Structural and functional MRI data differentially predict chronological age and memory performance

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Introduction

Human cognitive abilities typically decline with increasing chronological age, with explicit memory performance being particularly affected [1]. In order to track such developments [2], and especially to differentiate healthy physiological from pathophysiological aging [3], predictors of this decline need to be identified.

Whereas previous studies on age-related differences have focused on just a few potential predictors, we here compared behavioral data, task-based, resting-state and structural magnetic resonance imaging (MRI) as well as functional MRI scores in terms of their ability to predict chronological age and memory performance in two large samples of young and older adults.

Methods

We analyzed MRI data from 106 young (18-35 yrs, 47/59 m/f) and 153 older (51-80 yrs, 59/94 m/f) subjects that performed a visual incidental memory task [4,5,6] (see Figure 1). In the encoding session, novel and familiar images were presented and subjects performed an indoor-outdoor judgement. In the retrieval session, all old and several new images were shown and subjects provided a recognition-confidence rating (ranging from 1 for "sure new" over 3 for "undecided" to 5 for "sure old"). fMRI signals during the encoding session were acquired using the DELCODE protocol [3].

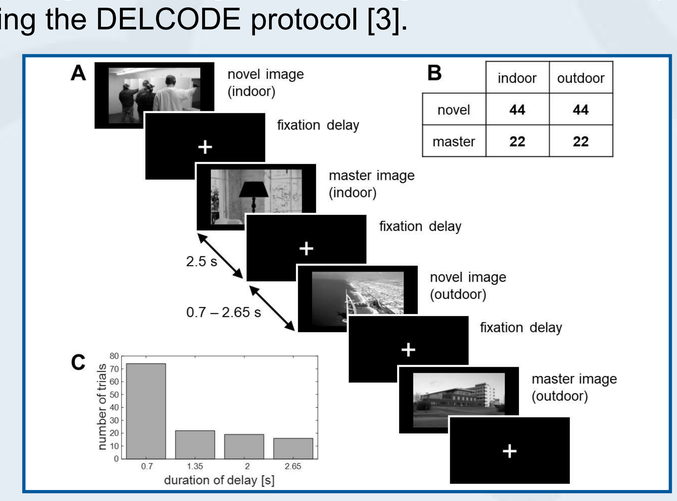

Figure 1. *Experimental design and stimulus timing during encoding.* The exemplary sequence of trials, each trial consisting of either a previously unseen novel image or a pre-familiarized master image.

As target variables for predictive analyses (see Figure 2, right), we used (i) age group (young vs. older), (ii) chronological age (in years) and (iii) memory performance, measured as area under the curve in an ROC analysis of the memory responses [6, p. 18].

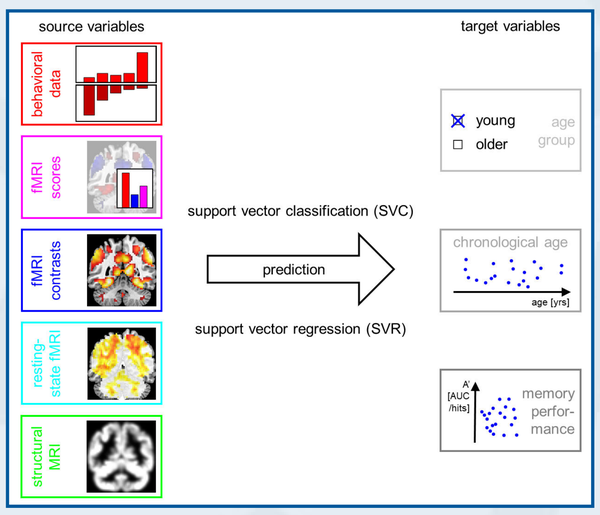

Figure 2. *Methodology of the present study.* Target variables of interest (right) are predicted using sets of source variables (left), thought to be markers of cognitive decline in old age, using machine learning techniques (center).

Analysis

Each analysis consisted in predicting one target variable from one set of source variables (see Figure 2, left):
(i) behavioral response frequencies, i.e. fractions of responses 1-5 for old vs. new items [5, tab. S2];
(ii) voxel-wise fMRI contrasts related to novelty processing and subsequent memory [5, fig. 7];
(iii) single-value fMRI scores (FADE & SAME score) computed from these contrasts [6,7];
(iv) voxel-wise mean percent of amplitude fluctuation (mPerAF), computed from resting-state fMRI scans; and
(v) voxel-wise gray matter volume (GMV), estimated with voxel-based morphometry from structural MR scans.
Target variables were predicted with support vector machines (SVM; see Figure 2, center) for classification (SVC) or regression (SVR) using a cost parameter of C = 1 and 10-fold cross-validation on subjects per group. For continuous target variables, distributional transformation (DT) [9] was applied after prediction.

Results

First, we assure that age group can be decoded from all source variables, with a clear hierarchy from behavioral over functional to structural variables (see Figure 3A). Second, we find that within age groups, structural MRI is superior at predicting chronological age (see Figure 3B). Third, we find that memory performance is best predicted from task-based fMRI and particularly single-value fMRI scores (see Figure 3C).

To follow up on these findings, we performed sub-group analyses in the older subjects (see Figure 5) and found a double-dissociation between structural MRI (and resting-state fMRI) vs. functional MRI and age vs. memory: (i) when partitioning subjects by chronological age, there are no significant effects on task-based fMRI, but strong differences in GMV (see Figure 4A); and (ii) when partitioning subjects by memory performance, there are no significant effects on structural MRI, but robust differences in memory-related brain activity (see Figure 4B).

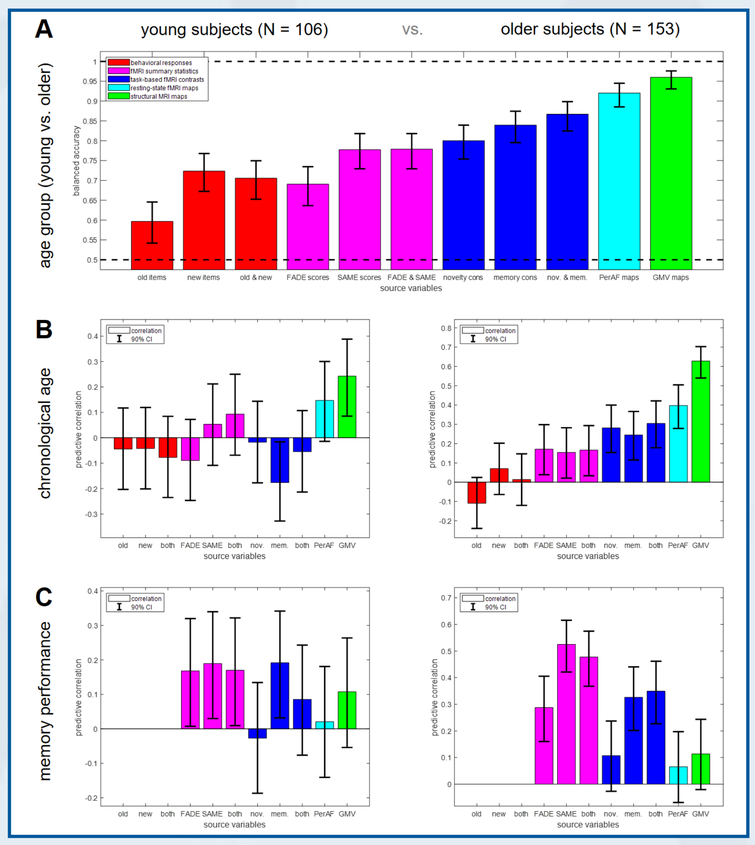

Figure 3. *Predictive analyses for chronological age and memory performance.* Performance for **(A)** classification of subjects into age groups and regression of subjects' **(B)** chronological age or **(C)** memory performance, based on behavioral data (red), fMRI scores (magenta), fMRI contrasts (blue), resting-state fMRI (cyan) and structural MRI (green).

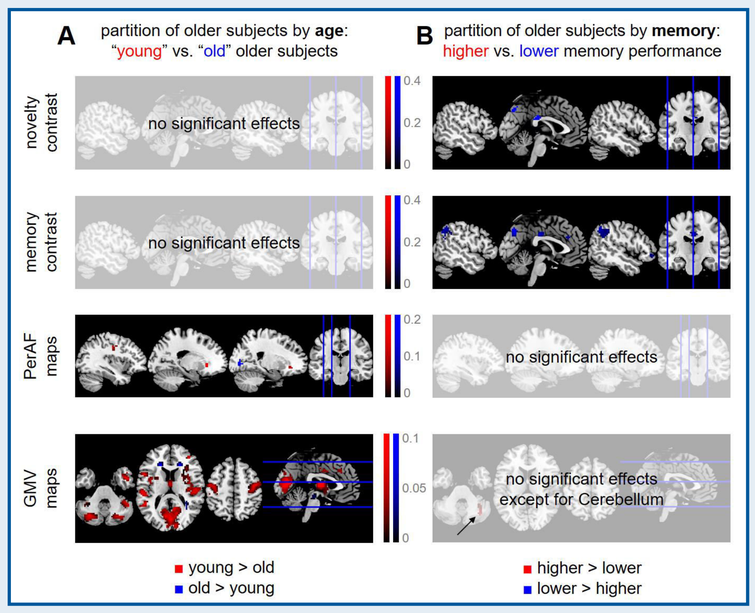

Figure 4. *Differential effects of age and memory in structural and functional MRI.* Significant differences **(A)** between "young" and "old" older subjects and **(B)** between older subjects with higher vs. lower memory performance, with respect to fMRI activity during novelty processing (1st row), subsequent memory (2nd row), fMRI amplitudes during rest (3rd row) and voxel-wise gray matter volume (4th row).

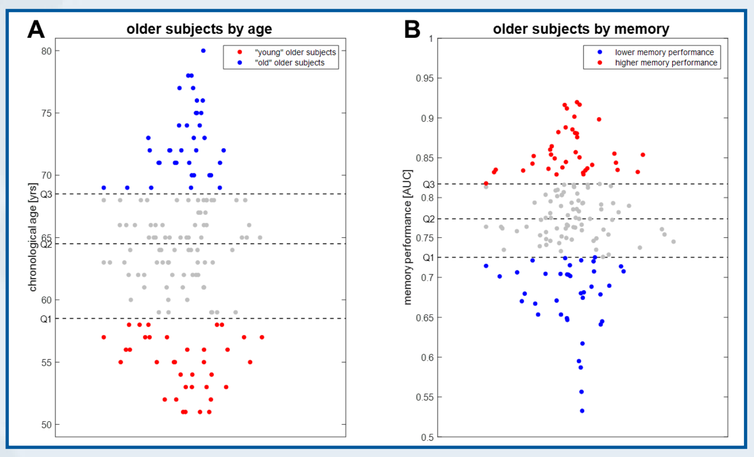

Figure 5. *Separation of older subjects by chronological age and memory performance.* Older subjects were partitioned into four groups based on **(A)** chronological age and **(B)** memory performance.

Conclusions

Our results suggest that older adults with memory performance comparable to young subjects are not characterized by fewer structural differences from, but higher functional similarities with young subjects (cf. Figure 4) [8]. This underscores that cognitive reserve is – at least to a degree – independent of brain maintenance. It is also noteworthy that resting-state fMRI behaved more similar to structural MRI than task-based fMRI (cf. Figure 3A/4A). In future work, we want to evaluate these feature sets for differentiating between clinical memory-impaired populations [3].

Preprint

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