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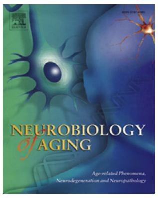

Spatial updating deficits in human aging are associated with traces of former memory representations

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ABSTRACT

The ability to update spatial memories is important for everyday situations, such as remembering where we left our keys or parked our car. Although rodent studies have suggested that old age might impair spatial updating, direct evidence for such a deficit in humans is missing. Here, we tested whether spatial updating deficits occur in human aging, whether the learning mode influences spatial updating, and what mnemonic mechanism underlies the presumed deficits. To address these questions, younger and older participants had to indicate the latest location of relocated items, following either incidental or intentional learning. Using eye tracking, we further quantified memory traces of the original and updated locations. We found that older participants were selectively impaired in recalling locations of relocated items. Furthermore, they depicted relatively stronger representations of the original locations, which were correlated with their spatial updating deficits. The findings demonstrate that stronger representations of former spatial contexts can impair spatial updating in aging, a mechanism that can help explain the commonly observed age-related decline in spatial memory.

1. Introduction

Previous learning can disrupt the recall of recently encoded information (Keppel and Underwood, 1962). This disruption—often termed proactive interference—pertains to the forgetting of information due to interference from the memory traces of events that occurred before the information to be remembered (Still, 1969). Studies from the last few decades show that susceptibility to proactive-interference increases with age (De Beni and Palladino, 2000; Lustig and Hasher, 2001; Lustig et al., 2001; May et al., 1999), suggesting that it may contribute to age-related memory deficits.

In the domain of spatial memory, increased susceptibility to proactive interference in old age has only been demonstrated in working memory tasks such as the retrieval of spatial sequences (Rowe et al., 2008). In addition, aging adversely affects path integration, the ability to update one's location during self-motion (Adamo et al., 2012; Allen et al., 2004; Harris and Wolbers, 2012; Stangl et al., 2018). However, it is important to study age-related proactive interference in long-term spatial representations because proactive interference may prevent the updating of essential, everyday spatial information, such as remembering where we left our keys or parked our car. Therefore, we aimed at investigating whether previous spatial learning could disrupt the retrieval of novel spatial information in older people. At present, such long-term age-related disruptions have only been observed in rodents (Wilson et al., 2004, 2006). These studies showed that in the aging hippocampus, spatial representations of previously learned environments can be abnormally maintained after the environment has changed (Wilson et al., 2004).

One important factor that could modulate susceptibility to proactive interference is the learning mode, that is, whether the encoding occurs incidentally or intentionally. Proactive interference has been demonstrated also in nonintentional memory processes (Lustig and Hasher, 2001), and it has been suggested that incidental encoding may even enhance age-related susceptibility to proactive interference in long-term associative memories (Merhav et al., 2014). Therefore, we further aimed at testing whether age-related deficits in spatial updating are more pronounced following incidental, rather than intentional, learning.

What could be the cause for the presumed age-related impairment in updating spatial information? The inhibitory deficit hypothesis (Hasher and Zacks, 1988) proposes that increased susceptibility to environmental distractions in older adults is due to

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an age-related reduction of the ability to suppress irrelevant information. Particularly, Hasher et al. (1999) proposed that age-related deficits in suppressing old information in the face of new goals underlie proactive interference in aging (Hasher et al., 1999). In the same line, findings in humans (Hasher et al., 2002; May and Hasher, 1998) and rodents (Wilson et al., 2006) have indicated that traces of previous experiences hinder the ability to retrieve the later memories, in old age. Accordingly, we hypothesized that inefficient suppression of previous spatial representations prevents spatial updating in aging. We thus aimed at testing whether the presumed deficit in spatial updating in older adults is associated with increased traces of the spatial information acquired previously.

To assess spatial updating deficits in aging, we designed a task in which items were relocated, overnight, on a 2-dimensional layout. Afterward, young and older adults had to indicate the latest locations of the items, and retrieval accuracy was compared to the retrieval accuracy of nonrelocated (control) items. To test the effect of learning mode on spatial updating, the item-location associations were either incidentally or intentionally encoded. To assess the proactive interference effect of the original locations on retrieval of the updated locations, we calculated the distance of the behavioral responses to the original loci relative to the updated loci (Nardini et al., 2008). To further quantify the spatial representations of the relocated items, we analyzed eye fixations on the original and updated loci, as an index for spatial memories (Hannula et al., 2010). To preview, we found that older adults depicted deficiencies in spatial updating abilities, which were associated with increased representation of the original locations.

2. Experiment 1

2.1. Materials and methods

2.1.1. Participants

Thirty two young and 30 older adults were recruited for experiment 1 (Table 1). In the incidental learning condition, there were 16 young (mean age was 24.38 ± 1 year old, 8 women) and 15 older (mean age was 70.33 ± 1.25 year old, 7 women) participants. In the intentional learning condition, there were 16 young (mean age was 22.5 ± 0.67, 8 women) and 15 older (mean age was 69.8 ± 0.9, 8 women) participants. Participants signed an informed consent form and were paid €6.50 per hour. The experiment was approved by the local ethics committee. All participants performed the Montreal Cognitive Assessment [MoCA] (Nasreddine et al., 2005) and the divided attention test from the test battery of attentional performance (Zimmermann and Fimm, 2002) to screen for mild cognitive impairment and attentional deficits, respectively. In addition, 2 older participants were excluded from experiment 1; one older female was excluded from the incidental-learning condition due to poor performance in the MoCA test [lower than 23 (Luis et al., 2009)], and one older male was excluded from the intentional-learning condition due to poor spatial learning for the control items (mean distance-error larger than 2 standard deviations above the group mean).

2.1.2. Experimental design

The aims of experiment 1 were to test whether older adults are impaired in updating long-term spatial memories and to test the effects of the learning mode on spatial updating abilities. An additional aim was to assess whether memory traces of the original loci influence the retrieval of the updated locations.

The stimuli for the task were presented in a square white area (30 × 30 cm), containing 36 cells, formed by a 6 × 6 invisible grid, and 24 images of everyday objects (e.g., furniture, musical instrument, clothes, toys, fruits, etc…). Each image appeared in a defined cell within the square scene, forming a specific item-location association. Additional 7 full-screen images were used for practice purposes. The task was displayed on a standard PC monitor, via MATLAB (2013b).

The experiment took place over 2 consecutive days and comprised 3 sessions: “Encoding 1,” “Encoding 2,” and “Retrieval” (Fig. 1A). “Encoding 1” took place on the first day. In this session, participants were presented with 12 item-location associations (Fig. 1A, top). The presentation of the 12 associations was repeated 6 times in different pseudorandom orders.

“Encoding 2” took place on the second day, during which 24 item-location associations were presented. Twelve of the associations contained images that were already shown during “Encoding 1,” but in different locations. Thus, those items served as the relocated condition (Fig. 1A). The other 12 item-location associations contained novel images and served as the control condition (Fig. 1A). There was no overlap between the 24 loci of “Encoding 2” and the 12 loci of “Encoding 1.” As in “Encoding 1,” the presentation of the 24 associations was repeated 6 times in different pseudorandom orders. The item-location associations of the control and the relocated conditions were counterbalanced between participants to avoid a mnemonic bias toward specific items and/or locations. The mean distance from the original to the updated loci was 19.36 ± 0.92 cm (min = 14.14 cm, max = 26.93 cm) and was similar across the 2 counterbalanced conditions ($t(22) = 1.34$, $p = 0.195$).

In the Incidental learning condition, participants were not informed that the task involves mnemonic skills. Instead, they were told that the task assesses age-related differences in perceptual judgment over time and repetitions. In the first 3 presentation rounds of each encoding session, participants were instructed to assess the colorfulness of each image by pressing the corresponding key (1 = less than 2 colors, 2 = 2 colors, 3 = more than 2 colors). In the last 3 presentation rounds of each encoding session, participants had to assess the size of each image by pressing the corresponding key (1 = smaller than a cat, 2 = about the size of a cat, 3 = bigger than a cat). We changed the perceptual task between the first and the second halves of the 6 repetitions to maintain the motivation and the attention of the participants, during encoding. Each image remained on the screen until the participant pressed the key and then the next image appeared. Both Encoding 1 and Encoding 2 started with 7 practice trials, using 7 full-screen size images.

In the Intentional learning condition, encoding was similar to the incidental learning condition, but participants were explicitly informed that the task assessed spatial memory and were asked to memorize the precise location of each item to subsequently retrieve it. To generate a similar experience to the incidental learning mode, we asked the participants to indicate the location of each image on the screen, by pressing the corresponding key (1 = top; 2 = middle; 3 = bottom, in the first 3 presentations, and 1=left; 2=middle; 3=right, in the latter 3 presentations). As in the incidental encoding, we changed the task between the first and the second halves of the 6 repetitions to maintain the motivation and the attention of the participants, during encoding.

Retrieval took place on day 2, 2 hours after the end of the second encoding, and was identical for both learning modes. In each retrieval-step (Fig. 1A), participants saw a full-screen version of one of the 24 images that had been presented earlier that day. After hitting the space bar, the image disappeared and the participants were instructed to click on the precise location on the screen in which the item had appeared 2 hours earlier, at “Encoding 2”—this will be referred to as the updated (second) location. Participants used the computer mouse to move a cursor on the screen and to click at the selected locations. If participants did not remember the location, they had to guess.

Table 1
Mean age (±SE), gender distribution (female ∖ male), MoCA scores and % miss trials at the TAP, in the young and older participants, in experiments 1 and 2

	Mean age		Gender F∖M		MoCA		TAP, % missed	
	Young	Old	Young	Old	Young	Old	Young	Old
Experiment 1, incidental	24.38 ± 1	70.33 ± 1.3	8 ∖ 8	7 ∖ 8	28.2 ± 0.4	27.2 ± 0.6	1.2 ± 0.2	2.2 ± 0.4
Experiment 1, intentional	22.5 ± 0.7	69.8 ± 0.9	8 ∖ 8	8 ∖ 7	28.3 ± 0.3	27.0 ± 0.5	1.4 ± 0.2	2.1 ± 0.3
Experiment 2	26.1 ± 0.8	69.4 ± 0.8	10 ∖ 9	10 ∖ 9	27.7 ± 0.2	27.2 ± 0.4	1.2± 0.1	2.1 ± 0.3

Key: MoCA, montreal cognitive assessment; TAP, test battery of attentional performance.

Retrieval accuracies for the control and relocated conditions were quantified as the mean Euclidean distances from the responses to the correct locations. We used an analog measure of distance errors, to probe the quality, rather than the quantity of the spatial memories (Ma et al., 2014). The experiment comprised 2 between-subject factors of (1) age (young vs. old) and (2) learning mode (incidental vs. intentional) and one within-subject factor of item-type condition (control vs. relocated items).

2.1.3. Statistical analyses

The dependent behavioral variables were (1) retrieval accuracy and (2) the effect of the original loci on retrieval of the updated ones (i.e., the proactive interference effect). Retrieval accuracy was quantified as the mean Euclidean distance between the response and the correct, updated location. The degree to which memory traces of the original locations affected participants' responses was assessed by the relative proximity to the original locations. If distance to the updated location is dUpd and distance to the original location is dOrig (Fig. 2A), then the relative proximity (i.e., 1/distance) to the original location (rproxOrig) is given by: $rProxOrig = \frac{1/dOrig}{1/dUpd+1/dOrig} = \frac{dUpd}{dUpd+dOrig}$ (Nardini et al., 2008) (Fig. 2A). Accordingly, a higher rProxOrig value reflects a greater effect of the original location on retrieval of the updated loci. If the distance error to the updated and to the original loci are the same, then rProxOrig = 0.5. If the distance error to the original location is larger than the distance to the updated location, then 0 < rProxOrig <0.5. If the distance error to the original location is smaller than the distance to the updated location, then 0.5 < rProxOrig <1. SPSS (IBM SPSS Statistics 21) was used for analyses of variances (ANOVAs) of multifactorial effects, which were followed by post hoc, corrected pairwise comparisons. G*Power (3.0.10) was used for sensitivity analyses to calculate effect sizes. Notably, the analysis of experiment 1 was performed twice, first with 50 participants and then with 62 participants, as we added 12 participants in response to the review process. As the data were analyzed twice, the alpha level was adjusted to 0.025, according to Bonferroni correction for 2 significance tests.

2.2. Results

To test for age-related deficits in spatial updating, the distance errors to the correct locations were analyzed in a mixed model ANOVA with one within-subject factor (the relocated condition vs. the control condition) and 2 between-subject factors (age and learning mode), (Fig. 1B). Analysis of between-subject factors revealed a significant main effect of age [F (1, 58) = 24.89, $p < 0.001$, effect size f = 0.86], indicating larger distance errors among older adults. The analysis also revealed a significant main effect of learning mode [F (1, 58) = 10.42, $p = 0.002$, effect size f = 0.57], indicating larger distance errors following incidental encoding. The analysis revealed no learning mode × age interaction [F (1, 58) = 2.48, $p = 0.12$].

Analyses of the within-subject factor revealed a significant main effect of condition [F (1, 58) = 30.50, $p < 0.001$, effect size f = 0.44], indicating larger distance errors in the relocated condition. The analysis revealed a significant condition × age interaction effect [F (1, 58) = 11.7, $p = 0.001$, effect size f = 0.31]. Pairwise comparisons indicated larger distance errors in the relocated condition, among the older participants [F (1, 58) = 38.73, $p < 0.001$, effect size f = 0.44] but not among the young [F (1, 58) = 2.29, $p = 0.136$], (Fig. 1B). Thus, the interaction reveals age-related impairment in the ability to update long-term spatial representations. The analysis revealed a nonsignificant condition × learning mode interaction [F (1, 58) = 5.21, $p = 0.026$] according to alpha level of 0.025. The

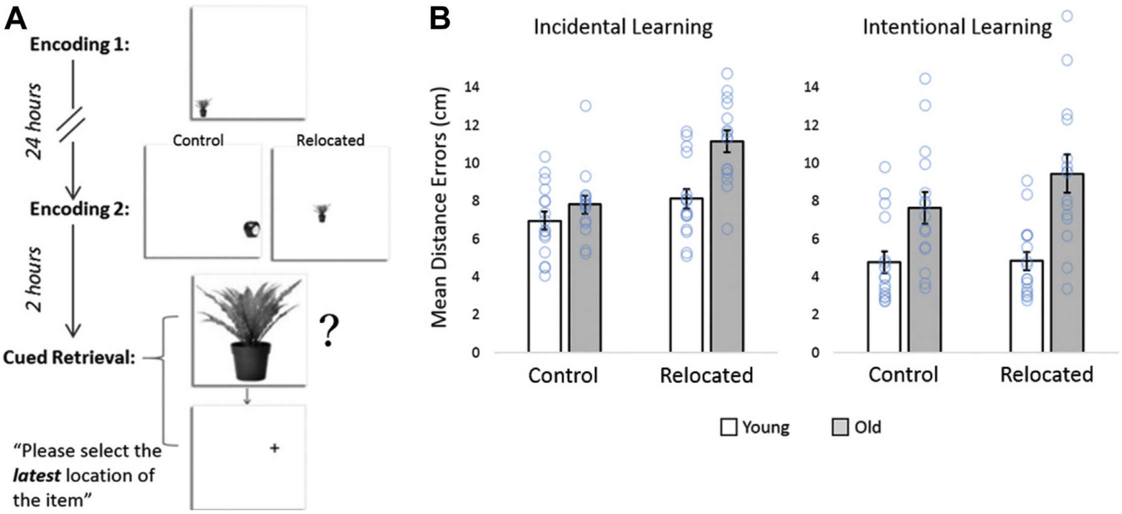

Fig. 1. Age-related deficits in spatial updating. (A) Experimental procedure. In the relocated conditions, the items were relocated, overnight. At retrieval, participants had to recall the latest locations of the relocated and the control (nonrelocated) items, as appeared on the 2nd day. (B) Age-related deficits in spatial updating. The distance errors to the correct locations revealed that the older participants were selectively impaired in retrieving the locations of relocated items. Data are presented as mean ± SE.

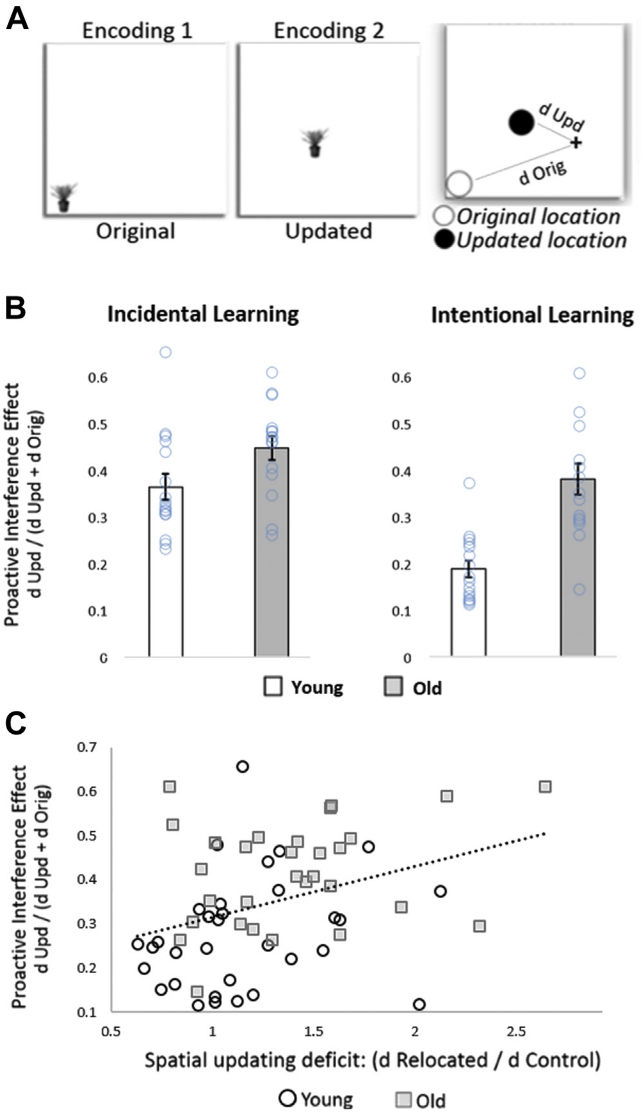

Fig. 2. The proactive interference effect by the original locations on retrieval of the updated loci. (A) The proactive interference effect. The effect of the original loci on retrieval of the updated loci was defined by the relative proximity to the original location (d Upd/[d Upd + d Orig]). (B) The proactive interference effect by the original locations on retrieval of the updated loci was stronger among the older adults. (C) The effect of the original loci on retrieval of the updated loci was positively correlated with spatial updating deficits (d relocated/d control). Data are presented as mean ± SE.

analysis also revealed no condition × age × learning mode interaction [F (1, 58) = 0.138, p = 0.711]. Thus, the deficit in updating spatial representation among older adults was not restricted to a specific learning mode (Fig. 1B).

Next, to assess the proactive interference effect, we explored whether the original spatial representations of the relocated condition interfered with the ability to retrieve the updated locations. The effect of the original loci on the retrieval of the updated loci was defined by the relative proximity to the original location (see Section 2.1.3, and Fig. 2A). The relative proximities were analyzed across age groups and learning modes. A 2-way ANOVA revealed a main effect of age [F (1, 61) = 27.09, $p < 0.001$, effect size f = 0.89], indicating higher proactive interference effect among older adults (Fig. 2B). There was also a significant main effect of learning mode [F (1, 61) = 21.62, $p < 0.001$, effect size f = 0.82], indicating a stronger proactive interference effect following incidental learning. The ANOVA revealed no age × learning mode interaction [F (1, 58) = 4.179, p =0.045] according to alpha level of 0.025. The fact that in most of the cases, the relative proximity to the original location was smaller than 0.5 suggests that in both groups, the responses were closer to the updated location than to the original location. However, the higher values among the older participants indicate a stronger effect of the original loci on the retrieval of the updated ones (Fig. 2B).

To test whether the effect of the original loci on retrieval of the updated loci is associated with a spatial updating deficit, we correlated the relative proximity to the original locations with the spatial updating deficit. The latter was defined as the mean distance errors in the relocated condition divided by the mean distance errors in the control condition (i.e., dupd/dcon). Analysis of both age groups in both learning modes revealed an overall positive correlation between the relative proximity to the original location and the spatial updating deficit (r = 0.35, n = 62, p = 0.005) (Fig. 2C). Next, we ran moderator analyses to test whether the correlation between the proactive interference effect and the spatial updating deficit is modified by (1) age, (2) learning mode, or by (3) age × learning mode interaction. All moderator analyses indicate that the addition of the interaction terms did not significantly increase in the variation explained (age: 0.4%, p=0.63; learning mode: 1.8%, p=0.28; age × learning mode: 4.3%, p=0.086). Thus, the experimental factors did not modify the overall correlation between the proactive interference effect and the spatial updating deficit.

3. Experiment 2

3.1. Materials and methods

The aim of experiment 2 was to further explore the mnemonic mechanism that underlies the presumed age-related deficit in spatial updating. Given that eye fixations have been established as a sensitive indicator for the strength of memory representations (Hannula et al., 2010), we used eye movement recording to quantify the memory traces for the original and the updated locations of items in the relocated condition.

3.1.1. Participants

Nineteen young (mean age was 26.1 ± 0.8 year old, 10 women) and 19 older (mean age was 69.4 ± 0.8 year old, 11 women) participants were recruited for experiment 2 (Table 1). The participants in experiment 2 did not take part in experiment 1 and thus were naïve to the experimental procedure. As in experiment 1, participants performed the MoCA (Nasreddine et al., 2005) and the divided attention test from the test battery of attentional performance (Zimmermann and Fimm, 2002) to screen for mild cognitive impairment and attentional deficits, respectively. According to our exclusion criteria (as mentioned previously), 2 additional older participants were excluded from the experiment, one due to poor performance in the MoCA test and one due to poor spatial learning.

3.1.2. Experimental procedure

The behavioral task of experiment 2 was similar to the incidental learning task of experiment 1, but several changes were implemented to adapt the task for eye-tracking data collection. Specifically, to better quantify the memory traces in the relocated condition, we increased the number of relocated items in the task. Yet, to avoid intense memory load and spatial overlap, we did not increase the number of control items.

Twenty nine images of everyday items were presented in a square white scene (28 × 28 cm) that contained 49 cells, formed by a 7 × 7 invisible grid. Each image appeared within a defined cell, forming a specific, item-location association. Thus, the areas in which the images were presented in experiment 2 (4 × 4 cm) was smaller than the areas in experiment 1 (5 × 5 cm). None of the 29 images was presented at the central cell, which was used for the calibration of pupil detection between trials. Three further images were used for practice purposes, and were presented in the central cell of the square. In the task, 19 items served for the relocated condition and thus were presented on 2 different locations, across the 2 encoding sessions (Fig. 1A). The other 10 items served for the control condition. The relocated and control sets were counterbalanced between participants to avoid a mnemonic bias toward specific items and/or locations. The mean distance from the original to the updated loci in the relocated condition was 19.06 ± 0.49 cm (min = 14.42 cm, max = 24.33 cm) and was similar across the 2 counterbalanced sets [t (36) = 0.79, $p = 0.432$]. In both Encoding 1 and Encoding 2, each item was presented 4 times, each time in a different pseudorandom order. Each presentation had a fixed duration of 3 seconds. In the first 2 presentations, participants had to assess the colorfulness of each image, as described in experiment 1. In the latter 2 presentations, participants had to assess the size of each image as described in experiment 1. Both encoding sessions started with 3 practice trials.

In each retrieval trial (Fig. 4A), participants first saw a full-screen version of one of the 29 images from Encoding 2, for 1.5 seconds. Then, the image disappeared, and for 2.5 seconds, the participants had to think where the item appeared last. Then, a black screen appeared for 200 ms, with a cross-shaped cursor. Then, the cursor remained on the screen and participants used the computer mouse to select the second location of the item, within the white square (Fig. 4A). The retrieval session started with 3 practice steps, using the images from the practice steps of the Encoding phases. In each retrieval trial, the cursor appeared in a different random location on the screen.

3.1.3. *Eye movement recording*

In Experiment 2, eye movement recording was performed using a head-mounted Eyelink II (SR Research Ltd). Participants were positioned 65–70 cm from the screen, thus the stimuli (items) in the scene, which filled 4 cm × 4 cm areas, subtended visual angles of 3.1°–3.5°. Pupils were detected using cameras placed below the eyes. Because we used a head-mounted eye tracker, participants could move their head (although were asked to sit still). To detect head motion, infrared markers were placed on the 4 corners of the monitor. These markers were detected by the head camera and used to correct for head motion.

Before each session, participants performed a calibration, which included fixation on 9 points on the screen and was followed by a validation test. Successful validation was defined by a maximum average error of 1 cm, compared to the calibration grid. A drift correction took place at the beginning of each trial (both encoding and retrieval), in which participants had to gaze at a circle in the middle of the screen and press the space bar. The maximum acceptable error value for the drift correction was 1°, otherwise, participants had to repeat the calibration steps described previously.

Eye movements were recorded at a sampling rate of 250 Hz. Saccades, blinks, and fixations were calculated in the following way: Saccades were eye movements greater than 0.1° visual angle, faster than 30°/s velocity and $8000°/s^2$ acceleration. Blinks were defined as missing pupil data over 3 consecutive samples. Fixations consisted of all other recordings, and we added a cutoff of 50 ms minimum duration.

Eye-tracking data were collected during Encoding 2 and the retrieval sessions. The areas of interest were the original and the updated loci of the 19 items of the relocated condition and the single loci of the items in the control condition. The areas of interest were defined by a cell-width diameter circle around the centers of the cells in which the items were presented. The analysis comprised one between-subject factor of age (young vs. old) and one within-subject factor of areas of interest (original loci vs. updated loci).

3.1.4. *Statistical analyses*

As in experiment 1, the dependent behavioral variables were (1) retrieval accuracy and (2) the effect of the original loci on retrieval of the updated ones (see Experiment 1, section 2.1.3). The dependent eye-movement variables were number of fixations and number of stimuli containing fixations on the areas of interest. Eye-tracking data were processed using R (version 3.0.2). SPSS (IBM SPSS Statistics 21) was used for ANOVAs of multifactorial effects, followed by corrected pairwise comparisons. The robust linear regression was analyzed via R.

3.2. *Results*

In experiment 1, we found that following incidental learning, older participants were impaired in their ability to update spatial information. We also found that among the older participants, there was a greater influence of the original spatial context on retrieval of the updated locations. The later assessment of relative proximity to the original locations, however, can only partially reveal the spatial representations of an item due to the following reasons: (1) if one item is associated with several locations, a single behavioral response may not fully reflect the spatial representations of it. (2) Participants were explicitly instructed to retrieve the latest (updated) location of the items. Accordingly, it could be that participants remembered the original location but explicitly avoided responding near it. (3) We cannot infer whether the higher relative proximity to the original loci among the older participants is due to poor memory of the updated loci or due to enhanced memory of the original loci. (4) The behavioral response may not reflect implicit spatial representations.

To overcome these limitations and to further investigate the mnemonic mechanism which underlies the age-related deficits in spatial updating, we used eye-tracking to quantify the memory representations for the original and the updated loci of the items. Eye-movement behavior, and particularly fixation, is known to be influenced by previous experiences and thus can serve as a tool to assess memories [for review see (Hannula et al., 2010)]. Eye-tracking behavior can also detect implicit memories (Hannula et al., 2010) and allows an assessment of several spatial representations per item.

3.2.1. *Behavioral performance*

First, to assess behavioral performance, we analyzed the distance errors in the control and relocated conditions, in both age groups (Fig. 3A). A mixed model ANOVA revealed a significant effect of age [F (1, 36) = 9.55, $p = 0.004$, effect size f = 0.68], indicating larger distance errors among older participants, and a significant effect of condition [F (1, 36) = 26.89, $p < 0.001$, effect size f = 1.0], indicating larger distance errors for items in the relocated condition. The analysis also revealed a significant age × condition interaction [F (1, 36) = 6.05, $p = 0.019$, effect size f = 0.23]. Pairwise comparisons indicated larger distance errors among older adults in the relocated condition [F (1, 36) = 15.25, $p < 0.001$, effect size f = 0.9] but not in the control condition [F (1, 36) = 2.97, $p = 0.093$]. Therefore, in line with experiment 1, the behavioral findings of Experiment 2 demonstrate age-related deficits in the ability to update long-term spatial representations (Fig. 3A).

We then compared the influence of the original spatial representations on retrieval of the updated ones (i.e., the proactive interference effect) between both age groups. The relative proximity to the original locations was higher among the older participants [t (36) = 3.575, $p = 0.001$, effect size d = 1.53] (Fig. 3B), indicating a stronger proactive interference effect among the older adults. A correlation analysis of both age groups revealed that the relative proximity to the original loci was positively correlated with the spatial updating deficits (r = 0.363, n = 38, $p = 0.025$), (Fig. 3C). However, subsequent analyses of each age group separately revealed no significant correlation between the relative proximity to the original loci and the spatial updating deficits (young: r = 0.43, n = 19, $p = 0.067$; older: r = 0.14, n = 19, $p = 0.57$). No significant difference was found between the 2 correlation coefficients (z = 0.9, $p = 0.18$).

3.2.2. Fixations during retrieval

Retrieval of the spatial representations could occur throughout the whole retrieval trial. Accordingly, we analyzed fixations from the whole retrieval trial except for the 200 ms when the cursor first appeared, to avoid analysis of fixations on the location in which the cursor was shown (Fig. 4A).

First, to assess the effect of age on memory representations for nonconflicting spatial information, we analyzed age-related differences in spatial representations of items in the control condition. The items of the control condition did not appear during Encoding 1 and thus were associated with a single location each. The young participants showed more control items with fixations on the correct areas of interest (t (36) = 2.03, $p = 0.049$, effect size d =0.59) (Fig. 4B), thus depicting superior spatial memory in the control condition.

Then, to explore what mnemonic mechanism contributes to the poor spatial retrieval in the relocated condition, among older adults, we tested for age-related differences in the spatial representations of the relocated items. We compared the number of items that triggered fixations on their original loci with the number of items that triggered fixations on their updated loci across the 2 age groups (Fig. 4B). Notably, there was no difference in the number of fixations per item, and no difference in the duration of fixations between the age groups [t (36) = 1.36, $p = 0.18$ and t (36) = 0.8, $p = 0.43$, respectively]. A mixed model ANOVA revealed a main effect of location [F (1, 36) = 179.91, $p < 0.001$, effect size f = 1.0] indicating more items with fixations on the updated locations. There was a significant effect of age [F (1, 3 6) = 4.753, $p = 0.036$, effect size f = 0.38] indicating more items with fixations among young participants. Importantly, there was a significant age × location interaction [F (1, 36) = 10.848, $p = 0.002$, effect size f = 0.38] (Fig. 4B). Pairwise comparisons revealed that the older adults showed fewer items with fixations on the updated loci [F (1, 36) = 9.28, $p = 0.004$, effect size f = 0.33] but not on the original loci [F (1, 36) = 1.03, $p = 0.316$]. To test what proportion of relocated items which triggered fixations on the original loci, we divided the number of items containing fixations on the original loci by the number of items containing fixations on the original + the number of items containing fixations on the updated loci (i.e., original/[original + updated]), (Fig. 4C). We found that the proportion of items which triggered fixations on their original loci was higher among the older participants [t (36) = 2.19, $p = 0.035$, effect size d = 0.76], (Fig. 4C).

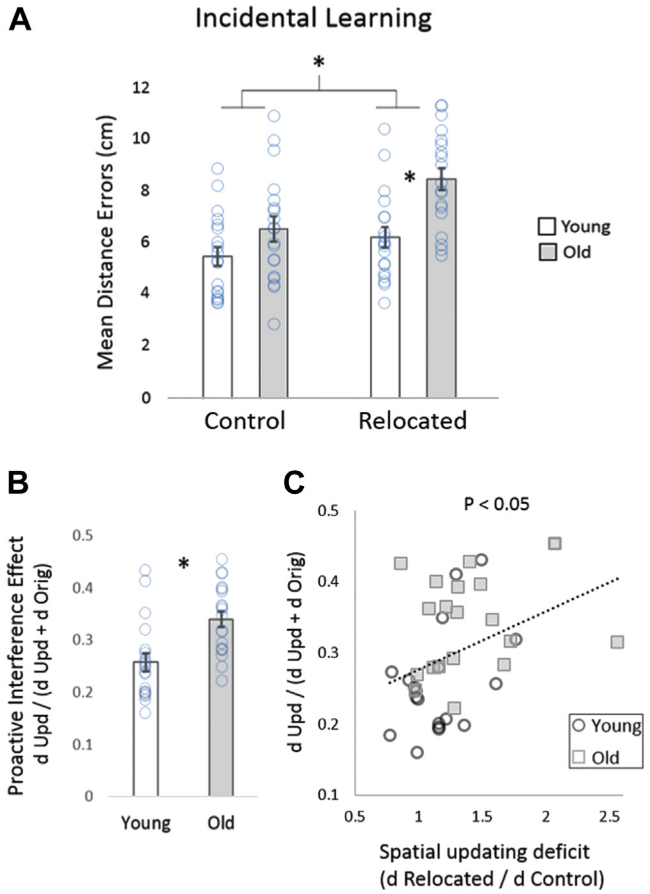

Fig. 3. Behavioral findings of experiment 2. (A) Age-related deficit in spatial updating. As in experiment 1, the older participants were selectively impaired in recalling the locations items from the relocated condition. (B) The proactive interference effect. The effect of the original loci on retrieval of the updated loci was stronger among the older participants. (C) The effect of the original loci on retrieval of the updated loci was positively correlated with spatial updating deficits. Data are presented as mean ± SE. *$p < 0.05$.

Last, we tested whether the amount of items which triggered fixations on their original loci was predictive of spatial updating deficits. Therefore, we correlated the relative number of items containing fixations on the original loci (nori/nupd) with the spatial updating deficit, which defined by dupd/dctrl (Fig. 4D). To minimize the effect of outlier responses, we applied a robust correlation analysis, which revealed a significant positive correlation between the proportion of items containing fixations on the original loci and the spatial updating deficits (Fig. 4D, r = 0.597, n = 38, $p < 0.001$). Then, we ran the same correlation analyses in each age group separately. The correlation analyses revealed significant positive correlations in both young and older participants (r = 0.495, n = 19, $p = 0.031$; r = 0.485, n = 19, $p = 0.035$; respectively). The positive correlations suggest that the spatial updating deficit is associated with elevated traces of the original spatial context.

3.2.3. Fixations during the “Encoding 2” session

Was the increase in original spatial representations among the older participants already manifested before the retrieval process? To address this question, we measured the number of fixations on the original loci, during the “Encoding 2” session while the updated loci were presented. The results revealed that during “Encoding 2,” older participants fixated more on the original loci than the younger participants [1.53 ± 0.39 and 0.47 ± 0.19, respectively; t (36) = 2.46, $p = 0.022$, effect size d = 1]. Given that a general age-related increase in the number of fixations could have caused this result, we normalized the numbers of fixations on the original loci by the number of fixations that were *not* on the updated loci ($\frac{nf_{Ori}}{nf_{total}-nf_{upd}}$). The normalized number of fixations on the original loci was still significantly larger for the older participants (t (36) = 3.1, $p = 0.005$, effect size d = 1.35). Notably, the age groups did not differ in the number of fixations on the updated loci, at “Encoding 2” [t (36) = 0.12, $p = 0.91$].

4. Discussion

In the present study, we found that the older participants were selectively impaired in recalling locations of items that had appeared at a different set of locations, 24 hours earlier. This finding indicates that updating long-term spatial representations is impaired in old age and is consistent with the increased rigidity of hippocampal place cell firing, observed in rodents (Wilson et al., 2004). So far, age-related deficits in updating spatial information were found in the retrieval of spatial sequences (Rowe et al., 2008), and during path integration (Adamo et al., 2012; Allen et al., 2004; Harris and Wolbers, 2012; Stangl et al., 2018), which could reduce the accuracy and stability of positional computations. Critically, however, in all of these studies, spatial updating operated on transient working memory representations over periods of seconds. In contrast, the present study provides the first evidence that aging also affects our ability to update long-term memory representations that may have undergone overnight consolidation. We also found that the age-related deficits in spatial updating abilities were associated with relatively stronger spatial representations of the former experience.

In experiment 1, the learning-mode factor did not significantly alter the levels of the age-related deficit in spatial updating. Thus, the age-related impairment in spatial updating was not restricted to a specific encoding procedure. It could be that the similarity of the spatial updating deficit across the 2 learning modes was due to the specific encoding procedures that were used in the present study (indicating the perceptual attributes vs. the locations of the items). Nevertheless, the learning mode factor significantly influenced the ability to retrieve spatial memories.

In experiment 1, stimuli were presented until participants responded. In contrast, in experiment 2, we used fixed encoding durations. Yet, the behavioral findings of experiment 2 showed age-related susceptibility to proactive interference, as was found in experiment 1. This suggests that the age-related deficits in spatial updating observed in experiment 1 were not due to differences in encoding durations.

In both experiments 1 and 2, we explored the mnemonic mechanism that contributes to the age-related deficits in spatial updating. We found that among older participants, the retrieval of the updated locations was highly affected by traces of the original loci of the items (Figs. 2B and 3B). We also found spatial updating deficits were correlated with a stronger effect of the original loci on the retrieval of the updated loci (Figs. 2C and 3C).

In experiment 2, we used eye fixations to explore the mnemonic mechanism that could underlie the age-related deficits in spatial updating. Specifically, we tested whether the age-related deficit in spatial updating was associated with increased representations of the original spatial information, relatively to the updated representations. We found that during retrieval, the relative amount of items that triggered fixations on their original spatial representation was higher among the older participants (Fig. 4C, section 3.2.2). Moreover, the relative number of items containing fixations on the original locations was positively correlated with the deficit in spatial updating abilities (Fig. 4D, section 3.2.2).

Similarly, during “Encoding 2,” while the updated loci were presented, the older participants exhibited more fixations on the original loci of the items (section 3.2.3). The latter finding implies that among the older adults, the exposure to the updated locations may have further elaborated the original spatial contexts. Moreover, it indicates that age-related proactive-interference is not simply a failure in retrieval because age-related alternations in memory representations emerged already at the presentation of the conflicting locations.

Overall, the patterns of fixations and relative proximities of responses suggest that traces of the original spatial representations may hinder spatial updating in old age. The increased representation of the original loci in older participants could be explained by (1) inefficient suppression of the original experience or by (2) enhanced consolidation of it. Several lines of evidence point to

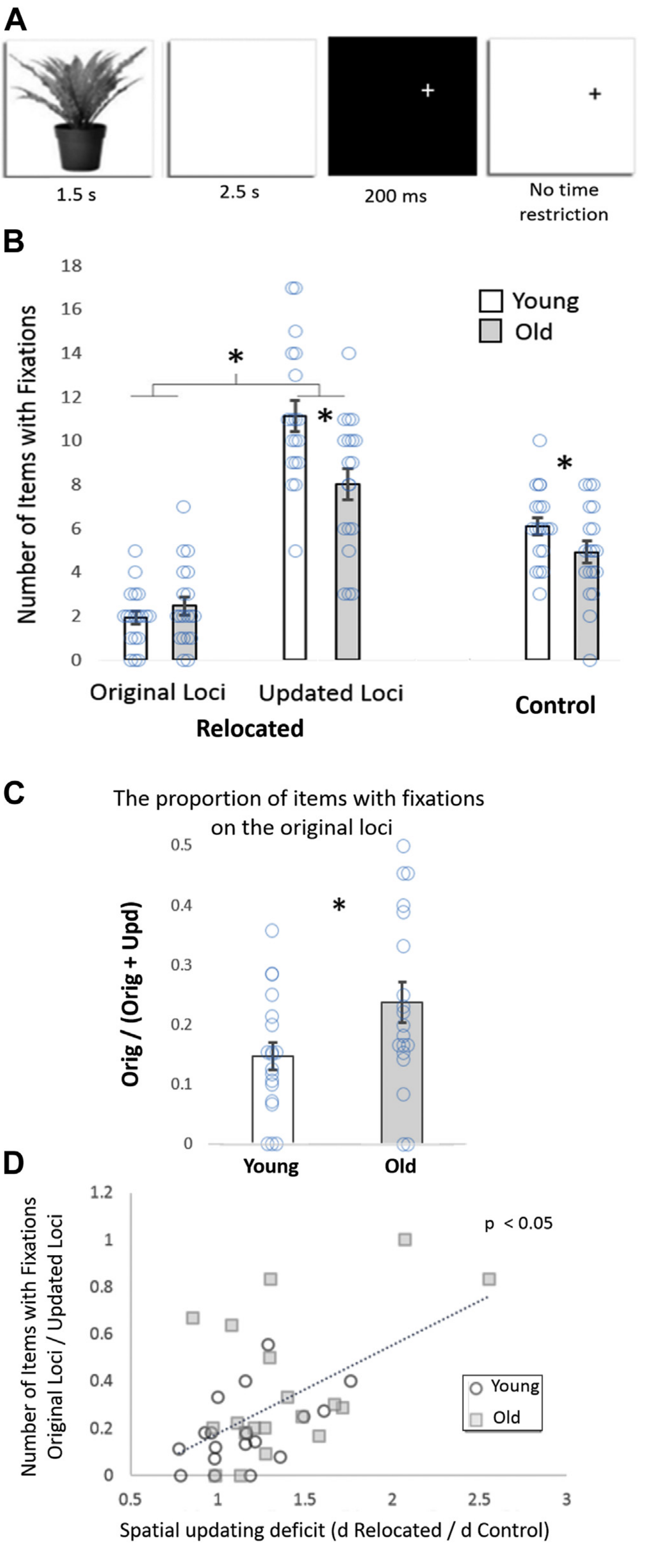

Fig. 4. Eye tracking findings. (A) Retrieval procedure. The timeline of a retrieval trial in experiment 2. (B) The amount of items with fixations on the original and updated locations. The older participants showed fewer items which triggered fixations on their updated location. (C) The relative amount of items that triggered fixations on their original loci was higher among the older adults. (D) Spatial updating deficit is associated with stronger representations of the former spatial context. The relative amount of items that triggered fixations on their original loci was positively correlated with individual spatial updating deficit. Data are presented as mean ± SE. $^{*}p < 0.05$.

inefficient suppression as the key mechanism. First, it has been suggested that overnight sleep-dependent consolidation processes are reduced in old age [(Scullin, 2013), for review, see (Harand et al., 2012)]. Moreover, studies on word recall have demonstrated that the ability of older humans to escape the past and redirect to the present is impaired (Hasher et al., 2002, May and Hasher, 1998). And finally, findings in old rodents show that encoding of new spatial contexts was weakened by proactive interference from representations of already-stored contexts (Wilson et al., 2006).

Notably, eye movement behavior does not only reflect memory representations (Hanulla et al.,) but also attention levels (Corbetta, 1998; Corbetta et al., 1998) and importantly, levels of spatial attention (Van der Stigchel and Theeuwes, 2005). Moreover, age-related differences in mnemonic abilities can be driven by selective age-related attention deficits (Verhaeghen and Cerella, 2002). Therefore, we propose that the age-related changes in spatial updating, in the eye movement behavior in the present study, may stem from age-related shifts in attention level rather than in memory processes. Those attentional shifts could have led to the reduced suppression of the original spatial memories during the encoding of updated locations.

The "inefficient suppression" mechanism resembles the effect of low cholinergic modulations on learning and memory because low cholinergic levels lead to a weaker novel input relative to the strength of pre-existing memory traces (Hasselmo, 2006; Hasselmo and Bower, 1993). We therefore hypothesize that low cholinergic levels have led to inefficient suppression of the pre-existing spatial knowledge, which in turn hindered the formation of the novel spatial information. This hypothesis would be in line with role of acetylcholine in resistance to proactive interference (De Rosa and Hasselmo, 2000; De Rosa et al., 2001), and we suggest that low cholinergic modulation underlies the susceptibility to proactive-interference in aging. The hypothesis also matches the notion that age-related changes in attentional levels could underlie the inefficient suppression of former memories, as it has been suggested that while low acetylcholine levels set dynamics for consolidation, high acetylcholine levels set circuit dynamics for attention and encoding (Hasselmo and McGaughy, 2004).

Although resistance to proactive interference has been associated with increased hippocampal cholinergic levels (Caplan et al., 2006; De Rosa et al., 2001), hippocampal responsivity to cholinergic input was found to decrease in aging [(Haigler et al., 1986; Lippa et al., 1980), for review see (Decker, 1987)]. Thus, age-related reduction in hippocampal responsivity to acetylcholine could be the underlying mechanism for spatial updating deficits in old age. Indeed, inefficient suppression of existing memory traces following low cholinergic modulation was observed in a CA3 hippocampal slice preparation (Hasselmo et al., 1995). Finally, Wilson et al. (2006) have linked between susceptibility to proactive interference in aging to age-related shifts toward pattern completion [the retrieval of already stored information (Vieweg et al., 2015)] and away from pattern separation [the encoding of new, distinct events (Toner et al., 2009; Yassa et al., 2011)]. Those shifts were suggested to occur due to age-related reduction in cholinergic modulation in the CA3 hippocampal subfield (Wilson et al., 2006).

What are the wider implications of our findings? Navigational abilities are known to decline in aging (Lester et al., 2017; Moffat, 2009), but we only have a limited understanding of the underlying mechanisms. The present study proposes a mechanism that could explain navigational deficits in aging, especially in situations that require updating of long-term spatial memories, that is, where former memory traces interfere with the most recent ones. For instance, when looking for a car in a frequently visited parking lot, one has to retrieve today's parking place over yesterday's location. Importantly, because spatial processing of small 2-dimensional layouts—as studied in our experiments—is not identical to navigation in large 3-dimensional environments (Hegarty et al., 2006), it remains to be determined whether older adults are also impaired in updating spatial memories during navigation.

5. Conclusions

We found that older humans are impaired in their ability to update long-term spatial memories. The findings also suggest that representations of former spatial contexts impair spatial updating abilities in older humans. We suggest that the age-related deficit in spatial updating is a result of inefficient suppression of the former spatial memories. We discuss the potential roles of reduced attention and reduced hippocampal cholinergic levels in the inefficient suppression of the former spatial memories among older adults. Given that updating memory traces of spatial information is required in many everyday situations, the present study proposes a mechanism that could contribute to the age-related deficits in spatial cognition.

Disclosure

The authors have no conflicts of interest to disclose.

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