Neurobiology of Aging 60 (2017) 20–33

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

Neural correlates of durable memories across the adult lifespan: brain activity at encoding and retrieval

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ARTICLE INFO

Article history:
Received 27 February 2017
Received in revised form 14 August 2017
Accepted 18 August 2017
Available online 30 August 2017

Keywords:
Aging
fMRI
Encoding
Episodic memory
Retrieval
Durable memory

ABSTRACT

Age-related effects on brain activity during encoding and retrieval of episodic memories are well documented. However, research typically tests memory only once, shortly after encoding. Retaining information over extended periods is critical, and there are reasons to expect age-related effects on the neural correlates of durable memories. Here, we tested whether age was associated with the activity elicited by durable memories. One hundred forty-three participants (22–78 years) underwent an episodic memory experiment where item-context relationships were encoded and tested twice. Participants were scanned during encoding and the first test. Memories retained after 90 minutes but later forgotten were classified as transient, whereas memories retained after 5 weeks were classified as durable. Durable memories were associated with greater encoding activity in inferior lateral parietal and posteromedial regions and greater retrieval activity in frontal and insular regions. Older adults exhibited lower posteromedial activity during encoding and higher frontal activity during retrieval, possibly reflecting greater involvement of control processes. This demonstrates that long-lasting memories are supported by specific patterns of cortical activity that are related to age.

1. Introduction

Despite the extensive literature on neurocognitive aging of memory, no study has focused on the brain correlates of long-lasting memories. It is well known that some events can be remembered after extended periods of time, whereas other memories quickly fade or are even forgotten. Yet, most research tests memory just once, typically during the same day, remaining blind to key processes linked to the creation of long-lasting, durable memories. Thus, we lack knowledge about how older adults encode and retrieve such durable memories compared with younger adults. Here, we tested whether activity patterns specific to durable—relative to transient—memory were affected by age, both at encoding and at retrieval. Participants completed an episodic memory task where item-context (source memory) associations were implicitly encoded and tested twice, after ≈90 minutes and ≈5 weeks. By repeated testing of the same stimuli, durable memories were distinguished from memories initially retrieved but later forgotten (transient memories). Functional magnetic resonance imaging (fMRI) data during the encoding and the short-delay retrieval sessions were collected to identify the specific patterns of activity associated with subsequent durable memories and their association with age.

Age is associated with a marked reduction in episodic memory function (Nyberg et al., 2012; Rönnlund et al., 2005) and changes in activity patterns supporting memory formation and retrieval (Davis et al., 2008; Grady, 2012; Maillet and Rajah, 2014). A much-used approach in memory research is the subsequent memory paradigm. Subsequent memory paradigms contrast stimulus encoding activity between trials that are later remembered versus those that are forgotten. Research using this paradigm has identified successful memory with increased activity in widespread cortical areas as well as in the hippocampus, and decreased activity in Default-Mode Network (DMN) regions (Kim, 2011; Spaniol et al., 2009). Decreased activity in task-positive and reduced deactivation in task-negative areas are the most characteristic features of successful memory encoding in older adults when tested at short intervals (Maillet and Rajah, 2014; Wang and Cabeza, 2016). The parieto-occipital cortex, involved visuospatial processing (Dennis et al., 2007; Park et al., 2013), together with the prefrontal cortex (Dennis et al., 2008; Miller et al., 2008) consistently exhibit lower encoding-related activity with higher age. Lower subsequent memory effects in older adults may arise from a reduced ability to allocate neural resources into relevant memory and attentional

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http://dx.doi.org/10.1016/j.neurobiolaging.2017.08.017

networks. Thus, based on evidence that tested older adults' memory after short delays, we hypothesized that with higher age, participants would show less activity associated with durable memories. Specifically, we expected age-related differences in core encoding regions such as in parieto-occipital and prefrontal regions, reflecting compromised encoding mechanisms. When compared with the patterns of activity supporting transient memories, the neural correlates supporting durable memory encoding would be less distinct in aging. For memory retrieval, different activity patterns have repeatedly been reported with advancing age (Addis et al., 2014; Angel et al., 2013; Cansino et al., 2015; but see; Wang et al., 2016). During the retrieval of context memories, higher frontal activity emerges as a recurrent finding (Dulas and Duarte, 2012; Leshikar and Duarte, 2014; Morcom et al., 2007), allegedly reflecting increased retrieval effort in older adults. In addition, age-related differences in retrieval activity might interact with testing effects as more effortful retrieval increases the benefit of testing effects (Wing et al., 2013). Consequently, we hypothesized older adults would exhibit higher frontal activity when retrieving durable memories.

Further, we aimed to expand the current knowledge on the neural correlates sustaining durable memories at encoding and retrieval with the largest sample of participants to date. For encoding, we envisioned 3 possible scenarios. First, durable memories could be represented by an extension of the activity-based principle governing initial memory success. Compared with transient memories, long-lasting memories would be characterized by the increased levels of activity in the same regions that support initial memory. Second, durable memories could rely on an activity-based principle but on different networks than those sufficient for initial memory formation. If this scenario is true, the blood-oxygen-level–dependent (BOLD) signal will reflect increased likelihood of an item being available for a long period of time but in areas not typically associated with encoding success. Both scenarios are not necessarily in conflict. Finally, durable memories could be undistinguishable at encoding or rely on additional mechanisms and thus appear unrelated to the degree of cortical activity during encoding.

The available evidence points in different directions. Most studies found that durable memories were associated with increased activity in the memory encoding network such as medial temporal, prefrontal, and parietal regions (Uncapher and Rugg, 2005; Wagner et al., 2016), including the hippocampus (Carr et al., 2010). In addition, frontal and posteromedial encoding activity has specifically been linked to memory durability (Liu et al., 2014; Uncapher and Rugg, 2005) as well as the amygdala when emotional stimuli were considered (Ritchey et al., 2008). Memory durability has also been associated with factors other than encoding strength, such as hippocampal-neocortical connectivity (Sneve et al., 2015), possibly related to postencoding system consolidation processes, or encoding similarity, mostly in DMN regions (Wagner et al., 2016).

The same 3 general scenarios described for encoding were also considered for retrieval. The only existing report on retrieval activity of durable memories showed increased activity in posteromedial, occipital, and fusiform areas during durable versus transient memories (Wagner et al., 2016). The results to some degree overlapped with the "core recollection network" (Johnson and Rugg, 2007), and with areas related to retrieval success of visually encoded material, that is, in partial agreement with the overlapping scenario suggested above. In addition, when the material is tested twice, as in the present study, there might be benefits from retrieval practice (Carpenter et al., 2008; Rowland and DeLosh, 2015). Thus, the initial, short-delay retrieval is also a process by which item-context associations can be strengthened. Testing effects seem to be contingent on processes that support memory success at encoding (Liu and Reder, 2016; Wing et al., 2013). Thus at retrieval, durable memory activity in regions involved in cognitive control—such as in anterior cingulate, frontal, and insular cortices—could be considered evidence in support of memory-strength modifying re-encoding processes.

Hence, in the present study, participants implicitly encoded source memory associations that were later tested twice, in a short- and a long-delay retrieval. The main goal was to identify cortical patterns of activity at encoding and at the short delay retrieval specifically associated with long-lasting memories and test whether such patterns of activity varied as a function of age.

2. Material and methods

2.1. Participants

One hundred forty-three participants (females = 90, mean age = 51.0 [standard deviation (SD) = 15.8], age range = 22–78) were included in the final sample. All participants completed the experimental design that included 1 incidental episodic encoding task and 2 retrieval tests. All participants were scanned during encoding and the first retrieval task. All participants were screened through health and neuropsychological interviews (see Supplementary Information; see Table 1 for main neuropsychological and sociodemographic variables). Participants were also excluded on the basis of bad quality or incomplete MRI data (n = 12), long retrieval span ≥90 days (n = 15) or insufficient numbers of items belonging to a given experimental condition (n = 14; <8 items belonging to any condition-of-interest). All participants gave written informed consent, and the study was approved by the Regional Ethical Committee of South Norway. Data were independent of an earlier report by our group (Sneve et al., 2015). Participants were compensated for their participation.

2.2. Experimental design

The stimulus material consisted of 300 black and white line drawings depicting everyday objects and items. The experiment consisted of an incidental encoding task and 2 tests; 1 after a short interval (≈90 minutes) and the other after, on average, 34.1 (SD = 15.8) days. The main experimental design has been thoroughly described elsewhere (Sneve et al., 2015). Briefly, the encoding and the first—but not the long delay—retrieval task took place in the MRI scanner. The encoding and the retrieval tasks consisted of 2 and 4 runs, respectively, that included 50 trials each. All runs started and ended with an 11 seconds baseline recording period in which a central fixation cross was present. An additional baseline period was also presented once in the middle of each run. In the encoding runs, a trial started with a voice asking into the participant's headphones, either "Can you

Table 1
Main demographic and neuropsychological variables

Sample descriptives	All	Age (t [p])
Sex (female:male)	90:53	–
Age	55.6 (13.7)	–
Age range	22:78	–
MMSE	29.0 (1.0)	−1.1 (0.3)
Vocabulary	65.0 (7.2)	2.7 (0.008)*
CVLT learning	56.0 (8.8)	−3.3 (0.001)*
CVLT 30′	12.6 (2.5)	−3.2 (0.001)*
Intertest interval (d)	34.1 (14.2)	−3.1 (0.002)*

Main demographic and neuropsychological variables. When appropriate, effects of age on each variable (right side; GLM with age and sex as predictors). Descriptive statistics represent $\bar{x}$ (SD), range or frequencies.
*Bonferroni corrected at $p <$ [0.05/5] 0.01.

eat it?“ or “Can you lift it?” (in Norwegian, Fig. 1A). Each question was asked 25 times in each run in a pseudorandomized order. One second after question onset, a picture of an item appeared on the screen together with a response indicator that instructed the participant which button to press to respond “Yes” or “No” to the previous questions. Button-response mapping was counterbalanced across subjects. The subject had 2 seconds to produce a response before the object was replaced by a central fixation cross which remained on the screen throughout the intertrial interval, that lasted between 1 and 7 seconds (exponential distribution over 4 discrete intervals; mean duration = 2.98 [SD 2.49] s).

Participants were asked to perform 2 surprise memory tests. The first one took place inside the MRI scanner approximately 1.5 hours after the last encoding trial. The long delay retrieval session occurred ≈5 weeks after the encoding, when participants returned to the experimental laboratory for a debrief meeting. All encoding trials were presented in both retrieval sessions. Test trials started with a recorded voice asking the following (Question 1): “Have you seen this item before” (Fig. 1B). Then, a picture of an item appeared on the screen, and the participant was instructed to indicate Yes (seen) or No (not seen) with a button press. In each run, 25 old items (presented during encoding) and 25 new items (not presented during

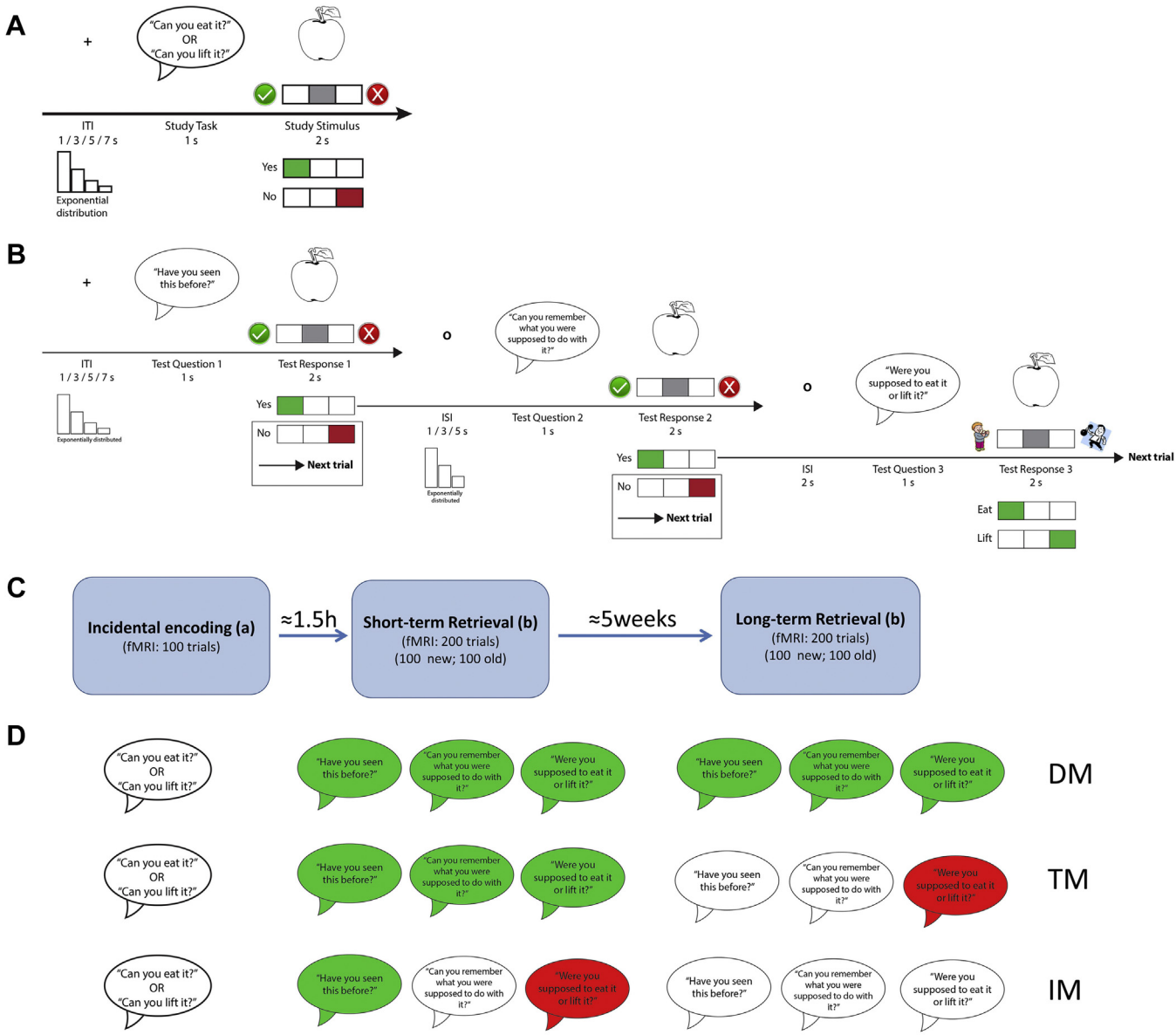

Fig. 1. Experimental paradigm. (A) Schematic of an encoding trial. The green ✓and the red X symbols were present on the screen to indicate which button indicated Yes and No. (B) Schematic of a retrieval trial. Test Questions 1 and 2 required a Yes/No response, whereas question 3 consisted of a two-alternative forced choice task. The trial ended if the participant responded No to either one of the two first questions. Response cues (✓, X, eating, lifting) were also here present on the screen. (C) Overview of the study design. An incidental memory encoding task was followed by a surprise memory test after 1.5 hours later where the old trials were randomly mixed with new items. Approximately 5 weeks after the initial encoding, participants underwent a second surprise memory test where the old items were re-tested and mixed with new items; (D) Schematic of the behavioral conditions of interest: durable memories (DMs) included those items with source memory in both, short- and long-interval retrievals; transient memories (TMs) included trials with correct source memory at the first, but not in the second retrieval while item memory (IM) was based on trials with only IM during the first retrieval. The red-colored bubble can indicate either incorrect or no source memory—as the participant could also stop the trial on the second question. Adapted from Sneve et al. (2015). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

encoding) were presented in a pseudorandomized order. Each object stayed on the screen for 2 seconds; if the participant responded that the item was new or did not respond, the trial ended. When the participant remembered seeing the item (pressed Yes), a new question followed (Question 2): "Can you remember what you were supposed to do with the item?". A No response ended the trial, whereas a Yes response, indicating that the participant also remembered the action associated with the item during the encoding, was followed by a final control question (Question 3): "Were you supposed to eat it or lift it?". Here, the participant got a two-alternative forced choice between the 2 encoding actions "Eat" or "Lift" (I was supposed to judge whether it would be possible to eat/lift it). Note that the specific questions asked during scanning were simplified to fit within the temporal limits of the paradigm, but that all participants were instructed in detail before the test session that the questions pertained to the item-action evaluation performed at encoding.

2.3. Behavioral analysis

Each test trial response to old items was behaviorally classified as follows: (1) source memory (Yes response to question 1 and 2 and correct response to question 3); (2) item memory (correct Yes response to question 1 and either a No response to question 2, or incorrect response to question 3); or (3) miss (incorrect No response to question 1). New items were classified either as (4) correct rejections or (5) false alarms (see Table 2 for behavioral results in each test session). To estimate memory performance strength, we additionally corrected the number of source memory trials by the number of incorrect source judgments (correct answers in question 3—incorrect answers in question 3). This correction tentatively accounts for processes such as false memories, threshold criteria in question 2 or guessing behavior that affects the raw estimates of source memory performance. Test trial responses in both retrieval tests were combined to create the fMRI behavioral conditions (described in Section 2.6 fMRI analysis).

All non-vertex-wise statistical analyses were performed in R-environment (https://www.r-project.org/; v.3.2.5). We did not find strong support for a nonlinear relationship between age and memory performance as assessed with the Bayesian information criterion. Thus, only the linear effects of age were tested in subsequent analysis. The association between age and behavioral and neuropsychological data was tested with general linear models (GLMs) with age and sex as predictors. Statistical significance was considered at $p < 0.05$, if not otherwise stated, and Bonferroni corrections were applied when appropriate. When not explicitly specified, data refer to mean (SD) and error bars to standard errors of the mean. Proportions are considered with respect to the new and old items as pertinent (e.g., source vs. old trials; false alarms vs. new trials).

Table 2
Behavioral measures

Behavioral measures	Short delay retrieval $\bar{x}$ (SD)	Age (t [p])	Long delay retrieval $\bar{x}$ (SD)	Age (t [p])
Source memory corrected	0.40 (0.18)	−5.8 (5.0e^{-8})*	0.10 (0.08)	−4.9 (2.4e^{-6})*
Source memory	0.51 (0.13)	−3.8 (2.1e^{-4})*	0.25 (0.10)	0.7 (0.5)
Item	0.23 (0.08)	3.8 (2.1e^{-4})*	0.38 (0.12)	−0.7 (0.5)
Miss	0.23 (0.13)	0.6 (0.6)	0.35 (0.15)	−0.3 (0.76)
Wrong recollection	0.10 (0.07)	6.6 (6.1e^{-10})*	0.15 (0.10)	5.2 (6.6e^{-7})*
Correct rejections	0.91 (0.08)	−3.9 (1.3e^{-4})*	0.82 (0.14)	−4.9 (2.3e^{-6})*
False alarms	0.09 (0.08)	4.1 (8.4e^{-5})*	0.17 (0.14)	5.1 (9.6e^{-7})*
Recognition corrected	0.65 (0.13)	−3.8 (2.2e^{-4})*	0.45 (0.14)	−5.1 (8.8e^{-7})*
Recognition d'	2.16 (0.63)	−5.1 (1.3e-^{6})*	1.45 (0.50)	−6.4 (2.5e^{-9})*

Main behavioral measures from the short- and long-delay retrievals. All measures but Recognition d' are expressed in proportions. Effects of age on each measure (GLM with age and sex as predictors). Recognition corrected = Item Hits−False alarms.
*Bonferroni corrected at $p <$ [0.05/8] 0.006.

2.4. MRI acquisition

Imaging data were collected using a 24-channel Siemens head coil on a 3T MRI (Siemens Skyra scanner, Siemens Medical Solutions, Germany) at Rikshospitalet, Oslo University Hospital. The functional imaging parameters were equivalent across all fMRI runs: 43 transversally oriented slices (no gap) were measured using a BOLD-sensitive T2*-weighted EPI sequence (TR = 2390 ms, TE = 30 ms, flip angle = 90°; voxel size = 3 × 3 × 3 mm; FOV = 224 × 224 mm; interleaved acquisition; generalized autocalibrating partially parallel acquisitions acceleration factor = 2). Each encoding run produced 131 volumes while the mean number of volumes per retrieval run was 208. At the start of each fMRI run, 3 dummy volumes were collected to avoid T1 saturation effects in the analyzed data. Anatomical T1-weighted MPRAGE images consisting of 176 sagittally oriented slices were obtained using a turbo field echo pulse sequence (TR = 2300 ms, TE = 2.98 ms, flip angle = 8°, voxel size = 1 × 1 × 1 mm, FOV = 256 × 256 mm). Visual stimuli were presented in the scanner environment with a 32-inch monitor while participants responded using the ResponseGrip device (both NordicNeuroLab, Norway). Auditory stimuli were presented to the participants' headphones through the scanner intercom.

2.5. MRI data preprocessing

Cortical reconstruction and volumetric segmentation of the T1-weighted scans were performed with FreeSurfer 5.3 pipeline (http://surfer.nmr.mgh.harvard.edu/fswiki), thoroughly described elsewhere (Dale et al., 1999; Fischl and Dale, 2000; Fischl et al., 1999). Briefly, the automatized processing pipeline includes removal of nonbrain tissue, Talairach transformation, intensity correction, tissue segmentation, and cortical surface reconstruction. Functional imaging data from the memory tasks were preprocessed using the Freesurfer Functional Analysis Stream (https://surfer.nmr.mgh.harvard.edu/fswiki/FsFast). After correction of functional images for distortions caused by B0 inhomogeneities in EPI scans, the images were motion corrected, slice timing corrected to the middle of each volume's TR, intensity normalized, and registered to each participant's anatomical volume. Then, each functional data set was resampled to a common space using a surface-based intersubject registration, bringing cortical hemispheres into *fsaverage* average space. After running first-level GLM analysis (see Section 2.6 fMRI analysis), surface smoothing was applied using a Gaussian kernel of 8-mm full-width half-maximum and each participant's surface map was introduced to a higher-level GLM analysis.

2.6. fMRI analysis

2.6.1. Main effects of memory contrasts

A first-level GLM consisting of the conditions of interest with onsets and durations corresponding to the experimental trial period (2s) was set up for each encoding and retrieval run and was

convolved with a 2-gamma canonical hemodynamic response function. Each event was assigned to a condition based on the participant's response to a given item during the test sessions. The experimental conditions were created by combining trial responses in both the short-delay and the long-delay tests (see Section 2.2 Experimental design and 2.3 Behavioral analysis) were defined as follows: (1) durable memory (DM) condition that consisted of items that were correctly identified with context information in both the short- and long-delay retrieval tests—correct question 3 in both tests; (2) transient memory condition (TM), that included those trials where the participant could correctly identify the item with context information in the first retrieval test but not in the second (long delay) retrieval—correct question 3 in the short-delay test but not in the long-delay test—and; (3) item memory condition that consisted of those items that were correctly recognized in the short-delay retrieval but without (or with incorrect) context information, correct question 1, but not question 3, in the short-delay test (Fig. 1D). The later condition-of-interest was only based on the first retrieval. In addition, several regressors were included to soak up BOLD variance associated with miss response trials and trials with no response. Four further regressors were added in the retrieval runs exclusively, modeling the second and the third test questions as well as false alarms and correct rejections associated with the presentation of the new items. In addition to the task regressors and their temporal derivatives, estimated motion correction parameters and a set of polynomials (up to the second degree) were included in the first-level GLM as nuisance regressors. The model and the data were high-pass filtered at 0.01 Hz, and temporal autocorrelations in the residuals were corrected using a prewhitening approach. For each individual, 2 contrasts of parameter estimates were computed for further statistical analysis: DM versus TM conditions (durable memory contrast) and DM and TM trials versus item memory (initial memory success contrast). To compute the latter contrast, we ran a separate first-level model in which a single regressor included both the DM and the TM trials. For fMRI analysis, on average 19.0 (8.3) memory trials were classified as durable memories, 31.5 (11.4) as transient memories, and 23.1 (8.4) as item memories.

Next, individual contrasts were introduced into group level ordinary least square GLM analysis to explore the main contrast effects. All statistical models additionally included sex and age as covariates (unless age was used as a variable of interest, see below). Statistical significance was tested at each cortical vertex, and the resulting maps were corrected for multiple comparisons using a cluster-based approach; vertices were thresholded at $p < 0.01$ and the remaining clusters were tested through permutation inference across 10.000 iterations using PALM scripts (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/PALM; Winkler et al., 2014). Cluster significance was considered at a family-wise error–corrected level of $p < 0.05$ (two-sided). The encoding and the retrieval fMRI data were independently processed. The reported results were robust to variations of the cluster-formation threshold (Supplementary Figs. 1 and 2).

2.6.2. Age-related effects on durable and initial memory contrasts

The abovementioned higher-order GLM analysis was additionally used to explore the effects of age on the memory contrasts. To better understand the age modulation over the memory contrasts, we extracted the mean signal change from the family-wise error–corrected clusters. The fitted signal change was assessed at age $= \pm 1$ SD and 99% confidence intervals (CIs) were computed to better interpret the contrast direction.

2.6.3. Relationship between durable and initial memory contrasts

The cortical patterns of activation associated with durable memories were compared to those associated with initial memory success, and to those reported in the literature through meta-analytical contrast maps. Meta-analytical contrasts mainly included studies that tested participant's memory after short periods of time (Kim, 2016, 2011). The map comparison was performed twofold: First, the cortical patterns of activity associated with the durable memories were compared to those associated with an initial memory success; thus we assessed the degree of anatomical overlapping between the two memory contrasts. Cortical signal change maps associated with durable memory and initial memory success contrasts, that is, durable versus transient memories and source versus item memory defined in the short delay test, were used to assess the spatial correspondence between both contrasts. Second, the durable memory and initial memory success signal change maps were compared with published meta-analytical contrast maps of memory success both during encoding (Kim, 2011) and retrieval (Kim, 2016). The reader is addressed to the original studies (Kim, 2011, 2016) for details on meta-analytical methods and on the specific study selection criteria. Note that the meta-analytical contrasts only included memory success contrasts, in which activity for memory success items was compared with activity associated to memory failure. The meta-analysis though included a variety of studies that were not necessarily constrained to source memory paradigms. We used a published meta-analysis—instead of an approach based on open databases—to avoid lexical confusions, select uniquely memory success contrasts and, isolate positive from negative activations. Activation likelihood estimation (ALE) maps were registered to the *fsaverage* template space, projected at mid surface using the *mri_vol2surf* tool and compared to the memory maps resulting from the present study. For each type of contrast estimates, data were merged across hemispheres, Z-standardized and fed to random subsampling statistical analysis. To avoid collinearity between adjacent vertices, subsets of vertices (1000 vertices) were randomly selected and bivariate Pearson's correlations between the different memory contrasts were computed within these subsets of vertices. This process was iteratively repeated ($n = 5000$). The mean correlation of all the iterations was selected as the index representing the spatial overlap between memory contrasts. The analysis was performed independently for those contrasts representing encoding and retrieval. In addition, initial memory success and durable memory significance maps, both at encoding and at retrieval, were binarized at $p < 0.01$ (uncorrected). Regions with unique or common patterns of activity were overlaid onto semi-inflated surfaces.

2.6.4. Hippocampal analysis

In addition to the surface-based analysis, contrast estimates were extracted from the left and right hippocampal ROIs—in the original functional space—based on the automatic subcortical segmentation implemented in FreeSurfer (Fischl et al., 2002), to

Table 3
Behavioral descriptives

fMRI behavioral measures	All $\bar{x}$ (SD)	Age (t [p])
Durable memory	0.19 (0.08)	−1.0 (0.3)
Transient memory	0.31 (0.11)	−3.6 ($4.0e^{-4}$)*
Item memory	0.23 (0.08)	−1.7 (0.1)
Miss memory	0.26 (0.11)	3.8 ($2.1e^{-4}$)*
Durable:Initial memory success	0.39 (0.14)	−1.7 (0.08)

Main behavioral measures in relation to the experimental fMRI conditions. All measures are in proportions. Effect of age on each measure (right column, GLM with age and sex as predictors).
*Significance was considered at $p < 0.01$ (0.05/5) after Bonferroni correction for the number of behavioral comparisons.

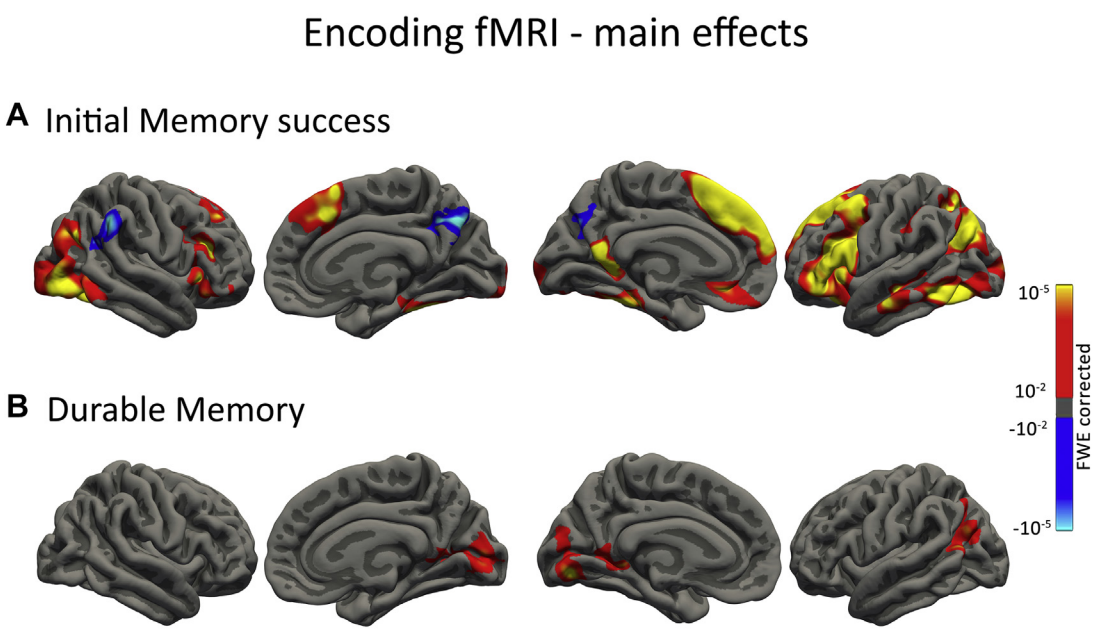

Fig. 2. Main memory effects of encoding activity. Parameter estimates of encoding activity. Vertex significance is displayed in clusters surviving multiple comparison correction by FWE (vertex-wise $p < 0.01$; cluster-based $p < 0.05$). BOLD activity during encoding associated with (A) initial memory success—source versus item memory on the first retrieval—and (B) durable memories—source memory during both retrievals versus source memory during the first but not during the second retrieval. Positive and negative significance patterns are shown in respective red-yellow and blue-light blue scales overlaid onto semi-inflated surfaces. See Supplementary Table 1 for cluster stats and Supplementary Fig. 1 for activity patterns during encoding associated with the different memory conditions at different correction thresholds. Abbreviation: BOLD activity, blood-oxygen-level–dependent activity. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

explore whether hippocampal activity was related to memory success as well as any effect of age. The relationship between hippocampal activity and durable memory and initial memory success estimates was tested independently with 4 mixed-effect ANCOVAs that included hemisphere, behavioral condition, age, and sex as independent variables. The different tests corresponded to encoding and retrieval data and initial memory success (behavioral condition levels: source and item memory during the first retrieval) and durable memory (behavioral condition levels: durable and transient memories) estimates.

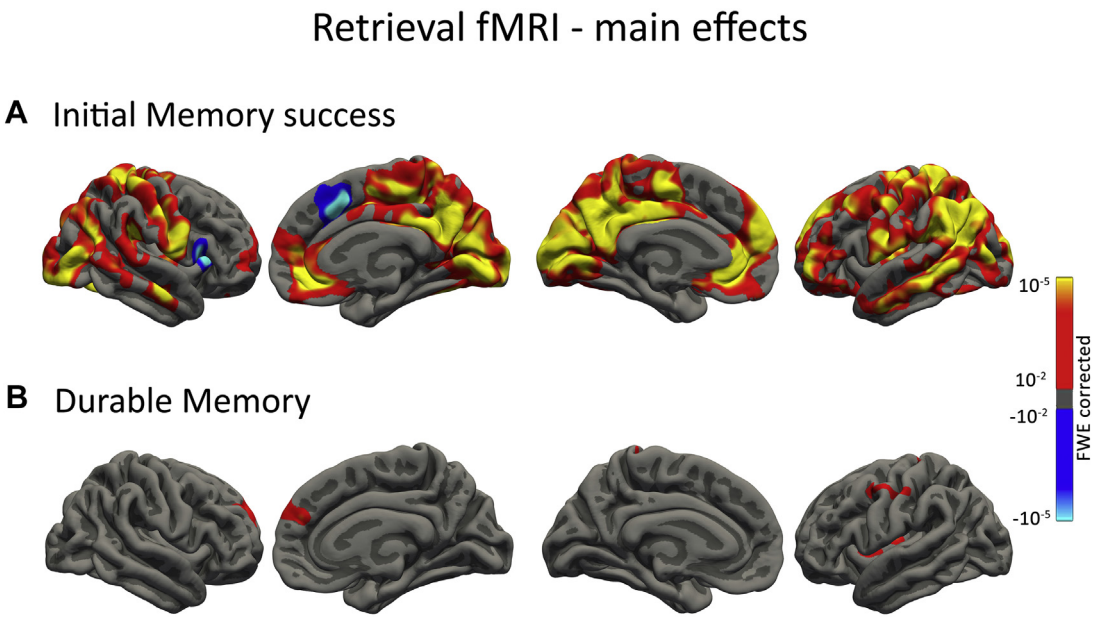

Fig. 3. Main memory effects of retrieval activity. Parameter estimates of retrieval activity. Vertex significance is displayed in clusters surviving multiple comparison correction by FWE (vertex-wise $p < 0.01$; cluster-based $p < 0.05$). BOLD activity during the first retrieval associated with (A) initial memory success, source versus item memory on the first retrieval, and (B) durable memories, source memory during both retrievals versus source memory during the first but not during the second retrieval. Positive and negative significance patterns are shown in respective red-yellow and blue-light blue scales overlaid onto semi-inflated surfaces. See Supplementary Table 1 for cluster stats and Supplementary Fig. 2 for activity patterns during retrieval associated with the different memory conditions at different correction thresholds. Abbreviations: BOLD activity, blood-oxygen-level–dependent activity; FWE, family-wise error. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

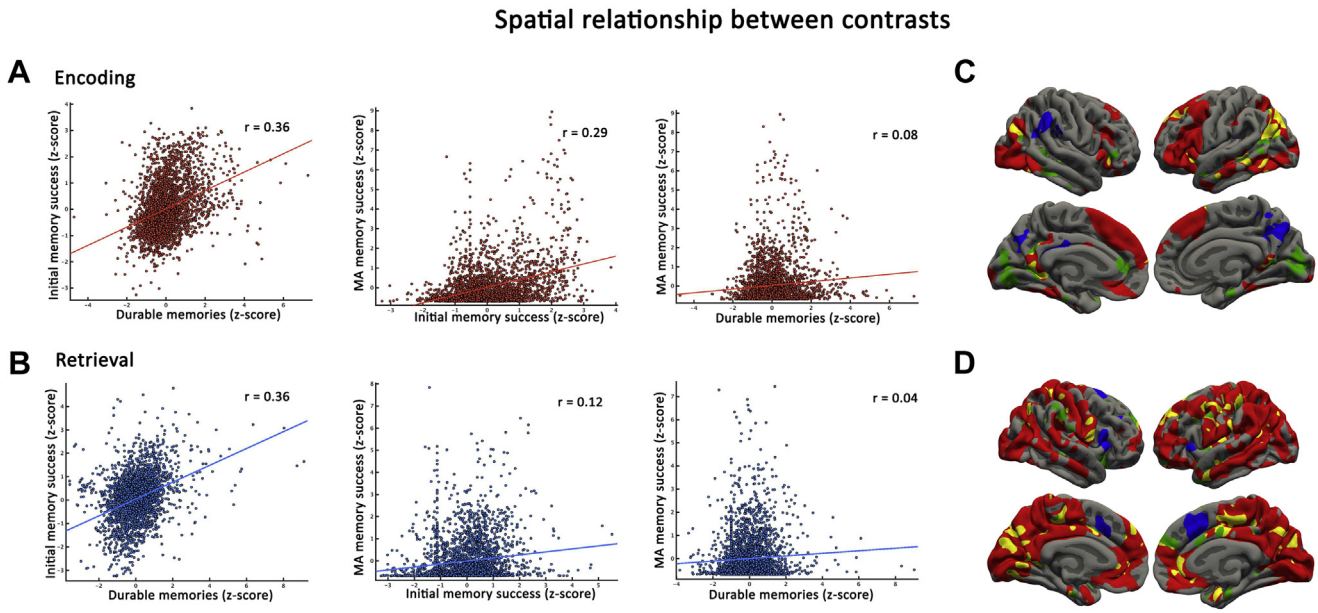

Fig. 4. Spatial overlapping between memory contrast maps. Spatial overlap between contrast (A) encoding and (B) retrieval maps in red and blue colors, respectively. Spatial overlap between: initial memory success and durable memory contrast maps (left column); durable memory and meta-analytic memory success contrast maps (middle column) and; initial memory success and meta-analytic memory success contrast maps (right column). For visual purposes, the plots only display the spatial correlation—after z-standardization—between a random subsample of vertices (n = 1000). See full stats in Section 3. Results. MA, meta-analytic. Overlay between initial memory success and durable memory contrast maps (thresholded at $p < 0.01$ uncorrected) during (C) encoding and (D) retrieval. The durable memory contrast is represented in green, the initial memory success contrast is represented in red and the overlap is represented in yellow. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

2.6.5. Content-specific retrieval activity within the sensorimotor cortex

As durable memories were characterized by higher retrieval activity within the sensorimotor cortex, we conducted a post hoc analysis to test whether sensorimotor patterns of activity varied according to the content of what was retrieved. That is, we studied whether content-specific patterns of activity corresponded to the different source questions ("can you eat/lift it?"). Briefly, the behavioral conditions of interest were redefined based on the short delay retrieval: (1) correct source memory for items presented in association with the source *Eat* question (source-eat memory); (2) correct source memory for items presented together with the source *Lift* question (source-lift memory); and (3) item memory trials. fMRI data were preprocessed as described above (Section 2.5 MRI data preprocessing). For each participant, the following contrasts of parameter estimates were computed for further statistical analysis: source-eat versus item memory (eat memory contrast) and source-lift versus item memory (lift memory contrast). GLM group-level analyses were carried out within the sensorimotor strip. Content-specific activity was defined by inclusively masking vertices with significant activity for one source question ($p < 1.0e^{-4}$) and exclusively masking for the alternative contrast ($p < 0.01$). Clusters of >100 vertices were considered significant. See Supplementary Information for further information.

3. Results

3.1. Behavioral results

After correcting for the number of incorrect source memories (correct answer in question 3 - incorrect answer in question 3) the proportion of source memory trials was 0.40 (0.18) and 0.10 (0.08) for the short- and long-interval memory tests, respectively, in both cases significantly above chance ($t = 27.1$ [$p < 2.2e^{-16}$] and $t = 12.9$ [$p < 2.2e^{-16}$] respectively; one-sample t-tests against 0). In both retrieval tests, corrected source memory was negatively related to age ($t = -5.8$ [$p = 5.0e^{-8}$] and $t = -4.9$ [$p = 2.4e^{-6}$]). Education level was not significantly associated with age nor with source memory performance at short- and at long-delay tests (analysis of variance; $p > 0.05$; Supplementary Table 3). See Table 2 for behavioral results in each retrieval session and the effects of age on memory performance. The proportion of items with source memory in the first retrieval that was also retrieved with source during the second retrieval (durable memories) was 0.39 (0.14). The remaining items were classified either as miss or as invalid, due to no response. Age was positively associated with the number of miss trials (in the first retrieval; $t = 3.8$ [$p = 2.1e^{-4}$]) and negatively related to the number of transient memory items ($t = -3.6$ [$p = 4e^{-4}$]). Notably, age was unrelated to the proportion of forgotten items between tests and the number of durable memory items (see Table 3; Bonferroni corrected for the number of behavioral tests at $p < 0.01$ [0.05/5]). See also Supplementary Tables 3 and 4 for behavioral and neuropsychological data sampled into age groups.

3.2. Main effects of memory contrasts

Cortical vertex-wise analyses on BOLD signal were performed for encoding and retrieval fMRI to identify the areas in which neural activity was related to initial memory success and to durable memory (multiple comparisons corrected). The initial memory success contrast—source versus item memory during the first retrieval—was associated with activity in widespread areas across the cortical mantle, showing encoding and retrieval patterns similar to those previously reported in the literature (Kim, 2011, 2016).

3.2.1. Encoding activity

During encoding, increased activity for initial memory success was found in large left-lateralized prefrontal, inferior, and medial temporal and parieto-occipital regions (Fig. 2A). Activity in the

bilateral posteromedial and the right inferior parietal cortex was associated with memory failure. During encoding, durable memories were associated with higher activity than transient memories in a bilateral posteromedial cluster that encompassed the lingual and the retrosplenial cortices, and in a left inferior parietal cluster (Fig. 2B).

3.2.2. Retrieval activity

During the first retrieval, initial memory success was associated with higher activity in widespread areas of the cortical mantle, especially in posteromedial, occipital and medial prefrontal regions (Fig. 3A), and reduced activity in restricted right medial superior frontal and lateral orbitofrontal areas. During retrieval, durable memories were associated with increased activity in the left sensorimotor cortex, the left insula, and the right superior medial frontal cortex (Fig. 3B). See Supplementary Table 1 for cluster stats and Supplementary Figs. 1 and 2 for the cortical maps corrected at different cluster-forming thresholds. See Supplementary Fig. 3 for activity associated with memory success during the second retrieval, regardless of behavioral classification at the first retrieval.

3.3. Spatial overlap between memory contrasts maps

The mean spatial overlap between the durable contrast and the initial memory success map was r = 0.36 (0.02) for encoding and 0.36 (0.02) for retrieval suggesting moderate relationships between both maps (Cohen, 1988). Next, these maps were compared with meta-analytical memory maps, thus avoiding the overlap derived from the identical nature of the task. The spatial overlap between initial memory success and meta-analytical memory maps was 0.29 (0.02) for encoding and 0.12 (0.02) for retrieval, showing small-to-medium and small anatomical correspondence with the meta-analytical results. In contrast, the spatial correspondence between durable memory and meta-analytical memory maps was trivial, both for encoding 0.08 (0.02) and retrieval 0.04 (0.02). Though exhibiting a similar general pattern, the spatial overlap between maps was slightly higher when the analyses were computed with durable memory and initial memory success contrast maps obtained only from a subsample of young participants (below 40 years; see Supplementary Information). See Fig. 4 for graphical representations of the spatial overlap.

3.4. Age-related effects on durable memory and initial memory success contrasts

Age was negatively related to posteromedial activity during the encoding of durable versus transient memories in a cluster centered in the retrosplenial cortex, extending also to adjacent posterior cingulate and precuneus regions (Fig. 5A). Post hoc analyses revealed that young participants exhibited higher activity in this posteromedial region for durable compared with transiently remembered memories, whereas older adults showed no significant differences between conditions (mean [CI] = 0.06 [0.03–0.09] and −0.02 [−0.05–0.02] for young and old participants, respectively, see Fig. 5C). In contrast, age was positively associated with durable memory compared with transient memory retrieval activity in the left inferior frontal cluster and in the right superior medial frontal gyrus (Fig. 5B). Post hoc analyses revealed that in both areas, activity for durable memories was larger than for transient memories in older adults, whereas no differences were seen in younger adults (mean [CI] = −0.02 [−0.04–0.01] and 0.03 [0.01–0.05] for young and old participants, in the left inferior

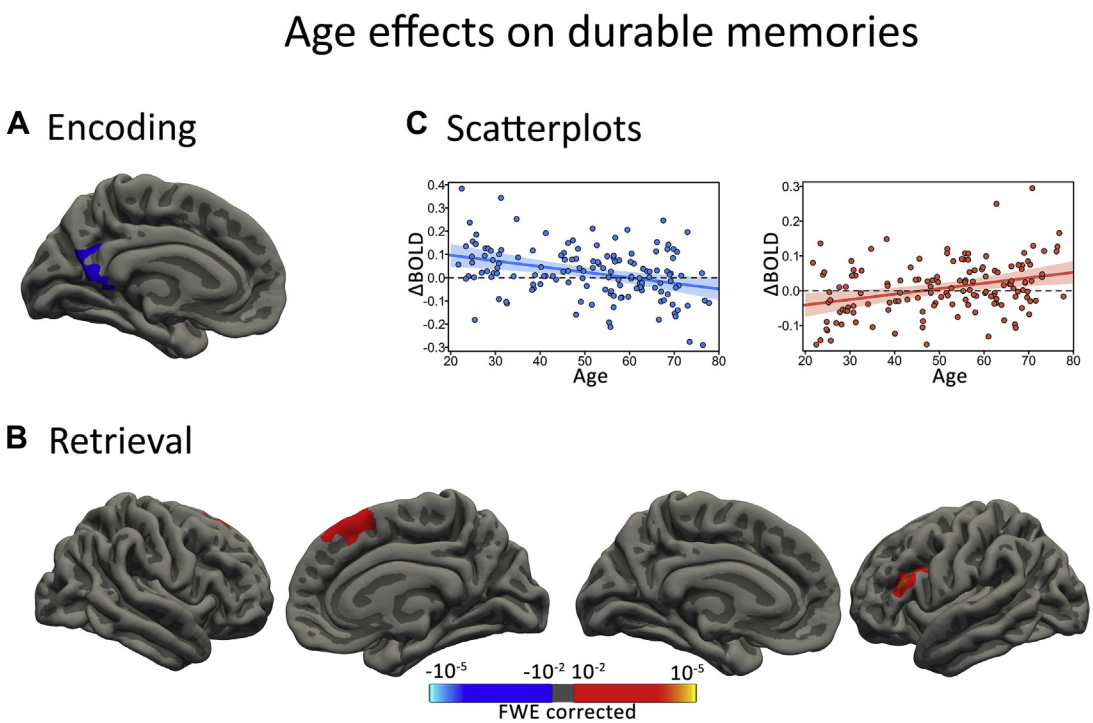

Fig. 5. Age-related differences on durable memory-associated activity. Parameter estimates of age effects on BOLD signal associated with durable memories. Vertex significance is displayed in clusters surviving multiple comparison correction by FWE (vertex-wise $p < 0.01$; cluster-based $p < 0.05$). Age effects on neural activity associated with (A) encoding of durable memories and, (B) retrieval of durable memories. Positive and negative significance patterns are shown in red-yellow and blue-light blue scales overlaid onto semi-inflated surfaces. In (C) mean signal change data across age are shown from clusters showing age effects. Data from the left posteromedial cortex during encoding and from the left inferior frontal gyrus during retrieval is plotted in the blue and red scatterplots, respectively. See Supplementary Table 2 for cluster stats. Abbreviation: BOLD activity, blood-oxygen-level–dependent activity. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

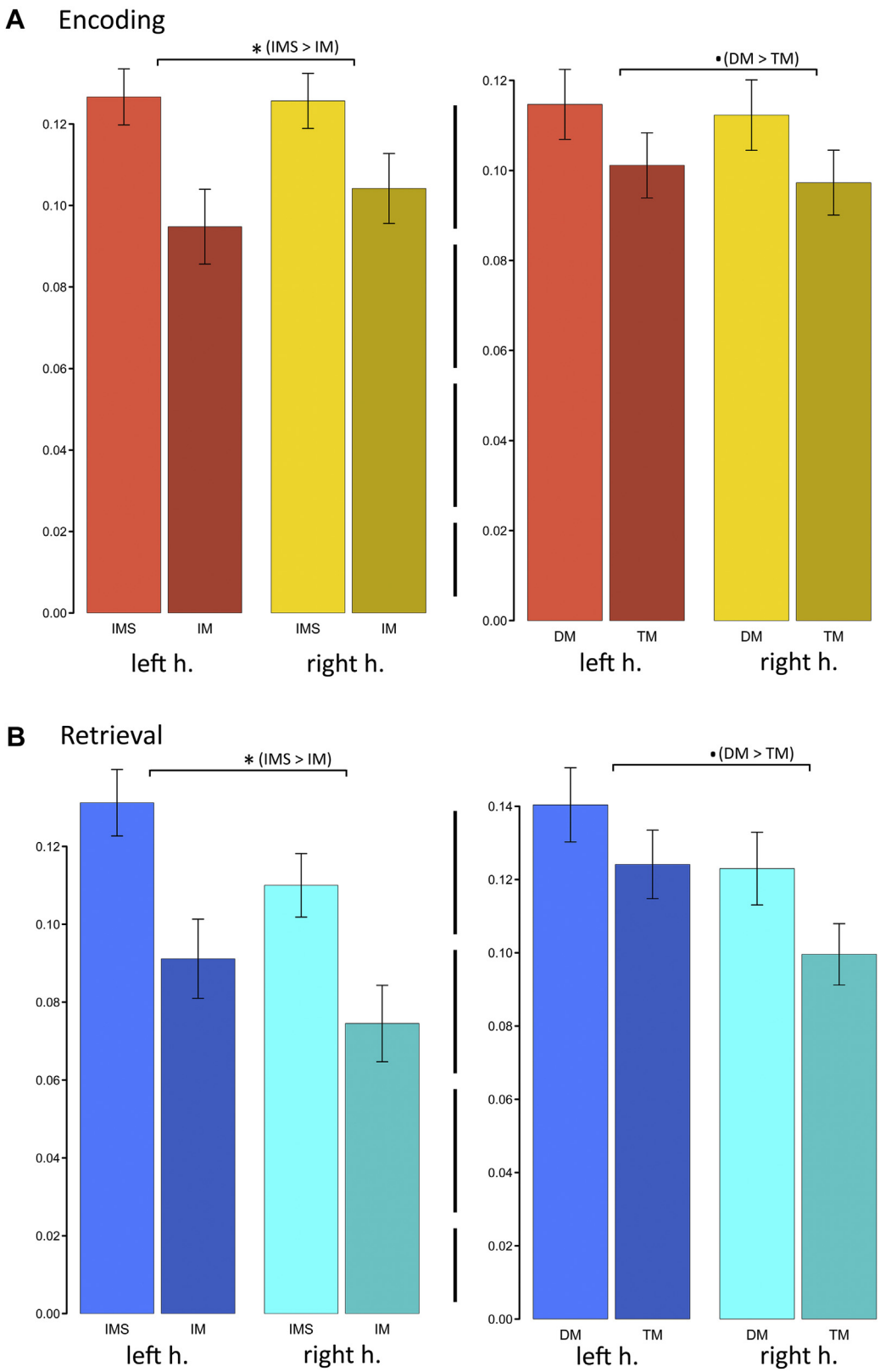

Fig. 6. Hippocampal activity on memory conditions. Left and right hippocampus activity during the main (A) encoding and (B) retrieval conditions. In the left-side figures, activity elicited by initial memory success and item memory trials is shown while the right-side figures represent durable and transient memory-elicited activity. Abbreviations: DM, durable memories; IM, item memory; IMS, initial memory success; TM, transient memories. * and ◦ symbols denote Bonferroni corrected ($p < 0.01$ [0.05/4]) and uncorrected significance ($p < 0.05$).

frontal cluster, shown in Fig. 5C; and mean [CI] = −0.03 [−0.06 to 0.00] and 0.05 [0.02–0.08] for young and old participants, in the right superior medial frontal cluster). Age-related effects on durable memories were not explained by thinner cortices in older adults as shown by post hoc GLMs on durable memory activity that included cortical thickness as an additional regressor. Cortical thickness was not associated with durable memory activity ($p > 0.3$) while age remained a significant predictor of durable memory activity ($p < 0.001$). See Supplementary Information for more details. There were no effects of age on encoding activity related to initial memory success. During retrieval of initial memory success items, age was associated with reduced posteromedial activity and increased right superior medial and right inferior frontal gyrus activity (Supplementary Fig. 4, and Supplementary Table 2).

3.5. Hippocampal analyses

Four mixed effects analyses of covariance (ANCOVAs) that included hemisphere, behavioral memory condition, age, and sex were performed to study whether memory success was related to hippocampal activity as well as any effects of age. The ANCOVAs tested BOLD differences between initial memory success and durable memory both for encoding and retrieval (Bonferroni corrected at $p = 0.01$ [0.05/4]; Fig. 6). Increased hippocampal activity was associated with initial memory success both during encoding and retrieval ($F = 13.0$ [$p = 4.3e^{-4}$], $F = 29.8$ [$p = 2.1e^{-7}$], for encoding and retrieval, respectively). In addition, an interaction between age and initial source memory was found for retrieval ($F = 9.65$ [$p = 0.002$]), caused by lower source memory activity with higher age. Both the encoding and retrieval ANCOVAs on durable memories showed trends toward increased hippocampal activity for durable versus transient memories ($F = 4.8$ [$p = 0.03$], $F = 6.0$ [$p = 0.01$] respectively). No age effects were found for encoding or retrieval activity of durable memories. See more ANCOVAs stats in Table 4.

3.6. Content-specific retrieval activity within the sensorimotor cortex

It is assumed that memory retrieval involves reactivation of content-specific relevant sensory and motor regions (Johnson and Rugg, 2007). To better interpret the association between sensorimotor activity and durable memories, we post hoc tested for differences in retrieval activity between the 2 encoding task instructions ("Can you eat it?" versus "Can you lift it?"). Content-specific retrieval activity was revealed within the sensorimotor cortex (Fig. 7). Content-specific activity for the eat memory contrast—source for eat compared with item memory trials—was found in the left inferior sensorimotor strip. This region is associated with lip and tongue representations. In contrast, the lift memory contrast was associated with higher activity in the middle part of the right sensorimotor strip; that grossly relates to the hand, arm, and elbow representations (Meier et al., 2008; Penfield and Boldrey, 1937). A post hoc mixed-effect linear model with content-type, cluster (as within-subjects) and age (as between-subjects) factors—that also included sex as a covariate of no interest—did not show *age* × *cluster* × *content-type* effects ($F = 0.3$, $p = 0.6$) suggesting that age was not associated with content-specific patterns of activity in the sensorimotor cortex. Content-specific retrieval results in the sensorimotor cortex suggested a somatotopic representation of the retrieved material. This strongly indicates that in the current paradigm retrieval of memories with source information involved content-specific reactivations.

4. Discussion

The results indicate that encoding and retrieval of durable memories are supported partly by increased brain activity in the same brain regions that support initial memory success and partly by activation of additional brain regions. In some regions, for example, the hippocampus, durable memories were supported by the same activity-based principle that governed initial memory success. Other regions, however, selectively supported durable memory processing, for example, posteromedial and frontal cortices at encoding and retrieval, respectively. Importantly, while encoding activity was reduced with aging, older adults' successful retrieval involved additional frontal recruitment. The implications of the results are discussed.

4.1. Brain signatures of encoding of durable versus transient memories

It is known that the degree of activity in perceptual, attentional, and storage brain networks during the encoding of events predicts subsequent memory over shorter time intervals (e.g., Kim, 2011). Here, we showed that hippocampal and neocortical activity predicted whether an item would be remembered for a long time or forgotten after being successfully recalled in a short delay test. High levels of activity in these regions might reflect the interaction of incoming information with existing representations (Burgess et al., 2001; Byrne et al., 2007). The relevance of hippocampal-posterior cortical circuitry that involves DMN and higher order visual processing nodes, for establishing durable memories is in good agreement with previous research. Hippocampal activity during encoding has previously been linked to durable memories (Carr et al., 2010; Wagner et al., 2016) as well as higher visuoperceptive (Wagner et al., 2016) and posteromedial (Liu et al., 2014) cortical activity.

High levels of encoding activity likely triggers initial consolidation processes involving a myriad of cellular mechanisms that ultimately lead to alterations of the synaptic efficacy (Dudai et al., 2015). Yet, consolidation processes do not occur homogeneously for all the encoded information. Likely, some encoding events are tagged as "salient" or "relevant" and consequently undergo system consolidation processes during postencoding periods and sleep (Payne et al., 2008; Saletin et al., 2011; Stickgold and Walker, 2013). Here, we show that the likelihood of an event being stabilized in long-term memory increases with increased recruitment of

Table 4
Hippocampal activity ANCOVA

ANCOVA	Memory	Hemisphere	Age	Sex	Memory*age
Encoding-durable memory	4.7 (0.03)°	0.5 (0.5)	0.0 (0.9)	0.8 (0.4)	1.9 (0.2)
Retrieval-durable memory	6.1 (0.01)°	20.9 ($1.05e^{-5}$)*	9.2 (0.003)*	0.2 (0.6)	1.7 (0.2)
Encoding-initial memory success	13.0 ($4.3e^{-4}$)*	0.7 (0.4)	2.9 (0.09)	0.0 (0.9)	0.0 (0.8)
Retrieval-initial memory success	29.8 ($2.1e^{-7}$)*	16.6 ($7.7e^{-5}$)*	19.7 ($1.81e^{-5}$)*	0.0 (1.0)	9.6 (0.002)*

Stats (F[p]) indicating differences in hippocampal activity across conditions of interest. Significance was considered at $p < 0.01$ (0.05/4) after Bonferroni correction for multiple comparisons. * and ° symbols denote corrected and uncorrected (trend toward) significance. None of the terms not shown in the table exhibited significance.

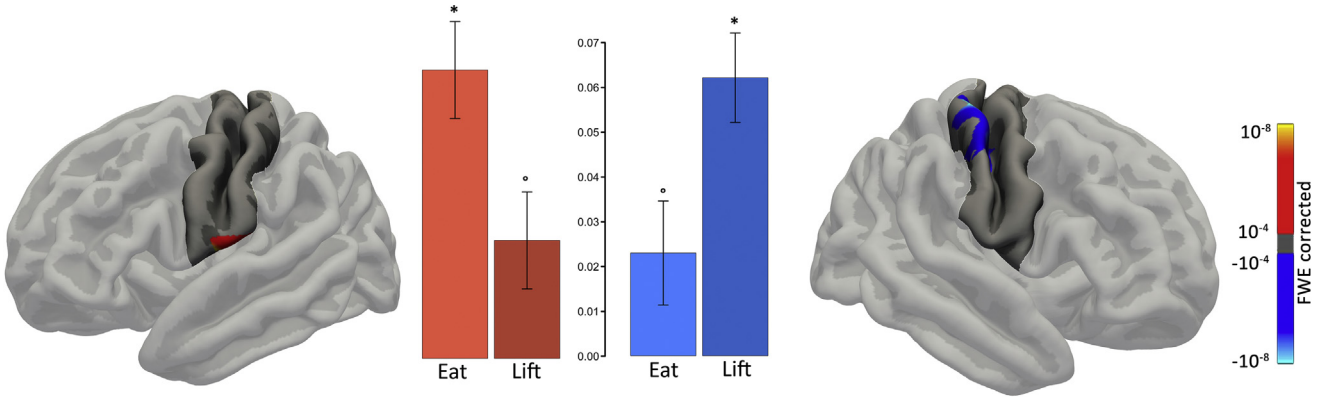

Fig. 7. Content-specific retrieval effects in the sensorimotor strip. Sensorimotor regions revealing content-specific retrieval effects. Red and blue clusters represent regions where content-specific successful source memory retrieval activity was seen for source Eat and Lift questions, respectively. The red and blue bar plots represent mean signal change of activity between source-Eat/Lift memory trials compared to item trials. * and ° symbols denote Bonferroni corrected ($p < 0.01$ [0.05/4]) and uncorrected significance ($p < 0.05$). Significance patterns are shown in red-yellow and blue-light blue scales overlaid onto semi-inflated surfaces and represent mean signal change of activity between the dominant content-specific condition compared with item memory. See Supplementary Information for more details. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

hippocampal and selected neocortical regions—including a subset of DMN nodes—during encoding. In agreement with the notion that hippocampal-neocortical ensembles constitute an initial memory trace for an episode (Nadel and Moscovitch, 1997; Squire, 2004), the degree of connectivity between the hippocampus and neocortical areas both during encoding (Sneve et al., 2015), sleep (Hu et al., 2015; Kaplan et al., 2016), and idle postencoding periods (Tambini et al., 2010; van Kesteren et al., 2010) has been shown to predict later retrieval. The results are somewhat coherent with recent system consolidation findings that suggest that both the neocortex and the hippocampus are involved during and initial encoding phase, but the involvement of the latter diffuses when predicting long-lasting memories (Kitamura et al., 2017).

Complementarily, cortical correlates of durable memories can reflect the beneficial engagement of cognitive processes. Activity in regions supporting durable memory might reflect the construction of more elaborate mental scenes, by means of deeper, self-referential and/or imagery richer encoding processes which are known to increase later memory performance (Craik and Lockhart, 1972; Richardson, 1980; Symons and Johnson, 1997; Trelle et al., 2015). A more elaborate mental scene construction (Andrews-Hanna et al., 2010; see also; Hassabis and Maguire, 2007), which requires the integration of new and existing information, is thought to be involved in the current encoding task and might constitute a basis for selective stabilization of memories. Altogether, with longer postencoding delays, correlates of subsequent memory success seem to shift from perceptual and attentional networks toward areas more involved in mnemonic processes.

4.2. Brain signatures of retrieval of durable versus transient memories

Durable memories were associated with higher retrieval activity in distributed frontal and insular cortical regions as well as—at a trend level—the hippocampus. Higher retrieval activity associated with durable memories might indicate reactivation of stronger memory traces. Hippocampal activity has been shown to characterize successful retrieval over shorter time intervals (Kim, 2010, 2016; Staresina et al., 2012). The present findings extend this intensity principle to durable memories which coincide with the suggestion that hippocampal activity co-varies with the amount of information retrieved and involves the reactivation of the memory trace (Ritchey et al., 2013; Xue et al., 2010). Activity in the sensorimotor cortex was related to both initial memory success and memory durability despite rarely being associated with successful memory retrieval. Here, activity in this region likely represents content-specific retrieval effects. A post hoc analysis confirmed that the patterns of activity within the sensorimotor strip varied according to the content of what was retrieved, following the somatotopic organization (Meier et al., 2008; Penfield and Boldrey, 1937) and suggesting the presence of content-specific reactivation of the material within the somatosensory cortex.

4.2.1. Testing effects

The retrieval-related activity associated with durable memories could also reflect testing effects. The effort and elaboration required during an initial cued retrieval could strengthen memory when tested in a later, delayed retrieval (Karpicke and Roediger, 2008; Pyc and Rawson, 2010; Roediger and Butler, 2011). It is likely that without the short delay test, some trials categorized as durable memories in the present study would have been forgotten if they had been tested only after a long period of time. Thus in the short delay retrieval, BOLD signal associated with the durable memory contrast might reflect testing effects and re-encoding processes that boost memory durability. More left anterior insular and right medial superior frontal activity during durable memory retrieval would fit with this interpretation. While activity in the anterior insula has occasionally been associated with successful retrieval measures (Kikyo et al., 2002; Slotnick and Dodson, 2005; Yonelinas et al., 2005), it consistently predicts subsequent memory during encoding (Addis and McAndrews, 2006; Kim, 2011; Kirwan et al., 2008). Insular activity possibly reflects monitoring demands and response selection processes, and its relationship with durable memories could be partially understood as the beneficial effect of effortful retrieval processes on item durability. The only available evidence indicated higher activity during the retrieval of durable memories in posteromedial cortex and in content-specific regions but also in the left insular cortex (Wagner et al., 2016). Further studies that rate memory strength and encoding strategies on a trial-by-trial basis are needed to clarify the processes supporting durable memories during the short delay retrieval.

4.3. Age-related effects on durable memory activity

Older adults exhibited lower left posteromedial activity during encoding of durable versus transient memories in a cluster centered

in the restrosplenial cortex and encompassing the neighboring posterior cingulate and the precuneus regions. The retrosplenial cortex (and adjacent PCC regions) is critical for integration of external visual information and stored representations as it is strongly connected both with the hippocampal formation and the visual cortex (Kobayashi and Amaral, 2003, 2007). Scarce evidence of age-related effects on subsequent memory activity in the retrosplenial cortex is available (Oh and Jagust, 2013; Park et al., 2013) in contrast to reduced deactivations in older adults in other regions of the posteromedial cortex (Maillet and Rajah, 2014; Miller et al., 2008; Park et al., 2013). Yet, aging is associated with thinning of the retrosplenial cortex (Fjell et al., 2013, 2014), diminished white-matter integrity of the fiber bundle connecting to the medial temporal lobe (Sala et al., 2012; Westlye et al., 2010) and marked source memory decline (Schacter et al., 1991, 1994), which relies on retrosplenial activity (Staresina and Davachi, 2006). Patients with Alzheimer's disease and mild cognitive impairment have been shown to have early retrosplenial hypometabolism (Chételat et al., 2016; Nestor et al., 2003), which again has been related to memory performance (Desgranges et al., 2002). The retrosplenial cortex also seems fundamental for memory consolidation (see Vann et al. (2009) for a detailed review of retrosplenial function). Monkeys with experimentally induced retrosplenial lesions exhibited diminished retention of information—as well as retrograde memory impairments—despite no evidence for impaired learning (Buckley and Mitchell, 2016) largely agreeing with the available neuropsychological evidence (Maguire, 2001). Those findings are in coherence with the present observation of weaker durable memory activity at encoding with increasing age. With increasing age, the retrosplenial cortex—and the adjacent PCC—might become increasingly ineffective in binding information, affecting the likelihood of an association being stabilized into memory.

The age-related activity reduction could also reflect the use of different encoding mechanisms. Older adults are less prone to engage deep or elaborative processes, relying more on structure or saliency of the encoding material (Craik, 1983; Kamp and Zimmer, 2015). During encoding, the ventral portion of the posteromedial cortex is involved in a deeper and more elaborate processing of the material (Daselaar et al., 2003; Schacter et al., 2007). Different engagement of cognitive processes, such as visual imagery and self-referential processing, could also explain the extension of age-dependent effects into the ventral portion of the precuneus (Andrews-Hanna et al., 2010). In contrast to the posteromedial cortex, durable memory activity in the hippocampus was invariant to age. This finding agrees with previous reports suggesting that subsequent memory effects during encoding remain stable with age (Duverne et al., 2009; Park et al., 2013), even though shorter retention intervals were used in that studies.

Older adults showed higher activity in the left inferior and right superior medial frontal cortices during retrieval of durable memories. This may indicate that older adults engage cognitive control processes to a greater extent during the retrieval of acquired source associations (i.e., retrieval effort, Wang and Cabeza, 2016). Older adults could increasingly depend on these processes to boost weaker memories, whereas younger adults would rely on more automatically driven reinstatement processes. The left inferior frontal cortex is a central region for a plethora of control mechanisms (e.g., selection mechanisms) that take place during recollection (Badre and Wagner, 2007) and is sensitive to higher task demands (Badre et al., 2005). The retrieval of weaker associative memories will require a more effortful processing, requiring higher task demands, and as a consequence may strengthen the memory binding of the retrieved information, increasing the likelihood of being correctly remembered in a later test. Previous research has revealed that testing effects rely on higher activity in the prefrontal cortex (Liu and Reder, 2016; Liu et al., 2014) and increased fronto-temporal connectivity (Wing et al., 2013). Thus, testing effects seem to facilitate later memory through mechanisms that normally support memory success at encoding (Wing et al., 2013).

4.4. General remarks

Memory performance declined with age both when tested after a short and a long delay. This finding is in agreement with the existing literature that shows marked decline on associative memory performance. Yet the rate of forgetting was unrelated with age. Although system consolidation processes (including sleep dependent consolidation) seem affected by age (Scullin and Bliwise, 2015; Scullin et al., 2017; cf.; Aly and Moscovitch, 2010) is still unclear whether older adults exhibit steeper forgetting rates (Macdonald et al., 2006; Wheeler, 2000) or else, are independent of participants' age (Fjell et al., 2005; Meeter et al., 2005). In the present study, either the relatively prolonged postencoding delay ($\approx$90 minutes) preceding the first retrieval or testing the same material twice (Wheeler, 2000) might have led to age-invariant forgetting rates.

In addition to the vertex-wise analyses, the spatial overlap comparison showed that durable memory patterns of activity at encoding and at retrieval are largely unrelated to the canonical patterns associated with memory success. The analysis suggests that durable memory formation does not reflect a mere extension of the same intensity principle leading to initial memory success and underscores the presence of additional mechanisms at encoding—and at short delay retrieval—involved in the establishment of long-lasting memories. Altogether, our results concur with previous studies such as in Wagner et al. (2016) where the authors showed that the formation of durable memories is supported both by an extension of the activity-based patterns leading to encoding success as well as by the presence of additional mechanisms that involve retrieval-related regions.

Testing the same memories twice allowed us to define prospectively memory durability—compared with studies that test half of the encoding material at each test. Yet the followed approach may induce testing effects, boosting weaker memories (Wagner et al., 2016), and making it difficult to interpret the retrieval results. Though the methodology also affects trial sorting at encoding, the impact is limited as reliable patterns of activity were associated with durable memory encoding. The main limitations of the study are inherent to the field, most importantly the correlational nature of the fMRI technique as well as the lack of longitudinal information.

5. Conclusions

The present study suggests that partially independent mechanisms support durable memories and initial memory success. Long-lasting memories rely on DMN and higher visual processing nodes at encoding and on frontal and insular activity during retrieval, possibly, to some degree, reflecting re-encoding processes. Further, older adults showed lower posteromedial activity, encompassing the retrosplenial cortex as well as adjacent posterior cingulate and precuneus regions associated with encoding and higher frontal activity during retrieval of durable memories. The age results may reflect an increased difficulty to integrate new information and a possibly beneficial effect of cognitive control mechanisms. However, whether the latter represents a compensatory mechanism is still unclear. Further multimodal studies are needed to better understand the association between the encoding and retrieval mechanisms and the ongoing long-term system consolidation processes such as overnight memory reactivation.

Disclosure statement

The authors have no conflicts of interest to disclose.

Acknowledgements

This work was supported by the Department of Psychology, University of Oslo (to K.B.W., A.M.F.), the Norwegian Research Council (to K.B.W., A.M.F.), and the project has received funding from the European Research Council's Starting Grant and Consolidator Grant scheme under grant agreements 283634 and 725025 (to A.M.F.) and 313440 (to K.B.W.). The authors would like to acknowledge Sara Fernández-Cabello and the anonymous reviewers for helpful comments. They are profoundly grateful to Dr Hongkeun Kim for providing the meta-analytical ALE maps.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.neurobiolaging.2017.08.017.

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