusing on separate individual tasks without consideration of commonalities between these tasks. This would allow us to more reliably explore the neural basis of aging's influence on key cognitive abilities. The Reference Ability Neural Network (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. In the RANN study, 12 tasks, three from each domain, that have reliably been associated with the corresponding RA, are administered to subjects in the scanner. Using analytic approaches that parallel those used to derive latent variables from cognitive psychometric data, we aim to determine whether four spatial fMRI networks can be derived that serve as the neural substrate for the latent cognitive structure of the reference abilities.

In a previous report (Stern et al., 2014) we introduced the RANN study and presented details of its acquisition and analysis procedures. We described an analysis intended to provide an initial representation of actual RANNs for each ability. We used a general linear model approach to summarize each subject's activation for each task into a single contrast. We then used a multivariate technique, linear indicator regression analysis, to derive four unique linear combinations of Principal Components (PC) of imaging data, one for each RA. We then investigated the ability of these constructed patterns to predict the reference domain using the activation of individual subjects for each task in held-out data. Median accuracy rates for associating component task activation with its corresponding reference ability were quite good: memory: 76%; reasoning: 82%; speed: 79%; vocabulary: 71%. We took this as an indication that it will be possible to identify unique networks associated with each reference ability.

Here we report an extension of this analysis in a larger group of participants. In our original report, we attempted to identify networks unique to each ability using data from subjects of all ages. Since the RANN study is intended to understand the sources of age-related cognitive change, it would be important to identify RANNs in younger people, and then investigate how these networks change as a function of aging. In the current study, we again used linear indicator regression analysis to derive a unique spatial covariance pattern (from a set of Principal Components) for each reference ability, but this analysis focused only on 64 individuals age 30 and below. We then investigated whether expression of these covariance patterns could successfully predict the reference domain associated with the activation of individual subjects and tasks in participants age 31 to 80. To the extent that these patterns are consistently expressed across age, this association should remain stable. However, a worsening in the ability to categorize abilities for older participants might indicate some age-related change. To the extent that we observed differences in classification accuracy, we planned to investigate the basis of these differences taking several approaches. Here we assessed whether classification accuracy 1) was lower for higher age for specific reference abilities or specific individuals, 2) was associated with the degree to which these patterns were expressed, and 3) was associated with observed age differences in mean cortical volume, cortical thickness and white-matter hyper-intensity burden. In addition to the activation particular to each reference domain, we also identified a common activation pattern in the derivation sample of participants aged 20–30. Brain-behavioral correlations and correlation with demographics was also assessed in the validation sample of participants aged 31 and above.

Material and Methods

Subjects

291 healthy adults were included in these analyses. All subjects native English speakers, strongly right-handed, and have at least a fourth grade reading level. Subjects were screened for MRI contraindications and hearing or visual impairment that would impede testing. Subjects were free of medical or psychiatric conditions that could affect cognition. Careful screening ensured that the elder subjects did not meet criteria for dementia or Mild Cognitive Impairment (MCI). A score greater than 130 was required on the Mattis Dementia Rating Scale (Mattis, 1988). Further, performance was required to be within age-adjusted normal limits on a list-learning test, and participants were required to have no or minimal complaints on a functional impairment questionnaire (Blessed et al., 1968).

Procedure

All subjects completed screening for dementia or MCI prior to participating in the remainder of the study. They participated in two 2-hour scanning sessions. Six tasks were administered in each session in the context of fMRI studies. One session presented three Vocabulary tasks and three Perceptual Speed tasks interspersed in a fixed order: Synonyms, Digit-Symbol, Antonyms, Letter Comparison, Picture Naming, and Pattern Comparison; and the other session presented three Episodic Memory tasks and three Fluid Reasoning tasks, also interspersed in a fixed order: Logical Memory, Paper Folding, Word Order Recognition, Matrix Reasoning, Paired Associates, Letter Sets. The order of tasks within session was not varied, but the order of the two sessions was counterbalanced across subjects, with equal numbers having each order. The activation tasks were supplemented with other imaging procedures described below. At a separate session subjects completed a battery of neuropsychological tests as well as a set of questionnaires. These will not be discussed in the current report.

Stimulus presentation

Task stimuli were back-projected onto a screen located at the foot of the MRI bed using an LCD projector. Participants viewed the screen via a mirror system located in the head coil and, if needed, had vision corrected to normal using MR compatible glasses (manufactured by SafeVision, LLC. Webster Groves, MO). Responses were made on a LUMItouch response system (Photon Control Company). Task administration and collection of reaction time (RT) and accuracy data were controlled by EPrime (v2.08) running on a PC computer. Task onset was electronically synchronized with the MRI acquisition computer.

Reference Ability tasks

In the scanner, participants performed a battery of twelve computerized tasks based on the cognitive tasks that have been used to derive the RAs that are addressed in this report. Prior to the scan session, computerized training was administered for the six tasks included in that session. At the completion of training for each task, participants had the option of repeating the training. The tasks are described in detail in (Stern et al., 2014). For all tasks, except picture naming, responses were differential button presses. During training, responses were made on the computer keyboard and during scans they were made on the LUMItouch response system.

In the remainder of the manuscript, we will use the following shorthand notation for the reference abilities: episodic memory — MEM, fluid reasoning — FLUID, perceptual processing speed — SPEED, and vocabulary — VOCAB.

Vocabulary Tests. The primary dependent variable for all VOCAB tasks is the proportion of correct items.

Synonyms (Salthouse, 1993). Subjects have to match a given word to its synonym, or to the word most similar in meaning. The probe word is presented in all capital letters at the top of the screen, and four numbered choices are presented below.

Antonyms (Salthouse, 1993). Participants match a given word to its antonym, or to the word most different in meaning.

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