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.

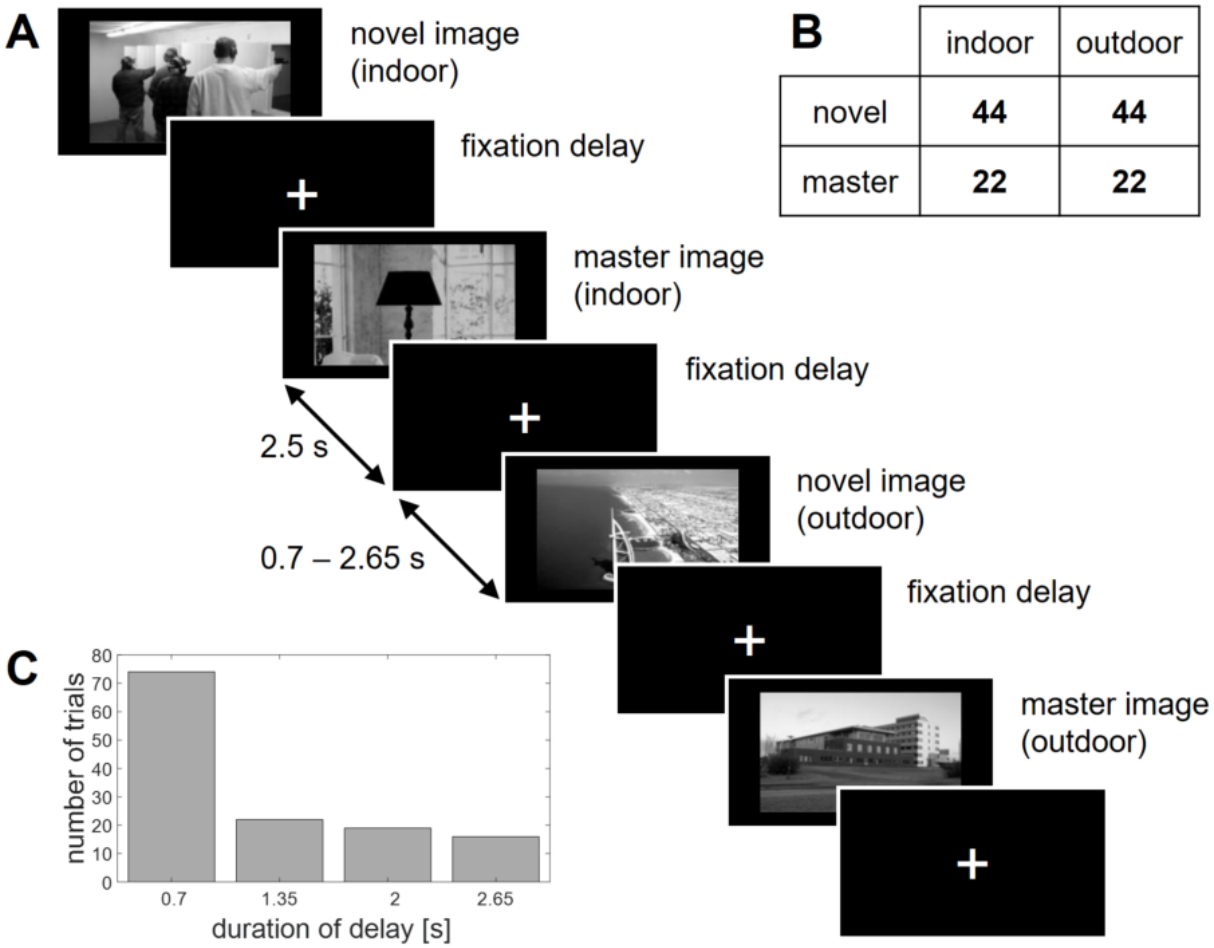

Figure 1. *Experimental design and stimulus timing during encoding.* **(A)** Exemplary sequence of trials, each trial consisting of either a previously unseen novel image or a pre-familiarized master image showing either an indoor or an outdoor scene. Each stimulus was shown for 2.5 s and followed by a variable inter-stimulus-interval (ISI) between 0.7 and 2.65 s. **(B)** Number of trials in the four experimental conditions. There were equally many indoor and outdoor scences and twice as many novel images as repetitions of the two previously familiarized master images. **(C)** Distribution of ISIs in the encoding session. ISIs were pseudo-exponentially distributed with shorter intervals occurring more often than longer ones.

(https://files.aievolution.com/prd/hbm2101/abstracts/abs_2321/Figure_1.png)

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].

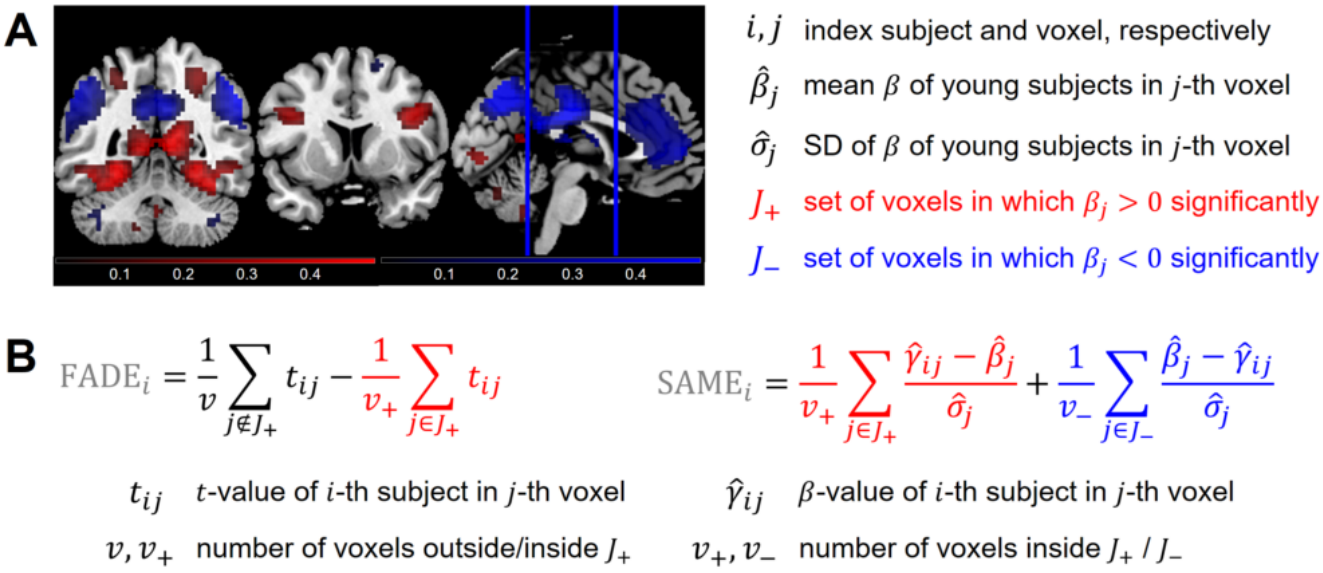

Figure 2. *Measures for quantifying successful aging in memory.* We compute two summary statistics from fMRI contrasts, which are both based on a group-level analysis across all young subjects and subject-wise computation in each older subject. **(A)** A reference map is obtained by significance testing of a contrast within the group of young subjects, resulting in voxels with significant activation (red) or significant deactivation (blue). **(B)** FADE and SAME score of older subjects are calculated as summary statistics by averaging single-subject contrast outcomes within selected sets of voxels.
(https://files.aievolution.com/prd/hbm2101/abstracts/abs_2321/Figure_2.png)

Conclusions:

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].

Disorders of the Nervous System:

Neurodegenerative/ Late Life (eg. Parkinson's, Alzheimer's) [2]

Learning and Memory:

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

Lifespan Development:

Aging

Modeling and Analysis Methods:

Activation (eg. BOLD task-fMRI)

Keywords:

Aging
Data analysis
Degenerative Disease
FUNCTIONAL MRI
Memory
NORMAL HUMAN
Other - neurocognitive aging

[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.

Task-activation

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
Neuropsychological testing

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 - MACS toolbox

Provide references using author date format

[1] Düzel E, Schütze H, Yonelinas AP, Heinze HJ. 2011. Functional phenotyping of successful aging in long-term memory: Preserved performance in the absence of neural compensation. Hippocampus 21:803–814. doi:10.1002/hipo.20834
[2] Maillet D, Rajah MN. 2014. Age-related differences in brain activity in the subsequent memory paradigm: A meta-analysis. Neurosci Biobehav Rev 45:246–257. doi:10.1016/j.neubiorev.2014.06.006
[3] Jessen F, Spottke A, Boecker H, Brosseron F, Buerger K, [...], Westerteicher C, Wiltfang J, Wolfsgruber S, Wagner M, Düzel E. 2018. Design and first baseline data of the DZNE multicenter observational study on predementia Alzheimer's disease (DELCODE). Alzheimer's Res Ther 10:1–10. doi:10.1186/s13195-017-0314-2
[4] Düzel E, Acosta-Cabronero J, Berron D, Biessels GJ, Björkman-Burtscher I, [...], Tosetti M, Uludag K, Vignaud A, Zwanenburg J, Speck O. 2019. European Ultrahigh-Field Imaging Network for Neurodegenerative Diseases (EUFIND). Alzheimer's Dement Diagnosis, Assess Dis Monit 11:538–549. doi:10.1016/j.dadm.2019.04.010
[5] Assmann A*, Richter A*, Schütze H, Soch J, Barman A, [...], Wüstenberg T, Behr J, Düzel E, Seidenbecher CI, Schott BH. 2020. Neurocan genome-wide psychiatric risk variant affects explicit memory performance and hippocampal function in healthy humans. Eur J Neurosci ejn.14872. doi:10.1111/ejn.14872
[6] Friston KJ, Holmes AP, Worsley KJ, Poline JP, Frith CD, Frackowiak RSJ. 1994. Statistical parametric maps in functional imaging: A general linear approach. Hum Brain Mapp 2:189–210. doi:10.1002/hbm.460020402
[7] Soch J*, Richter A*, Schütze H, Kizilirmak JM, Assmann A, [...], Maass A, Ziegler G, Richardson-Klavehn A, Düzel E, Schott BH. 2021. Bayesian model selection favors parametric over categorical fMRI subsequent memory models in young and older adults. NeuroImage. doi:10.1101/2020.07.27.220871
[8] Soch J*, Richter A*, Schütze H, Kizilirmak JM, Assmann A, [...], Yakupov R, Ziegler G, Wiltfang J, Düzel E, Schott BH. 2021. A comprehensive score reflecting memory-related fMRI activations and deactivations as potential biomarker for neurocognitive aging. bioRxiv. doi:10.1101/2021.01.16.426666