**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) 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.

**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).

**Discussion:**

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].

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