**Memory-related fMRI activations and deactivations**

**as a potential biomarker for neurocognitive aging**

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**Introduction:**

Older adults, particularly those at risk for developing dementia, typically show a decline in episodic memory performance, which has been associated with altered memory network activity detectable via functional magnetic resonance imaging (fMRI). There are two ways of assessing such episodic memory networks: (i) as neural correlates of *novelty processing* by contrasting familiar with novel items or (ii) as neural correlates of *subsequent memory* by contrasting items remembered with items forgotten in a later memory test [1]. Both, novelty and subsequent memory, are characterized by significant activations of medial temporal lobe, prefrontal and parietal cortical structures, and by significant differences between healthy young and older adults in these areas [2]. In this study, we evaluated two reductionist scores derived from memory-related fMRI activations as potential biomarkers for successful aging in episodic memory and tested whether they are predictive with respect to age and memory performance.

**Methods:**

We analyzed fMRI data from 106 young (18-35 yrs, 47/59 m/f) and 111 older (60-80 yrs, 46/65 m/f) subjects acquired within the “Autonomy in Old Age” (AiA) project (Leibniz Institute for Neurobiology, Magdeburg, Germany). Subjects performed the so-called “FADE task” [1], a visual incidental memory encoding task with indoor/outdoor judgement during encoding (see Figure 1) and recognition confidence rating on a five-point scale during retrieval (ranging from 1 for “sure new” to 5 for “sure old”). The fMRI data were acquired using the exact same protocol as in the ongoing DELCODE [3,4] study (German Centers for Neurodegenerative Diseases). There was another fMRI data set comprising 117 participants (19-33 yrs, 60/57 m/f) using the same task, but different trial timings and MRI acquisition parameters [5] which was used as a replication cohort for young AiA subjects.

Our analyses were based on a first-level general linear model (GLM) [6] parametrically modulating with a non-linear transformation of memory confidence ratings, which was previously identified as an optimal model of subsequent memory effects in fMRI signals [7]. Using this GLM, novelty and subsequent memory contrasts were computed and used to calculate two scores to quantify successful aging in memory.

**Results:**

Both scores are based on reference maps of prototypical activations seen in young subjects (see Figure 2A). The originally suggested *FADE score* (“functional activity deviation during encoding” [1]) quantifies the deviation of encoding-related *activations* from those templates in older adults; our newly developed *SAME score* (“similarities of activations during memory encoding” [8]) accumulates the average of reduced *activations* and reduced *deactivations* relative to young subjects in older adults (see Figure 2B).

We found that (i) both scores significantly differ between young and older adults when computed from the memory contrast, and the SAME score also does so for the novelty contrast; (ii) when controlling for age group, both scores are correlated with memory performance when computed from the memory contrast, which also holds for the SAME score on the novelty contrast; (iii) both scores are equally stable when computed for older adults using different reference samples of young subjects, and the SAME score is also stable when computed for young subjects acquired in different studies [8].

**Discussion:**

Taken together, we show that highly reductionist and easy-to-use fMRI scores reliably detect correlates of age-related alterations in human memory networks. Our results further suggest that the SAME score provides a comprehensive measure that accounts for both activations and deactivations as well as interindividual variability in the baseline cohort of young subjects [8]. In future work, we want to evaluate FADE and SAME score for differentiating between clinical memory-impaired populations, e.g. different stages of Alzheimer’s disease [3].

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