NeuroImage 172 (2018) 51–63

Contents lists available at ScienceDirect

NeuroImage

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

Reference ability neural networks and behavioral performance across the adult life span

Christian Habeck *, Teal Eich, Ray Razlighi, Yunglin Gazes, Yaakov Stern

Cognitive Neuroscience Division, Department of Neurology, Columbia University, New York, NY, 10032, United States

A B S T R A C T

To better understand the impact of aging, along with other demographic and brain health variables, on the neural networks that support different aspects of cognitive performance, we applied a brute-force search technique based on Principal Components Analysis to derive 4 corresponding spatial covariance patterns (termed Reference Ability Neural Networks –RANNs) from a large sample of participants across the age range. 255 clinically healthy, community-dwelling adults, aged 20–77, underwent fMRI while performing 12 tasks, 3 tasks for each of the following cognitive reference abilities: Episodic Memory, Reasoning, Perceptual Speed, and Vocabulary. The derived RANNs (1) showed selective activation to their specific cognitive domain and (2) correlated with behavioral performance. Quasi out-of-sample replication with Monte-Carlo 5-fold cross validation was built into our approach, and all patterns indicated their corresponding reference ability and predicted performance in held-out data to a degree significantly greater than chance level. RANN-pattern expression for Episodic Memory, Reasoning and Vocabulary were associated selectively with age, while the pattern for Perceptual Speed showed no such age-related influences. For each participant we also looked at residual activity unaccounted for by the RANN-pattern derived for the cognitive reference ability. Higher residual activity was associated with poorer brain-structural health and older age, but –apart from Vocabulary-not with cognitive performance, indicating that older participants with worse brain-structural health might recruit alternative neural resources to maintain performance levels.

Introduction

Cognitive aging can be described parsimoniously by a set of four reference abilities – Episodic Memory, Reasoning, Perceptual Speed, and Vocabulary – that serve as the "primitive types" of cognition in general (Salthouse and Ferrer-Caja, 2003). Our group has recently extended this line of research (Habeck et al., 2016; Stern et al., 2014) by collecting functional imaging data on a battery of tasks that tap each of the four reference abilities across the adult life span, in order to determine their neural correlates, i.e. Reference Ability Neural Networks (RANNs). Using a multivariate technique that married Principal Components Analysis (PCA) and Linear-Indicator Regression (Hastie et al., 2009), we previously derived spatial activation patterns that accurately classified the reference ability underlying each activation task. Indeed, even when these patterns were derived only in people below age 30, out-of-sample task classification performance of the four RANNs in people older than 30 was high, and did not decline with age, suggesting that these RANNs are age-invariant.

In this previous specification of the RANNs to their underlying reference ability, one crucial aspect that was not accounted for was behavioral performance: ideally, RANNs should not only be specific to the reference ability of the underlying cognitive process, but also account for behavioral performance. To reconcile this issue, we extended our previous findings, analyzing the data from 255 20–77 year old adults who underwent fMRI while performing three tasks for each of the four cognitive reference abilities, i.e. 12 tasks in total. In the current report, we combined PCA with a brute-force search that sought to maximize *both* the brain-behavioral correlation of the derived RANNs *and* cognitive specificity to the reference domain in question. Statistical inference was performed by resampling, and testing the prediction of cognitive process and behavioral performance in held-out data. This approach allowed us to investigate how well the RANNs could account for performance and cognitive specificity, and to understand how changes in performance concomitant with aging are reflected in these RANNs.

We stress that the current report is *not* methodological in focus: the approach we chose is conceptually simple, but algorithmically somewhat involved, lengthy and inelegant. We are not bringing a prime-time ready technique to the field that should be widely disseminated; rather, our focus here is on the results of our approach, i.e. the derived networks, their association with behavioral performance, demographics and brain structure across the adult life span.

* Corresponding author.
E-mail address: ch629@columbia.edu (C. Habeck).

https://doi.org/10.1016/j.neuroimage.2018.01.031
Received 2 November 2017; Received in revised form 21 December 2017; Accepted 12 January 2018

Methods

Participant sample and demographics

Analyses included data from 255 strongly right-handed, native English speaking healthy adults. Participants were recruited via random-market-mailing, and screened for MRI contraindications and hearing or visual impairment that would impede testing. Older adult participants were additionally screened for dementia and mild cognitive impairment prior to participating in the study, and participants who met criteria for either were excluded. Apart from these obvious cognitive exclusion criteria, we had a host of other health-related exclusion criteria including: myocardial infarction, congestive heart failure or any other heart disease, brain disorder such as stroke, tumor, infection, epilepsy, multiple sclerosis, degenerative diseases, head injury (loss of consciousness > 5 mins), mental retardation, seizure, Parkinson's disease, Huntington's disease, normal pressure hydrocephalus, essential/familial tremor, Down Syndrome, HIV Infection or AIDS diagnosis, learning disability/dyslexia, ADHD or ADD, uncontrolled hypertension, uncontrolled diabetes mellitus, uncontrolled thyroid or other endocrine disease, uncorrectable vision, color blindness, uncorrectable hearing and implant, pregnancy, lactating, any medication targeting central nervous system, cancer within last five years, Renal insufficiency, untreated neurosyphilis, any alcohol and drug abuse within last 12 months, recent non-skin neoplastic disease or melanoma, active hepatic disease, insulin dependent diabetes, any history of psychosis or ECT, recent (past five years) major depressive, bipolar, or anxiety disorder, objective cognitive impairment (dementia rating scale of <130), and subjective functional impairment (BFAS > 1). The prevalence of medication for hypertension, diabetes, and high cholesterol is as follows, respectively: 18%, 14%, and 7%. This compares favorably with CDC statistics for the adult US population at large (33.5%, 12.6%, and 12.1%, from www.cdc.gov/nchs/fastats). A complete description of the participants in terms of demographics and cortical thickness can be found in Table 1.

Procedure

FMRI data was acquired as participants performed 12 cognitive tasks, pertaining to the four reference abilities (Stern et al., 2014). In the remainder of the manuscript, we occasionally use the following short-hand notation for the reference abilities: episodic memory — MEM or just "Memory", reasoning — REASON, perceptual speed — SPEED or just "Speed", and vocabulary — VOCAB. We will refer to the Reference Ability Neural Networks (RANNs) as activation patterns, for brevity. Further, "cognitive reference ability" and "cognitive reference domain" will be used interchangeably.

Tasks were administered over the course of two 2-h scanning sessions, with six tasks administered in each scanning-session. One session presented three VOCAB tasks and three SPEED tasks interspersed in a fixed order: Synonyms, Digit-Symbol, Antonyms, Letter Comparison, Picture Naming, and Pattern Comparison; and the other session presented three MEM tasks and three REASON tasks, also interspersed in a fixed order: Logical Memory, Paper Folding, Word Order Recognition, Matrix Reasoning, Paired Associates, and Letter Sets. The order of tasks within session was not varied, but the order of the two sessions was counter-balanced across participants. Prior to each scan session, computerized training was administered for the six tasks to be administered during that session. At the completion of training for each task, participants had the option of repeating the training. For all tasks except Picture Naming, responses were differential button presses. During training, responses were on the computer keyboard. During scans, they were made on the LUMItouch response system (Photon Control Company).

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). Task administration and collection of reaction time (RT) and accuracy data were controlled by EPrime running on a PC computer. Task onset was electronically synchronized with the MRI acquisition computer.

Reference ability tasks

VOCAB tasks. The primary dependent variable for all VOCAB tasks was the proportion of correct responses.

Synonyms (Salthouse, 1993**):** Participants were instructed to match a given probe word to its synonym or to the word most similar in meaning. The probe word was presented in all capital letters at the top of the screen, and four numbered choices were presented below. Participants indicated which choice was correct.

Antonyms (Salthouse, 1993**):** Participants matched a given word to its antonym, or to the word most different in meaning. The probe word was presented in all capital letters at the top of the screen, and four numbered choices were presented below. Participants indicated which choice was correct.

Picture Naming: Participants verbally named pictures, adapted from the picture naming task of the WJ-R Psycho-Educational battery (Salthouse, 1998; Woodcock et al., 1989).

SPEED tasks. As accuracy for all three SPEED tasks was high, the primary dependent variable was reaction time (RT). For all tasks, participants were instructed to respond as quickly and accurately as possible.

Digit Symbol: A code table was presented on the top of the screen, consisting of nine number (ranging in value from 1 to 9)-symbol pairs. Below the code table, an individual number/symbol pair was presented. Participants indicated whether the individual pair was the same as that in the code table.

Letter Comparison (Salthouse and Babcock, 1991**):** Two strings of letters, each consisting of three to five letters, were presented alongside one another. Participants indicated whether the letter-strings were the same or different.

Pattern Comparison (Salthouse and Babcock, 1991**):** Two figures, consisting of varying numbers of lines connecting at different angles, were presented alongside one another. Participants indicated whether the figures were the same or different.

REASON tasks. The primary dependent variable for the REASON tasks was proportion of correct trials.

Paper Folding (Ekstrom et al., 1976**):** Participants selected which of

Table 1
Participant sample and demographics. Cortical thickness has strong negative linear age trends, $p < .0001$.

	<30	30–39	40–49	50–59	60–69	>70
N	35	44	38	40	62	36
NART-IQ	113 ± 9	112 ± 9	114 ± 9	115 ± 8	118 ± 9	120 ± 10
Education	15.3 ± 2.3	16.4 ± 2.5	15.9 ± 2.6	15.5 ± 2.3	16.0 ± 2.5	17.3 ± 2.5
Sex	23 F, 12 M	27 F, 17 M	17 F, 21 M	20 F, 20 M	32 F, 30 M	18 F, 18 M
DRS	140.4 ± 2.7	139.8 ± 2.3	139.1 ± 2.9	140.1 ± 3.3	139.7 ± 3.1	139.7 ± 3.0
Mean Cortical thickness	2.69 ± 0.11	2.66 ± 0.09	2.65 ± 0.09	2.59 ± 0.08	2.55 ± 0.11	2.51 ± 0.12