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 patho-physiological 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) in terms of their ability to predict chronological age and memory performance in two large

samples of young (N = 106) and older (N = 153) 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]. In the encoding session, 88 novel and 44 familiar images were presented and subjects performed an indoor-outdoor judgement. In the retrieval session, the 88 novel, now old and 44 unseen, now 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 were measured during the encoding session and acquired using the exact same protocol as the one used in the ongoing DELCODE study [3].
From our subjects, we used as target variables for predictive analyses: age group (young vs. older), chronological age (in years) and memory performance (measured as AUC in an ROC analysis [6, p. 18]). As source variables for predictive analyses, we extracted: (i) behavioral response frequencies, i.e. fractions of responses 1-5 for old vs. new items [4, tab. S2]; (ii) voxel-wise fMRI activity related to novelty processing (novel vs. familiar images) and subsequent memory (later remembered vs. forgotten novel items) [5, fig. 7]; (iii) two fMRI summary statistics (FADE & SAME score) computed from these contrasts [6,7]; (iv) voxel-wise percent of amplitude fluctuation (PerAF), computed from resting-state scans acquired directly before the task; and (v) voxel-wise gray matter volume (GMV), estimated with voxel-based morphometry (VBM) from T1-weighted MPRAGE images.
Target variables were predicted with support vector machines (SVC, 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.

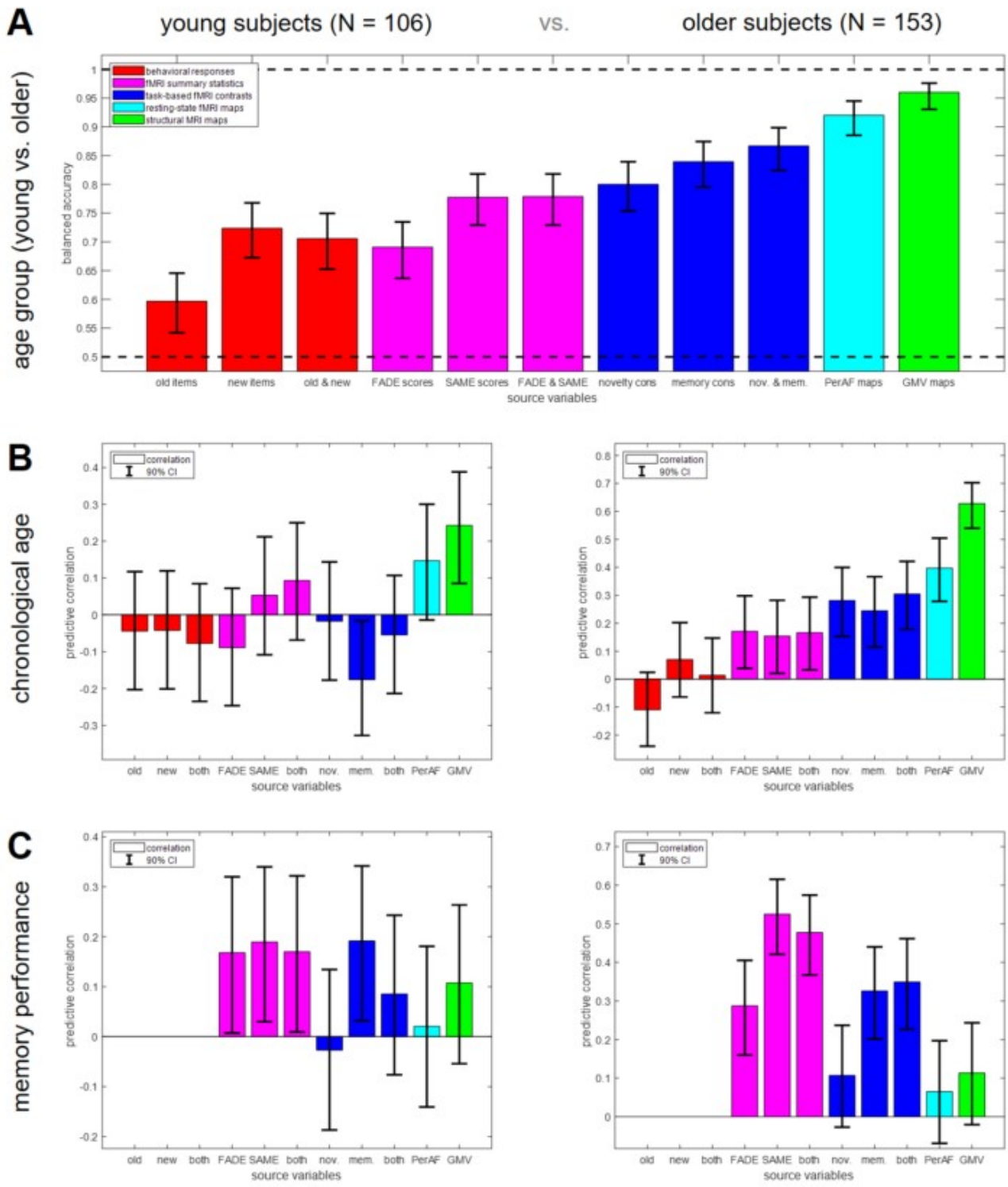

Figure 1. *Predictive analyses for chronological age and memory performance.* Performance for **(A)** classification of subjects into age groups and regression of subjects' **(B)** chronological age or **(C)** memory performance, based on behavioral data (red), fMRI scores (magenta), fMRI contrasts (blue), resting-state fMRI (cyan) and structural MRI (green). Bar plots show balanced accuracy (i.e. mean class accuracy) for classification and predictive correlation (i.e. correlation coefficient between actual and predicted values) for regression; error bars denote 90% confidence intervals; for explanation of source variables, see "Methods".

(https://files.aievolution.com/prd/hbm2201/abstracts/abs_2426/Figure_1_2021_12_17.png)

Results:

First, we validate that age group can be decoded from all source variables, with a clear hierarchy from behavioral over functional to structural variables (see Figure 1A). Second, we find that within age groups,

structural MRI (VBM-estimated GMV) is superior at predicting chronological age (see Figure 1B). Third, we find that memory performance is best predicted from task-based fMRI and particularly fMRI summary statistics (see Figure 1C).

To follow up on these findings, we performed sub-group analyses in the older subjects 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 2A); 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 2B).

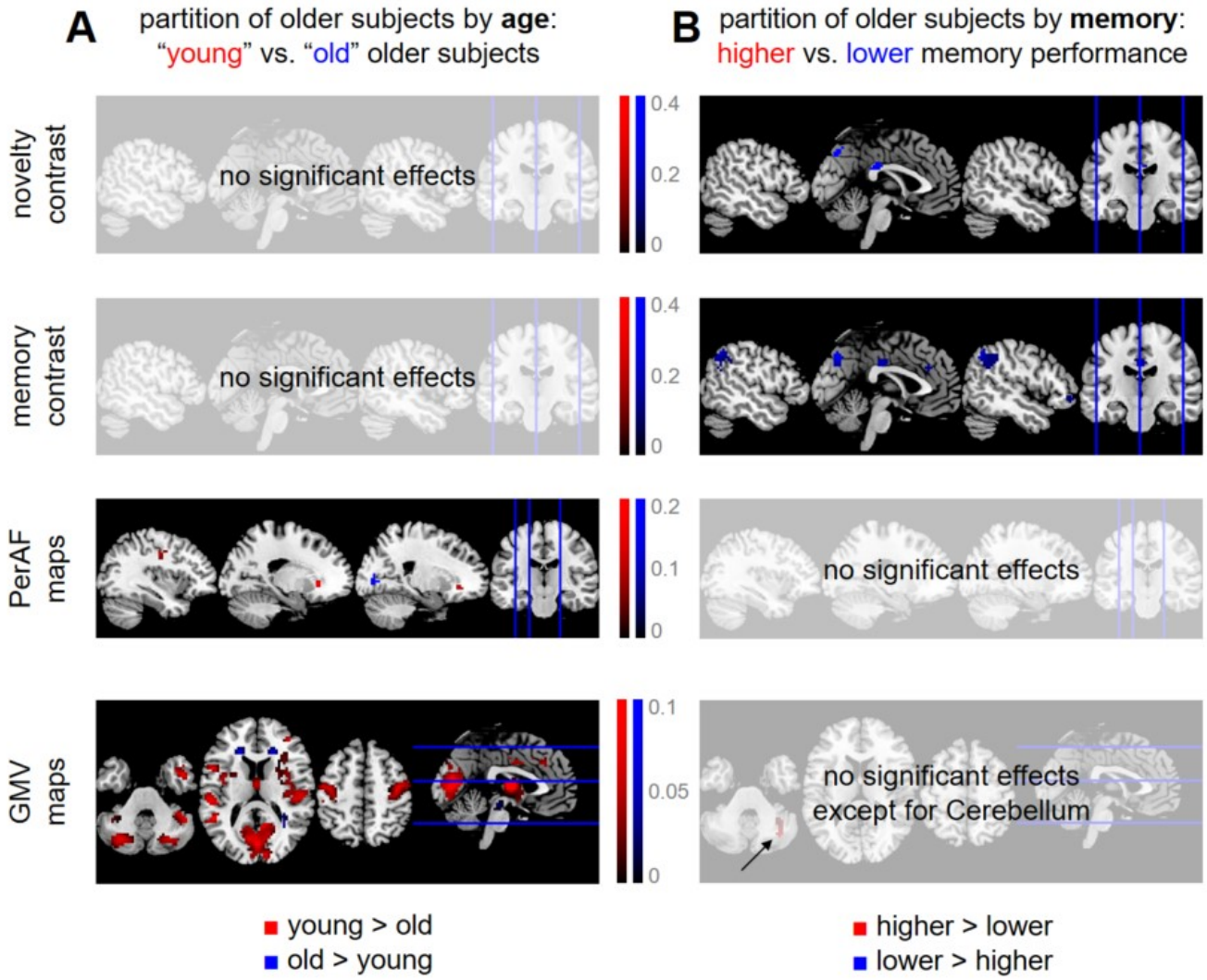

Figure 2. *Differential effects of age and memory in structural and functional MRI.* Significant differences **(A)** between "young" and "old" older subjects and **(B)** between older subjects with higher vs. lower memory performance, with respect to fMRI activity during novelty processing (1st row), subsequent memory (2nd row), fMRI amplitudes during rest (3rd row) and voxel-wise gray matter volume (4th row). Thresholded statistical maps are FWE-corrected for cluster size (CDT: $p < 0.001$; FWEc: novelty: $k = 42$; memory: $k = 27$; PerAF: $k = 23$; GMV: $k = 33$ [A], $k = 42$ [B]). Colored voxels indicate significantly higher values for either young subjects and those with higher memory (red) or old subjects and those with lower memory (blue).

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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 2) [8]. It is also noteworthy that resting-state fMRI behaved more similar to structural MRI than task-

based fMRI (cf. Figure 1A/2A). In future work, we want to evaluate these feature sets for differentiating between clinical memory-impaired populations, e.g. different stages of Alzheimer's disease [3].

Disorders of the Nervous System:

Neurodegenerative/ Late Life (eg. Parkinson’s, Alzheimer’s)

Learning and Memory:

Long-Term Memory (Episodic and Semantic) [1]

Modeling and Analysis Methods:

Classification and Predictive Modeling [2]

Novel Imaging Acquisition Methods:

Anatomical MRI
BOLD fMRI

Keywords:

Aging
Data analysis
FUNCTIONAL MRI
Learning
Machine Learning
Memory
Multivariate
Statistical Methods
STRUCTURAL MRI
Other - chronological age

[1|2]Indicates the priority used for review

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation” study.

Resting state
Task-activation
Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Functional MRI
Structural MRI
Behavior
Other, Please specify - resting-state fMRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

SPM
Other, Please list - ML4ML package

Provide references using author date format

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