# Age-related declines in neural selectivity manifest differentially during encoding and recognition

Claire Pauley[a,b], Verena R. Sommer[a], Malte Kobelt[c], Attila Keresztes[d,e], Markus Werkle-Bergner[a], & Myriam C. Sander[a]

[a] *Center for Lifespan Psychology, Max Planck Institute for Human Development, 14195 Berlin, Germany*

[b] *Faculty of Life Sciences, Humboldt-Universität zu Berlin, 10115 Berlin, Germany*

[c] *Institute of Cognitive Neuroscience, Ruhr-Universität Bochum, 44780 Bochum, Germany*

[d] *Brain Imaging Centre, Research Centre for Natural Sciences, 1117 Budapest, Hungary*

[e] *Faculty of Education and Psychology, Eötvös Loránd University, 1053 Budapest, Hungary*

Correspondence should be addressed to Myriam C. Sander at sander@mpib-berlin.mpg.de.

**Abstract**

One important factor contributing to age-related memory decline is the loss of distinctiveness with which information is represented in brain activity. This loss in neural selectivity may be driven by neural attenuation (i.e., reduced activation to target stimuli) or neural broadening (i.e., increased activation to non-target stimuli). In this fMRI study, we assessed age differences in neural selectivity during first encoding, repeated encoding, and recognition, as well as the underlying pattern (broadening versus attenuation). We found lower neural selectivity in older compared to younger adults during all memory stages. Crucially, while reduced selectivity in older adults was due to neural broadening during first encoding, it was driven by neural attenuation during recognition, but revealed no clear pattern during repeated encoding. Our findings suggest that intrinsic differences between memory stages may interact with neural activity to manifest as either neural broadening or attenuation. Moreover, despite these differential patterns, neural selectivity was highly correlated across memory stages, indicating that one common mechanism may underly distinct expressions of age-related neural dedifferentiation.



**Keywords:** Episodic memory, Memory retrieval, Aging, Neural selectivity, Neural dedifferentiation, fMRI

## 1. Introduction

A hallmark of cognitive aging is the decline of episodic memory function (Nyberg et al., 2012). Neurobiological models have proposed that an age-related reduction in the fidelity of neuronal signal transmission underlies this cognitive decline (Li et al., 2001). In particular, it has been suggested that neural representations of information are less distinctive in older adults – a phenomenon termed age-related neural dedifferentiation (for reviews, see Koen & Rugg, 2019; Koen et al., 2020).

Supporting neuroscientific evidence of age-related neural dedifferentiation has been provided by studies that took advantage of the functional specializations of regions within the ventral visual cortex (VVC), including the parahippocampal cortex (PHC) and fusiform gyrus (FFG). In younger adults, these regions are known to respond with increased neural activity preferentially to visual house and face stimuli, respectively (Epstein & Kanwisher, 1998; Kanwisher et al., 1997). Age comparative studies have found that the selectivity with which these regions respond to their preferred stimuli is reduced in older adults compared to younger adults (Carp et al., 2011; D.C. Park et al., 2004; J. Park et al., 2012).

In order to unpack age differences in neural selectivity at the population level, J. Park and colleagues (2012) demonstrated that reduced category selectivity, defined as the difference in activation in response to a region's preferred and non-preferred stimulus type, may be driven by a few possible mechanisms. First, older adults may have a similar response to preferred stimuli (e.g., houses in the PHC) compared to younger adults, but have a heightened response to the non-preferred stimulus (e.g., faces in the PHC) compared with younger adults. This process is commonly termed neural broadening, a concept initially reported in animal models of age-related neural dedifferentiation (Leventhal et al., 2003; Schmolesky et al., 2000). Second, older adults may exhibit a reduced response to the preferred stimulus of a region, but have a similar response to the younger adults for the non-preferred stimulus, a pattern termed neural attenuation. Finally, older adults may exhibit a combination of both neural attenuation and neural broadening. The initial findings of J. Park and colleagues (2012) revealed that an age-related decline in face selectivity was driven by region-specific mechanisms, namely neural broadening in the FFG and neural attenuation in the extended face network. Thus, the authors identified age-related

processing deficits both within the VVC as well as in regions outside of the VVC. They concluded that age-related neural dedifferentiation may not be a static construct, but may depend on regional processing differences.

Since this seminal work by J. Park and colleagues (2012), only few studies have investigated these intricacies and those yielded mixed evidence: There has been evidence for neural broadening (Hill et al., 2021; Kobelt et al., 2021), neural attenuation (Koen et al., 2019), and a combination of both (Carp et al., 2011). Importantly, all of the studies quantified neural dedifferentiation based solely on data from memory encoding tasks. As such, it remains unknown how cognitive and neural processes that differ between memory encoding and other memory stages (e.g., repeated encoding or retrieval) influence manifestations of neural dedifferentiation.



Repeated encoding and retrieval have been shown to be reflected in altered neural activity in comparison to the first encoding of a given event. Repeated study of the same stimulus is widely known to improve memory performance (Glenberg et al., 1977; Henson, 2003). On the neural level, stimuli presented multiple times are often subject to repetition effects, particularly repetition suppression, in which the activation to subsequent presentations of a stimulus is reduced (Grill-Spector & Malach, 2001; Grill-Spector et al., 2006; Larsson et al., 2016). Repetition suppression has been demonstrated in both young and older adults (Goh et al., 2010; Sommer et al., 2021). Consequently, repeated encoding is likely to affect measures of neural selectivity and the underlying pattern of neural dedifferentiation.

Processing differences between memory encoding and retrieval have been attributed to a multitude of factors. First, these differences are most salient when considering the distinct goals of the two memory stages. The utility of memory encoding is to translate incoming information into a lasting neural code (Tulving, 1983), whereas the utility of memory retrieval is to use incoming cues to search for stored information (Simons & Spiers, 2003). Additionally, it has been argued that while memory encoding relies on directing attention externally in order to process novel stimuli (Chun & Turk-Browne, 2007), memory retrieval requires orienting attention to internal mnemonic representations (Wagner et al., 2005). Furthermore, it has been suggested that passive memory encoding is less cognitively demanding

than memory retrieval (Favila et al., 2020). Accordingly, differences in neural activity supporting encoding and retrieval have been observed in a broad range of studies (Cabeza & Nyberg, 2000; Daselaar et al., 2009; Huijbers et al., 2009, 2011; Kim et al., 2010). For example, Daselaar and colleagues (2009) revealed that the posterior midline region and ventral parietal cortex showed reduced activity during successful encoding, but increased activity during successful retrieval, indicating a so-called encoding/retrieval flip of activation. Thus, it is important to consider the possible repercussions of the inherent differences between encoding and retrieval on neural dedifferentiation.

Together, age-related declines in neural selectivity have been attributed to neural broadening, neural attenuation, and a combination of both. However, these patterns have only been investigated during memory encoding tasks. Hence, it is unknown whether age differences in neural selectivity express differentially across memory processing stages, such as repeated encoding and retrieval. Therefore, we sought to investigate whether age differences in neural selectivity, or the corresponding manifestations of neural dedifferentiation, vary between first encoding, repeated encoding, and recognition.



## 2. Materials and methods

Parts of these data were previously published in Kobelt et al. (2021). Relevant methods and analyses to the current study are restated here. Importantly, the present analyses assessed a smaller sample of participants as well as adjusted regions of interest as compared to Kobelt et al. (2021; details reported below). Furthermore, Kobelt et al. (2021) focused on the first encoding run, whereas we incorporate both the second encoding run and recognition into our analyses.

### *2.1. Participants*

Data were collected from a total of 76 healthy adults. The initial sample comprised 39 younger adults (18–27 years) and 37 older adults (64–76 years). Twelve participants were excluded due to too much motion in the scanner (1 young adult and 2 older adults), memory performance below chance level (2 young adults and 1 older adult) and category-selective clusters below threshold (2 young adults and 4

older adults; for the definition of category-selective clusters, see Section 2.6. below). The final sample consisted of 34 young adults ($M_{age}$ = 22.2, $SD_{age}$ = 2.6 years; 15 females, 19 males) and 30 older adults ($M_{age}$ = 70.8, $SD_{age}$ = 2.3 years; 17 females, 13 males). Participants were screened via telephone interview for mental and physical illness, metal implants, and current medications. Additionally, all older adults were screened using the Mini-Mental State Examination (Folstein et al., 1975) and all exceeded the threshold of 26 points. The study was approved by the ethics committee of the German Society for Psychological Research (DGPs) and written informed consent was obtained from each participant prior to testing.



*2.2. Stimuli*

Stimuli consisted of 300 gray-scale images from three different categories: 120 neutral faces (adapted from the FACES database; Ebner et al., 2010), 120 houses (some adapted from D.C. Park et al., 2004, and some obtained from the internet), and 60 scrambled images (30 faces and 30 houses, constructed from randomly selected face and house images) serving as control stimuli. Three additional stimuli (one face, one house, and one scrambled image) were selected to serve as target images for the encoding target-detection task. Subjects were familiarized with these target stimuli prior to the task. Face and house stimuli were randomly divided into two sets of 120 images (60 faces and 60 houses). One stimulus set was presented during both encoding and recognition (old images) and the other stimulus set was presented only during recognition (new images). The stimulus sets were defined once and were used for all subjects.

*2.3. Paradigm*

The following work was completed within a larger overall study spanning two days of data collection. This study focuses only on the face-house task, which consisted of an incidental encoding phase and a surprise recognition test, both performed inside the fMRI scanner on the same day with a delay of approximately 30 minutes (see Figure 1). The encoding phase consisted of two identical runs each

comprised of nine stimulus blocks. For all blocks, each trial was presented for 1200 ms with a jittered fixation cross shown between trials ranging from 500 to 8000 ms. Stimuli were randomly distributed into blocks, such that each block had 20 images from the same category (faces, houses, or scrambled) plus the category's corresponding target stimulus. The order of the blocks was alternating and counterbalanced across participants, either starting with a face or house block. Stimulus order was pseudo-randomized with the restriction that the target image was presented neither in the first four nor last four trials of a block. Due to a technical issue, the same stimulus order was used for all participants starting with a face block and in 36 participants starting with a house block. In order to keep the subjects attentive to the stimuli, subjects were asked to perform a target-detection task in which they pressed a button when one of the three target images was presented. These target trials were excluded from further analyses. The second encoding run was presented identically to the first run; thus, subjects were exposed to each image twice during encoding. In total, the encoding phase lasted 22 minutes.



Following encoding, subjects remained briefly in the scanner while structural scans were collected (see below for details) and then had a break outside of the scanner while they received instructions for the surprise recognition test. The recognition test was divided in two runs, in each of which three face and three house blocks were presented in alternating order. Each block consisted of 20 old images (seen during encoding) and 20 new images from the same stimulus category. For each trial, subjects were asked whether the image was old or new. Each trial was presented for 1200 ms and followed by a gray screen for 3000 ms, in which subjects had the opportunity to respond via button press. Jittered fixation crosses separated the trials ranging from 500-8000 ms. Trial order was pseudo-randomized to ensure that no more than three old or new images were presented successively. Due to a technical issue, the same stimulus order was used for 13 subjects starting with a face block and 14 subjects starting with a house block. In total, the recognition task lasted 26 minutes.

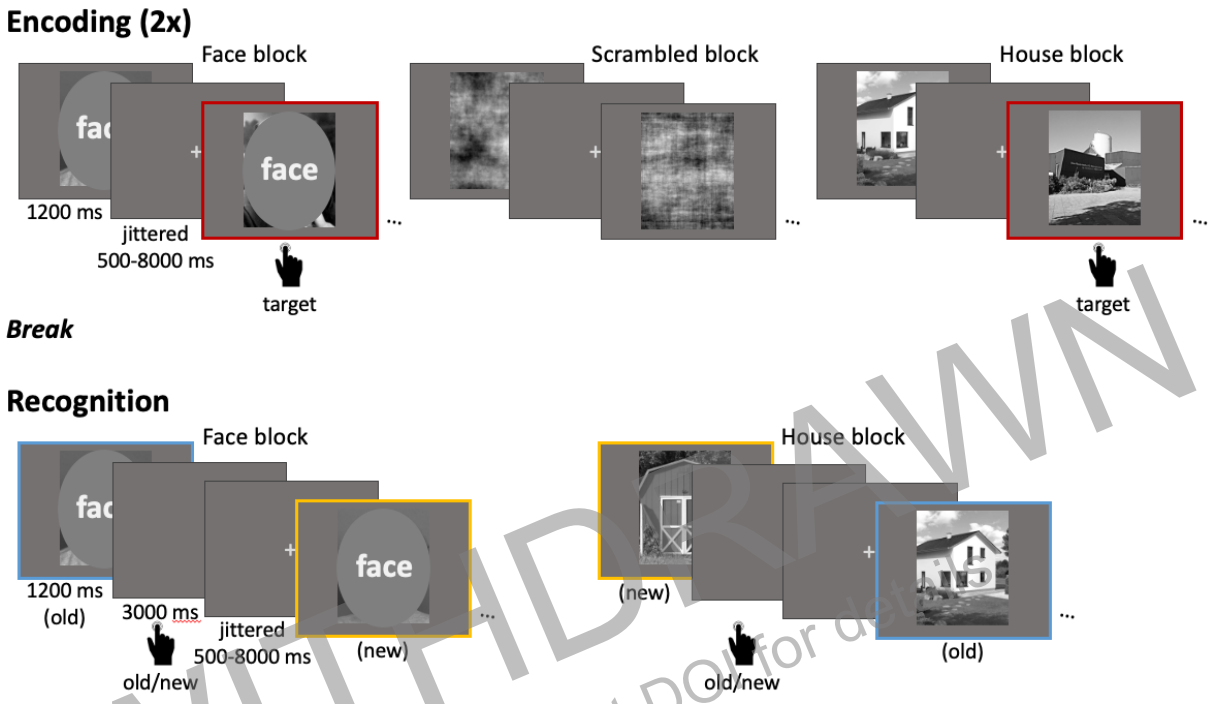




Figure 1. Face-house task. The fMRI paradigm consisted of an incidental encoding phase (top) and a surprise recognition test (bottom). During encoding, two identical runs of house, face, and scrambled baseline images were presented in a block design. Each encoding run was comprised of nine stimulus blocks (three alternating blocks from each stimulus category) with 21 trials per block. Subjects were instructed to complete a target-detection task in which they pressed a button when one of three pre-learned stimuli (outlined in red) was presented. Following a short break, subjects completed a surprise recognition memory test in which they indicated via button press whether each image was old (previously seen during encoding; outlined in blue) or new (not seen before; outlined in yellow). The recognition phase was divided into six alternating face and house blocks with 40 trials (20 old and 20 new) per block. Figure adapted from Kobelt et al., 2021.

*2.4. fMRI data acquisition and preprocessing*

Brain imaging was conducted on a Siemens Magnetom TrioTim 3T MRI scanner with a 32-channel head-coil. A T1-weighted (T1w) magnetization prepared rapid acquisition gradient echo (MPRAGE) pulse sequence image (voxel size = $1 \times 1 \times 1$ mm$^3$; TR = 2.5 ms; TE = 4.77 ms; flip angle = 7°; TI = 1.1 ms)

was collected following the encoding phase. Functional blood oxygenation level dependent (BOLD) scans were acquired using an echo planar imaging (EPI) sequence in two runs in both encoding and recognition phases. Encoding runs consisted of 270 volumes each and recognition runs consisted of 372 volumes each (voxel size = $3 \times 3 \times 3.3$ mm$^3$; TR = 2 s; TE = 30 ms). Additionally, turbo spin-echo proton density images (PDs), diffusion tensor images (DTIs), and fluid attenuation inversion recovery images (FLAIRs) were acquired, but not included in the following analyses. Experimental stimuli were displayed on a projector using the Psychtoolbox (Psychophysics Toolbox) for MATLAB (Mathworks Inc., Natick, MA), which subjects were able to view via a mirror mounted on the head-coil.

Data preprocessing was performed using *fMRIPrep* (version 1.4.0; Esteban et al., 2019) using the standard settings. The T1w image was corrected for intensity non-uniformity and used as the T1w-reference image for the rest of the workflow. This reference image was then skull-stripped and spatially-normalized to the *ICBM 152 Nonlinear Asymmetrical template version 2009c* using nonlinear registration. Functional scans were corrected for motion and slice time and finally co-registered to the normalized T1w reference image. Preprocessed functional data were spatially smoothed with a 4 mm full width half maximum kernel.



### *2.5. Behavioral data analyses*

Behavioral data were analyzed using custom MATLAB scripts. As previously reported in Kobelt et al. (2021), recognition memory performance (*Pr*) was calculated as the difference between the hit rate (proportion of correctly identified old items) and the false alarm rate (proportion of new items incorrectly identified as old items). Age differences in memory performance were assessed with an independent-samples *t*-test. Dependent-samples *t*-tests were conducted to determine whether memory performance differed between face and house stimuli and whether memory performance exceeded chance level.

*2.6. Defining category-selective regions of interest*

In order to identify subject-specific regions of interest (ROIs) preferentially active during face and house processing, face and house encoding blocks were contrasted to scrambled blocks for each subject in a block GLM design as in Kobelt et al. (2021). Using a cluster-based approach, adjacent voxels exceeding an uncorrected threshold of $p < 0.005$ were defined as a cluster. For each subject, the cluster with the highest average *t*-value for faces compared to scrambled images was designated as the face-selective ROI and the cluster with the highest average *t*-value for houses compared to scrambled images was designated as the house-selective ROI. To limit the search space to category-selective regions (see D.C. Park et al., 2004), only voxels within the bilateral VVC as defined by the automated anatomical labeling (AAL) atlas were considered. The VVC mask included the fusiform gyrus, parahippocampal gyrus, and inferior temporal gyrus. Furthermore, as an additional step to Kobelt et al. (2021), voxels lost to signal drop-out during recognition were removed from the clusters in order to keep face and house clusters congruent within subjects across the subsequent analyses on both encoding and recognition data (Olman et al., 2009). Only subjects with at least 10 voxels in both their face and house clusters were included in the analysis (leading to the exclusion of two young adults and four older adults, as stated in Section 2.1.; $M_{\text{FaceVoxels}} = 80$, $\text{Range}_{\text{FaceVoxels}} = 13–278$; $M_{\text{HouseVoxels}} = 78$, $\text{Range}_{\text{HouseVoxels}} = 10–264$).

Additionally, we explored the possibility that category-selective regions outside of the VVC may be susceptible to age-related neural dedifferentiation (see Carp et al., 2011; J. Park et al., 2012). Therefore, we identified all face and house clusters in the whole brain in which adjacent voxels exceeded an uncorrected threshold of $p < 0.005$ during the encoding contrast. We visually inspected the sum of the instances in which a given voxel appeared in either a face or house cluster across all subjects (see Figure 2). This revealed considerable agreement across subjects for high category selectivity in both the VVC and regions of the occipital cortex. Correspondingly, we added an occipital mask and defined an additional face- and house-selective ROI for each subject which had the highest average *t*-value for faces or houses compared to scrambled images, respectively. Voxels lost to signal drop-out during recognition were subsequently removed from the clusters. An additional four subjects (three young adults and one

older adult) were excluded from this analysis because their clusters were smaller than 10 voxels, however, since this analysis was not the main focus of the study, these subjects were not excluded from any other analyses.

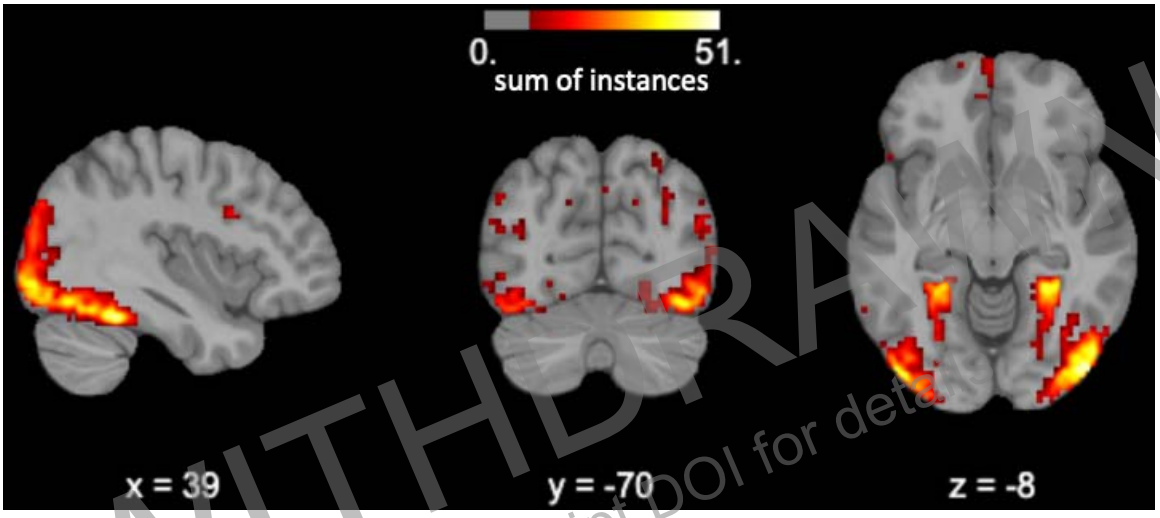




Figure 2. Sum of instances in which a given voxel was included in either a face or house cluster across all subjects (i.e., demonstrated high neural selectivity). Only voxels that appeared in at least 10 clusters are displayed. Upon visual inspection of this figure, we decided to assess the occipital cortex in addition to the VVC due to the high neural selectivity across subjects in both of these regions.

*2.7. Assessing neural selectivity and underlying patterns of neural dedifferentiation*

In order to assess mean BOLD activation for each subject, two block GLMs were constructed, one model for encoding and one model for recognition. For each encoding run, three separate regressors modeled face, house, and scrambled blocks and an additional six regressors modeled motion confounds. For each recognition run, two separate regressors modeled face and house blocks with the additional six motion regressors. The resulting voxel-wise beta maps were then averaged separately for faces and houses within the face and house clusters. The mean beta responses for the two recognition runs were collapsed. Mean beta for preferred stimuli (e.g., faces in the face cluster) and non-preferred stimuli (e.g., houses in the face cluster) were then averaged across stimuli, resulting in an average beta response to preferred and non-preferred stimuli respectively for each participant at the first and second encoding runs as well as at

recognition. Selectivity scores were computed by subtracting the response to non-preferred stimuli from the response to preferred stimuli within each subject.

A two-way mixed factorial analysis of variance (ANOVA) was then used to analyze mean beta values during each memory stage separately with the between factor "age group" (older vs. younger) and the within-factor "preferredness" (preferred vs. non-preferred). Significant interactions were subsequently investigated using independent samples *t*-tests with Bonferroni-corrected *p* values. Zero-order correlations were computed across participants as well as within groups using Pearson's *r* in order to assess the relationship of neural selectivity across memory stages.



*2.8. Analyzing repetition effects*

Since stimuli were presented twice during the encoding phase, we suspected repetition suppression may have influenced mean beta values during the repeated encoding run. Therefore, we examined whether there were general activation differences between the two encoding runs. Repetition suppression has been shown to primarily affect regions in response to their preferred stimulus category (Barron et al., 2016). Thus, a 2 (age group) $\times$ 2 (encoding run) mixed factorial ANOVA was computed on the mean beta values of the preferred stimuli in order to assess age differences in repetition effects.

*2.9. Determining the relationship between neural selectivity and memory performance using partial least squares correlation (PLSC)*

Finally, we implemented a PLSC analysis in order to understand the common impact of neural selectivity across the different memory stages on memory performance as well as to delineate the weights of the individual contributions of neural selectivity at each memory stage (Keresztes et al., 2017; Kobelt et al., 2021; Krishnan et al., 2011; McIntosh et al., 1996). First, a between-subject correlation matrix was calculated between an *n*-element vector containing memory performance (*Pr*) and a $n \times 3$ matrix of selectivity scores from the three memory stages. This correlation matrix was then decomposed using

singular value decomposition (SVD), producing a single estimate latent variable (LV) that optimally represents the association between neural selectivity and memory performance and depicts the memory stages showing the strongest relationship to memory performance. The significance of the LV was tested using 10,000 permutation tests of the singular value corresponding to the LV. Robustness estimates were measured using a bootstrapping procedure across 10,000 resamples of the data. Bootstrap ratios (BSRs; normalized robustness estimates) were then calculated by dividing the neural selectivity weights from the SVD by the standard errors of their robustness estimates. Similar to z values, BSRs are considered reliably robust with values above or below ±1.96. A selectivity-memory score was calculated for each subject by multiplying the neural selectivity weights by the empirical selectivity scores. This selectivity-memory score reflects the comprehensive impact of neural selectivity on memory performance within each subject.



## 3. Results

### *3.1. Behavioral results*

We repeated *t*-tests as in Kobelt and colleagues (2021) in order to reexamine possible age differences in recognition memory performance (i.e., *Pr* = hit rate – false alarm rate) in the current sample of participants, which slightly differed from that in Kobelt et al. (2021). Older adults demonstrated a strong response bias, responding "old" more often than young adults to both old stimuli ($M_{young}$ = 0.50, $SD_{young}$ = 0.14, $M_{older}$ = 0.62, $SD_{older}$ = 0.12, $t(62) = -3.67$, $p < 0.001$) and new stimuli ($M_{young}$ = 0.26, $SD_{young}$ = 0.11, $M_{older}$ = 0.42, $SD_{older}$ = 0.13, $t(62) = -5.35$, $p < 0.001$). We corroborated that memory performance did not differ between age groups ($M_{young}$ = 0.24, $SD_{young}$ = 0.12, $M_{older}$ = 0.20, $SD_{older}$ = 0.12, $t(62) = 1.45$, $p$ = 0.15) and that memory performance exceeded chance in both young ($t(33) = 11.93$, $p < 0.001$) and older adults ($t(29) = 9.02$, $p < 0.001$). Furthermore, memory performance did not differ between face and house stimuli in either young ($t(33) = -0.88$, $p = 0.39$) or older adults ($t(29) = -1.61$, $p = 0.12$).

*3.2. Age differences in neural selectivity*

3.2.1. First encoding

The following analysis of the first encoding run was reported in Kobelt et al. (2021). Due to differences in the participant sample and voxels included in the face and house clusters, we reanalyzed the data here to ensure the results are corroborated. During the first encoding run, results of a 2 (age group) × 2 (preferredness) mixed factorial ANOVA on mean activation in the VVC revealed a main effect of preferredness demonstrating category selectivity ($F(1,62) = 709.64$, $p < 0.001$), but no main effect of age ($F(1,62) = 1.02$, $p = 0.32$). Furthermore, we found an interaction between age group and preferredness ($F(1,62) = 13.85$, $p < 0.001$), indicating greater neural selectivity in young adults ($M_{young} = 1.48$, $SD_{young} = 0.41$) than in older adults ($M_{older} = 1.12$, $SD_{older} = 0.37$; see Figure 3A left). Pairwise comparisons revealed no significant age differences in the mean beta response to preferred stimuli ($t(62) = 0.12$, $p = 0.91$), but a trending age difference in the mean beta response to non-preferred stimuli ($t(62) = 1.86$, $p = 0.067$) with older adults ($M = 0.70$, $SD = 0.67$) demonstrating greater activation to non-preferred stimuli than younger adults ($M = 0.31$, $SD = 0.96$) in line with the neural broadening hypothesis (see Figure 3B left). Thus, these results are in agreement with the findings of Kobelt et al. (2021).

In the occipital clusters, results of a 2 (age group) × 2 (preferredness) mixed factorial ANOVA on mean activation revealed a main effect of preferredness demonstrating category selectivity ($F(1,58) = 730.91$, $p < 0.001$), but no main effect of age ($F(1,58) = 0.36$, $p = 0.55$). Furthermore, we did not find an interaction between age group and preferredness ($F(1,58) = 0$, $p = 0.99$), indicating no age differences in neural selectivity between young adults ($M_{young} = 1.10$, $SD_{young} = 0.30$) and older adults ($M_{older} = 1.10$, $SD_{older} = 0.33$).

3.2.2. Repeated encoding

During the repeated encoding run, results of a 2 (age group) × 2 (preferredness) mixed factorial ANOVA on mean activation in the VVC revealed a main effect of preferredness demonstrating category selectivity

($F(1,62) = 611.57$, $p < 0.001$), but no main effect of age ($F(1,62) = 0.003$, $p = 0.96$). We found an interaction between age group and preferredness ($F(1,62) = 7.14$, $p = 0.01$), indicating greater neural selectivity in young adults ($M_{young} = 1.39$, $SD_{young} = 0.40$) than in older adults ($M_{older} = 1.12$, $SD_{older} = 0.41$; see Figure 3A middle). Pairwise comparisons revealed no significant age differences in the mean beta response to preferred stimuli ($t(62) = -0.62$, $p = 0.54$) or in the mean beta response to non-preferred stimuli ($t(62) = 0.53$, $p = 0.60$; see Figure 3B middle). Therefore, despite the observed age-related decline in neural selectivity during repeated encoding, there was no clear evidence for neural broadening or attenuation.

In the occipital clusters, results of a 2 (age group) × 2 (preferredness) mixed factorial ANOVA on mean activation revealed a main effect of preferredness demonstrating category selectivity ($F(1,58) = 450.03$, $p < 0.001$), but no main effect of age ($F(1,58) = 0.84$, $p = 0.36$). Furthermore, we did not find an interaction between age group and preferredness ($F(1,58) = 0.24$, $p = 0.63$), indicating no age differences in neural selectivity between young adults ($M_{young} = 1.09$, $SD_{young} = 0.40$) and older adults ($M_{older} = 1.04$, $SD_{older} = 0.37$).



### 3.2.3. Recognition

During recognition, results of a 2 (age group) × 2 (preferredness) mixed factorial ANOVA on mean activation in the VVC revealed a main effect of preferredness demonstrating category selectivity ($F(1,62) = 171.20$, $p < 0.001$), but no main effect of age ($F(1,62) = 2.92$, $p = 0.09$). We found an interaction between age group and preferredness ($F(1,62) = 12.87$, $p < 0.001$), indicating greater neural selectivity in young adults ($M_{young} = 0.82$, $SD_{young} = 0.43$) than in older adults ($M_{older} = 0.46$, $SD_{older} = 0.33$; see Figure 3A right). Pairwise comparisons revealed a significant age difference in the mean beta response to preferred stimuli ($t(62) = -2.23$, $p = 0.029$) with older adults ($M = 1.59$, $SD = 1.00$) demonstrating lower activation to preferred stimuli than younger adults ($M = 2.21$, $SD = 1.20$; see Figure 3B right). No age

differences were found in the mean beta response to non-preferred stimuli ($t(62) = -1.07$, $p = 0.29$). The pattern exhibited at recognition is in line with the neural attenuation hypothesis.

In the occipital clusters, results of a 2 (age group) × 2 (preferredness) mixed factorial ANOVA on mean activation revealed a main effect of preferredness demonstrating category selectivity ($F(1,58) = 186.35$, $p < 0.001$), but no main effect of age ($F(1,58) = 0.05$, $p = 0.82$). Furthermore, we did not find an interaction between age group and preferredness ($F(1,58) = 0.03$, $p = 0.87$), indicating no age differences in neural selectivity between young adults ($M_{young} = 0.48$, $SD_{young} = 0.27$) and older adults ($M_{older} = 0.47$, $SD_{older} = 0.27$). Due to the absence of age differences in neural selectivity in the occipital cortex in all three memory stages, further analyses followed up only on the VVC.



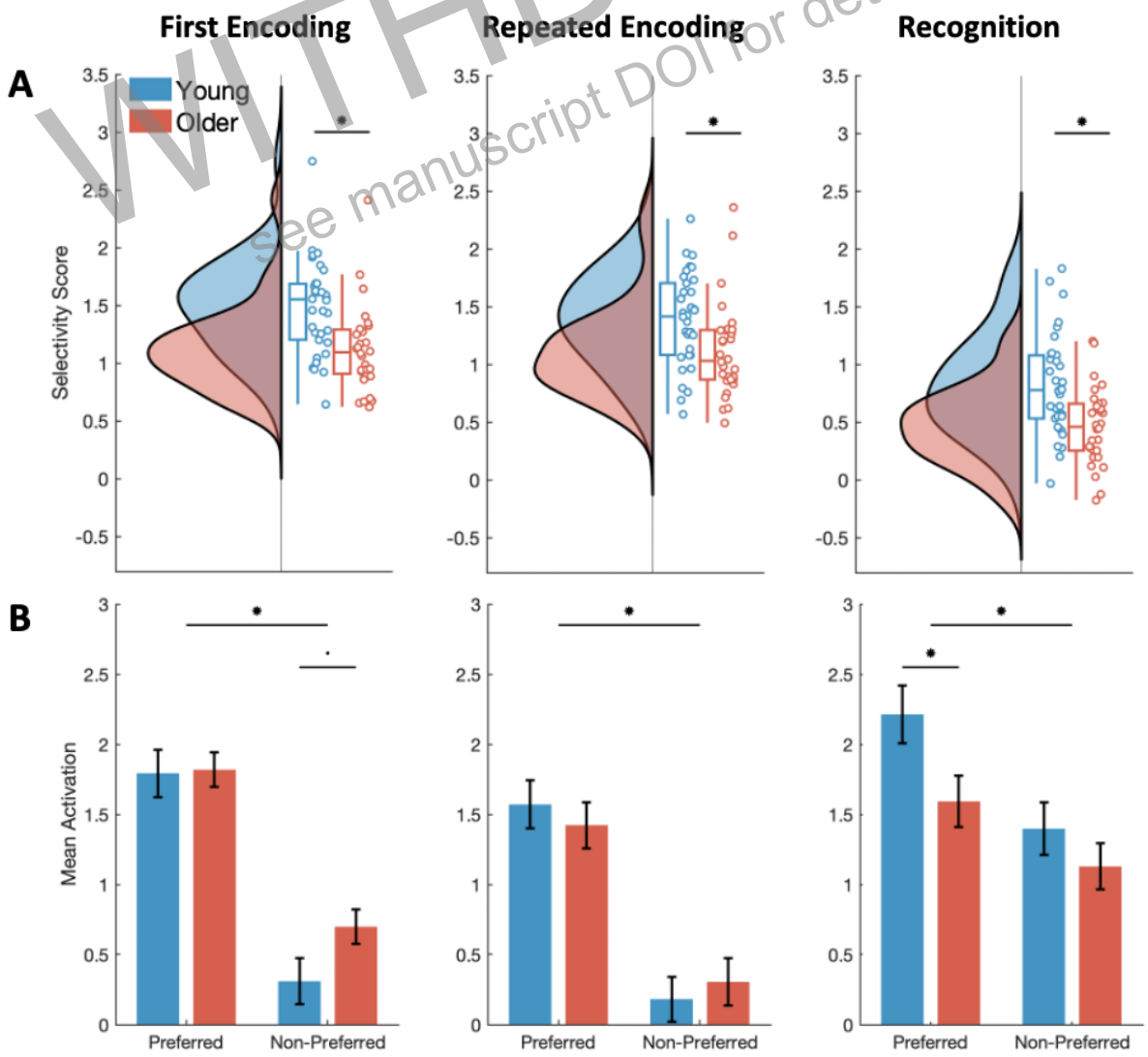

Figure 3. Age differences in neural selectivity (A) and underlying activation patterns (B). Young adults (blue) demonstrated greater neural selectivity than older adults (red) during first encoding (left), repeated encoding (middle), and recognition (right). Group distributions are displayed in unmirrored violin plots and boxplots with medians and 95% confidence intervals with whiskers representing the 2nd and 98th percentiles (Allen et al., 2019). Selectivity scores of individual participants are reflected in jittered data points. Error bars in the bar charts denote standard error of the mean. Significant group differences ($p < 0.05$) are indicated by asterisks and trend group differences are indicated by periods.



*3.3. Stability of interindividual differences in neural selectivity across memory stages*

We sought to elucidate whether interindividual differences in neural selectivity remained stable across the memory stages. Thus, Pearson correlations were computed to investigate how measures of neural selectivity were related within individuals across memory stages. Neural selectivity was positively correlated between first encoding and repeated encoding ($r = 0.79$, $p < 0.001$, $r_{young} = 0.87$, $p_{young} < 0.001$, $r_{older} = 0.64$, $p_{older} < 0.001$), first encoding and recognition ($r = 0.84$, $p < 0.001$, $r_{young} = 0.86$, $p_{young} < 0.001$, $r_{older} = 0.71$, $p_{older} < 0.001$), and repeated encoding and recognition ($r = 0.65$, $p < 0.001$, $r_{young} = 0.77$, $p_{young} < 0.001$, $r_{older} = 0.36$, $p_{older} = 0.05$). These findings indicate that interindividual differences in neural selectivity were strongly related across memory stages (see Figure 4).

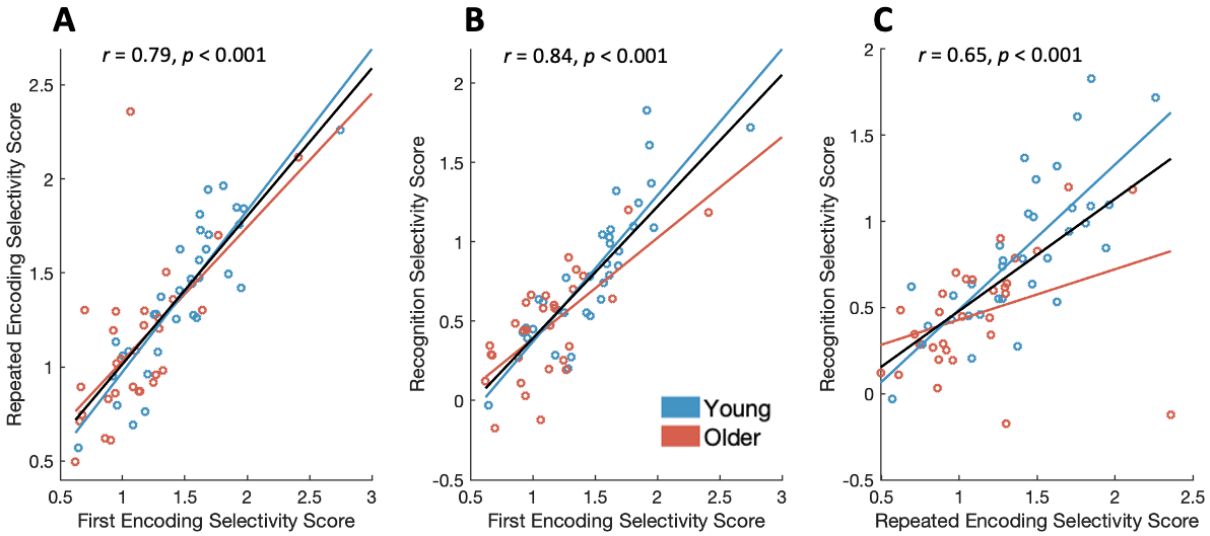

Figure 4. Neural selectivity was strongly correlated between first encoding and repeated encoding (A), first encoding and recognition (B), and repeated encoding and recognition (C). Young adults shown in blue and older adults in red. Black lines and corresponding Pearson correlation values reflect correlations for both groups combined. Note: axis scale varies between plots.



*3.4. Repetition effects between first and repeated encoding*

A 2 (age group) × 2 (encoding run) mixed factorial ANOVA on preferred mean beta values revealed no main effect of age group ($F(1,62) = 0.13$, $p = 0.72$), but a main effect of encoding run ($F(1,62) = 4.27$, $p = 0.04$). No interaction was found between age group and run ($F(1,62) = 0.34$, $p = 0.56$). Mean comparisons show that the repeated encoding run ($M = 1.50$, $SD = 0.95$) demonstrated lower preferred activation than the first encoding run ($M = 1.80$, $SD = 0.85$). In sum, we found evidence for repetition suppression between the first and repeated encoding runs, but no evidence for age differences therein.

*3.5. Relation to memory performance*

In order to disentangle the relative contribution of neural selectivity during each memory stage to memory performance, we performed a PLSC analysis to extract a single composite score that depicts individual differences in neural selectivity. This analysis identified a marginally reliable latent variable (LV; $p = 0.051$) that optimally represents the relationship between neural selectivity and memory ($r = 0.25$; see Figure 5). Bootstrap ratios (BSRs) revealed higher neural selectivity during first encoding (BSR = 2.49) and recognition (BSR = 2.19) as the two stable components of the LV explaining the largest amount of information common to memory performance and the multivariate pattern of neural selectivity.

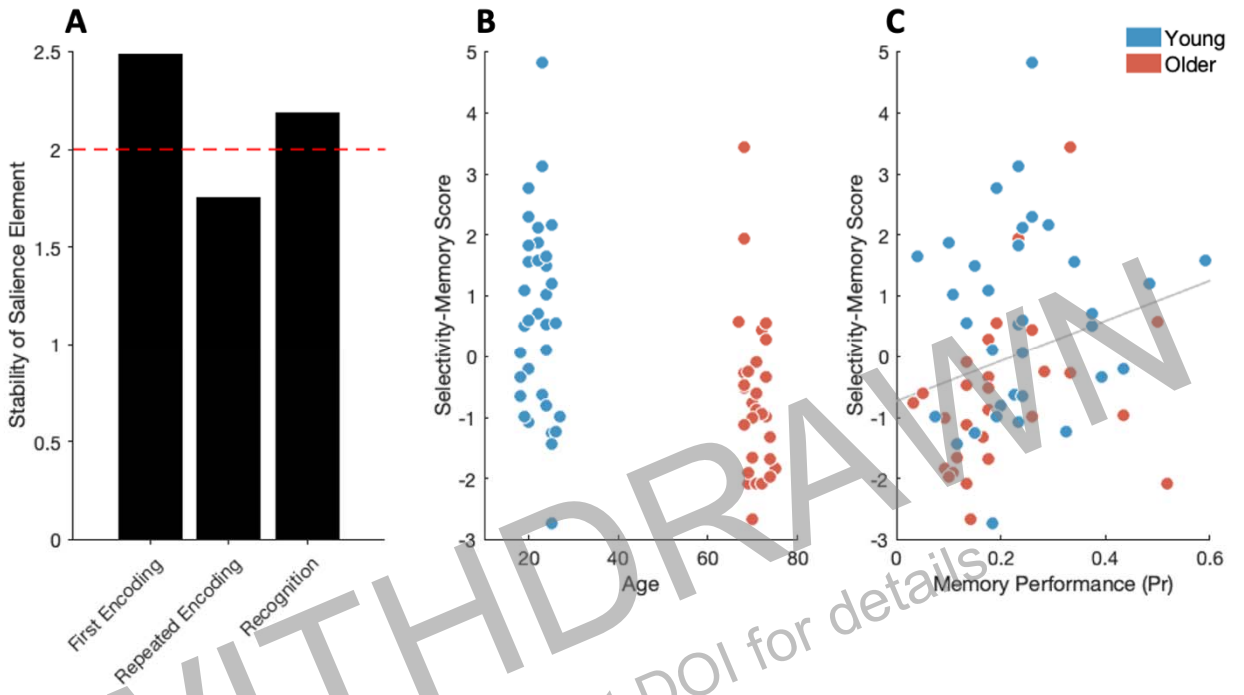




Figure 5. Association between neural selectivity and memory identified by PLSC. Bootstrap ratios of the LV profile show first encoding and recognition as the stable components with the robustness cutoff indicated by the dashed red line (A). Selectivity-memory scores were lower in older adults compared with younger adults (B) and positively correlated with memory performance (C). Blue denotes young adults and red denotes older adults.

## 4. Discussion

Evidence for age-related neural dedifferentiation has been established as a reduction in the distinctiveness of categorical visual processing in the VVC in older adults (Carp et al., 2011; Kobelt et al., 2021; Koen & Rugg, 2019; D.C. Park et al., 2004; J. Park et al., 2012). Studies often explore these differences as a possible mechanism for age-related memory decline (Kobelt et al., 2021; Koen et al., 2019, 2020). Importantly, age differences in neural selectivity are typically investigated using data collected during passive viewing or encoding tasks despite the fact that age-related neural deficits have also been expressed during retrieval processing (Dulas & Duarte, 2012; Johnson et al., 2015; St-Laurent et al., 2014). Therefore, we expanded the scope of this research line by assessing measures of age-related neural

dedifferentiation across different memory processing stages (i.e., initial encoding, repeated encoding, and recognition) in a group of young and older adults.

We replicated the results of previous studies by demonstrating that older adults exhibit reduced neural selectivity in the VVC during encoding compared to younger adults (Kobelt et al., 2021; D.C. Park et al., 2004), and expanded the literature by showing that this age deficit in neural selectivity is also salient during repeated encoding. Furthermore, we found evidence for reduced neural selectivity in older adults during recognition, supporting findings that age-related neural dedifferentiation also manifests during memory retrieval processing (Dulas & Duarte, 2012; Johnson et al., 2015; St-Laurent et al., 2014). In addition, a multivariate measure of neural selectivity showed a significant relationship with memory performance, in line with the idea that neural dedifferentiation is associated with poorer episodic memory independent of age (Kobelt et al., 2021; Koen et al., 2019; for review, see Koen et al., 2020). Our findings support the idea that high fidelity neural representations are crucial in facilitating memory encoding and retrieval processes (Koen et al., 2020).



Importantly, age differences in neural selectivity can manifest as one of three possible underlying patterns: neural broadening, neural attenuation, or both (J. Park et al., 2012). The underlying pattern can be determined by examining the average BOLD activation in response to preferred and non-preferred stimuli. Using this method, we have previously determined that the pattern driving age differences in neural selectivity during first encoding resembled neural broadening (Kobelt et al., 2021). This finding is also in line with several other studies which established neural broadening during encoding (Hill et al., 2021; J. Park et al., 2012; but see Koen et al., 2019). Expanding on the findings reported by Kobelt and colleagues (2021), we investigated neural broadening and attenuation during subsequent memory stages, namely repeated encoding and recognition. Interestingly, although we observed age differences in neural selectivity during repeated encoding, the underlying pattern did not clearly indicate either broadening or attenuation. During recognition, we found evidence promoting neural attenuation as the pattern driving age differences in neural selectivity. Hence, our results provide rare evidence for differential mechanisms

underlying age-related neural dedifferentiation across memory processing stages (i.e., neural broadening during encoding and neural attenuation during retrieval).

Considering that neural selectivity was assessed in the same region at all three timepoints, the differences in the observed pattern likely arose from processing differences between the memory stages. Comparing first and repeated encoding, we found evidence of repetition suppression, which may explain these differential observed patterns. We did not find age differences in the repetition effect, but a similar overall reduction in neural activation during repeated encoding in both age groups. Interestingly, a previous study has reported that older adults exhibited broader repetition effects than younger adults (Goh et al., 2010). In that study, the authors assessed age differences in the repetition effect for pairs of identical faces presented one after another as well as pairs of faces in which the second face had been slightly morphed. They found that younger adults demonstrated the repetition effect only for identical faces, but older adults demonstrated the repetition effect for both identical and morphed faces, indicating an age-related reduction in neural selectivity in line with the neural broadening hypothesis. Note that Goh and colleagues (2010) evaluated the repetition effect at a single trial level, whereas we utilized a block design. It thus remains an intriguing possibility that age differences in repetition suppression effects can themselves serve as neural markers for age differences in neural differentiation (see Sommer et al., 2021).

We further identified differences in the pattern of activation between first encoding and recognition. Differences between encoding and retrieval have been previously observed in mean activity (Cabeza & Nyberg, 2000; Daselaar et al., 2009), functional connectivity (Huijbers et al., 2011; Simons & Spiers, 2003), and object representations (Long & Kuhl, 2021). These discrepancies may reflect differences in the utility of the tasks (Simons & Spiers, 2003) or in differences in orienting attention between the memory stages (Chun & Turk-Browne, 2007; Wagner et al., 2005), which may be represented in neural activity leading to differential manifestations of neural dedifferentiation.

Another explanation for the observed differences in activation patterns between encoding and recognition may be differences in task demands. It has been suggested that task demands may modulate expressions of age-related neural dedifferentiation (Koen & Rugg, 2019) and that memory retrieval

imposes greater task demands than passive memory encoding (Favila et al., 2020). In this study, the task demands were implicitly varied, with a passive encoding task employing few cognitive resources, but an active recognition task requiring higher cognitive resources. This subtle modulation of cognitive engagement may have interacted with the neural representations of categorical information leading to differences in activation. Age differences in neural distinctiveness have previously been shown to be highly susceptible to variation in cognitive load (Carp et al., 2010). Carp and colleagues (2010) provided evidence for greater neural differentiation in older adults compared to younger adults under low cognitive load, but greater neural differentiation in younger adults compared to older adults under high cognitive load. These findings demonstrate the malleability of measures of neural dedifferentiation under changing task demands, which may offer an additional explanation for the differences we observe between encoding and recognition.



It is an open question whether neural broadening and neural attenuation are manifestations of distinct underlying mechanisms or different manifestations of a singular underlying mechanism. We found that reduced neural selectivity in older adults was driven by neural broadening during first encoding, but by neural attenuation during recognition. Furthermore, neural selectivity across all memory stages was highly correlated, despite exhibiting differential activation patterns. These findings suggest that the participants who demonstrated greater neural broadening during encoding also demonstrated greater neural attenuation during recognition, indicating that these distinct manifestations are likely related. It is thus possible that a “common cause” (see Lindenberger & Baltes, 1994), underlies both neural broadening and neural attenuation. One plausible “common cause” contributing to the expression of age-related neural dedifferentiation are age differences in neurotransmitter availability that act globally on neural activation. Early research using simulations of neurotransmitter systems pointed to an age-related decline in the integrity of dopaminergic pathways as the potential mechanism leading to cognitive decline (Li & Lindenberger, 1999; Li et al., 2001). Although the role of reduced dopaminergic activity in memory decline has been substantiated (Abdulrahman et al., 2017; Bäckman et al., 2006, 2010; Rieckmann et al., 2018), studies exploring the relationship between dopamine and dedifferentiation of

functional brain activation reveal mixed results, with some findings indicating a dopamine-related reduction in neural specificity (Abdulrahman et al., 2017) and others suggesting no relationship (Rieckmann et al., 2018). More recently, age differences in gamma-aminobutyric acid (GABA) have come into the research focus. Reduced GABA levels have been associated with lower neural distinctiveness in visual (Chamberlain et al., 2021) and auditory (Lalwani et al., 2019) regions. Of particular relevance to our study, Chamberlain and colleagues (2021) found a decrease in neural distinctiveness in the VVC in response to visual face and house stimuli, which coincided with a decrease in GABA concentration. Thus, a reduction in neurotransmitter availability (e.g., dopamine and GABA) is a likely candidate for a common cause of age-related neural dedifferentiation.

As an exploratory analysis, we also investigated age differences in neural selectivity in the occipital cortex. However, we found no evidence for an age-related decline in neural distinctiveness in this region, indicating that both young and older adults demonstrated high neural selectivity in the occipital cortex. This finding suggests that age differences in neural selectivity may influence higher-order perceptual networks and not lower-level perceptual processing regions. Furthermore, this finding is in line with a recent study by Koen and colleagues (2019), which also identified evidence for age-related neural dedifferentiation in ventral visual regions, but not in occipital regions. Interestingly, several studies have found age differences in neural distinctiveness in brain regions outside of the VVC (Carp et al., 2010, 2011; Kobelt et al., 2021; J. Park et al., 2012), however, they differ from the present analysis in that they did not identify subject-specific regions of interest and, with the exception of J. Park and colleagues (2012), they used a multivariate approach to assess neural distinctiveness. Note that the Kobelt et al. (2021) finding of age differences in neural distinctiveness in the occipital cortex was only identified by their item-level analysis, not in their category-level analysis, indicating that aging may impact fine-grained neural representations in the occipital cortex, which our analysis does not detect. Future research should seek a better understanding of how age-related neural dedifferentiation manifests across different brain regions.

Collectively, our findings demonstrate age-related declines in neural selectivity during first encoding, repeated encoding, and recognition, supporting the idea that aging affects neural representations of categorical information across memory stages. The underlying patterns of functional activation revealed that age differences in neural selectivity were driven by neural broadening during encoding, but neural attenuation during recognition, indicating how memory stages and possibly related task demands interact with neural activation. Importantly, neural selectivity was strongly associated across memory stages, suggesting that neural broadening and attenuation are unique manifestations of a common mechanism responsible for dedifferentiated neural responses in older age.



**Disclosure**

The authors declare no competing financial interests.

**Author statement**

**Claire Pauley:** Formal analysis, Software, Writing - Original Draft. **Verena R. Sommer:** Conceptualization, Investigation, Writing – Review & Editing. **Malte Kobelt:** Software, Writing – Review & Editing. **Attila Keresztes:** Investigation, Writing – Review & Editing. **Markus Werkle-Bergner:** Conceptualization, Writing – Review & Editing. **Myriam C. Sander:** Conceptualization, Project administration, Supervision, Writing – Review & Editing.

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