Angel L., Bastin C., Genon S., Balteau E., Phillips C., Luxen A., Maquet P., Salmon E., Collette F. Differential effects of aging on the neural correlates of recollection and familiarity. *Cortex (in press).*

Differential effects of aging on the neural correlates of recollection and familiarity

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Running title : fMRI correlates of recollection and familiarity in aging

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Abstract

The present experiment aimed to investigate age differences in the neural correlates of familiarity and recollection, while keeping performance similar across age groups by varying task difficulty. Twenty young and twenty older adults performed an episodic memory task in an event-related fMRI design. At encoding, participants were presented with pictures, either once or twice. Then, they performed a recognition task, with a Remember/Know paradigm. A similar performance was observed for the two groups in the Easy condition for recollection and in the Hard condition for familiarity. Imaging data revealed the classic recollection-related and familiarity-related networks, common to young and older groups. In addition, we observed that some activity related to recollection (left frontal, left temporal, left parietal cortices and left parahippocampus) and familiarity (bilateral anterior cingulate, right frontal gyrus and left superior temporal gyrus) was reduced in older compared to young adults. However, for recollection processes only, older adults additionally recruited the right precuneus, possibly to successfully compensate for their difficulties, as suggested by a positive correlation between recollection and precuneus activity.

Keywords: Aging, Recollection, Familiarity, fMRI

1. Introduction

Dual-process models of recognition memory postulate that the ability to recognize previously encountered information depends upon two mechanisms: recollection and familiarity (Mandler, 1980; see Yonelinas, 2002 for review). Recollection refers to processes allowing mental reinstatement of the previous episode, implying a conscious retrieval of contextual details associated with the stimulus, whereas familiarity corresponds to retrieval of the item without specific contextual information. The efficiency of recollection and familiarity processes is typically assessed by either objective or subjective methods. For instance, in source memory paradigms, participants are instructed to retrieve specific contextual details associated with the target item during the study phase (e.g. color, spatial location, temporal information). Another frequently used method is the Remember/Know paradigm (Tulving, 1985); during a recognition test, participants are asked to choose Remember responses if they are able to recollect something associated with the previous presentation of the item, or Know responses if the item is familiar but no contextual information is available. A large body of evidence from behavioral studies suggests a differential effect of aging on recollection and familiarity processes (Bastin and Van der Linden, 2003; Bugaiska et al., 2007; see Davidson and Glisky, 2002 for review); while familiarity-based recognition is relatively preserved, the ability to recollect the spatio-temporal context is strongly impaired in healthy older adults. This dissociation may be related to the fact that recollection processes are supposed to be more resource-dependent than familiarity processes (see Yonelinas, 2002 for review).

Functional neuroimaging (fMRI) methods have started to explore age-related changes in the neural activity associated with memory retrieval, helping understand the factors that contribute to recollection and familiarity performance in aging. Studies in the field of cognitive neuroscience of memory aging have described two distinct patterns of age-related differences. First, some studies have reported decreases in retrieval-related activity in some brain areas in older adults, reflecting presumably a decline in the functional integrity of these regions (see Dennis and Cabeza, 2008; Grady, 2008; Park and Reuter-Lorenz, 2009 for reviews). Second, and perhaps more unexpectedly, a growing body of research has revealed an age-related increase in activations in some brain areas, especially in frontal and parietal areas. For instance, several studies have reported that older adults recruit supplementary areas in the contralateral hemisphere when carrying out cognitive tasks that are associated with lateralized brain activity in young adults, resulting in more symmetrical patterns of memory-related activity in older than younger adults (HAROLD model, *Hemispheric Asymmetry Reduction in OLD age*; Cabeza, 2002). These findings have been interpreted either as reflecting a compensatory response to deficits in other brain areas (Cabeza et al., 2002; Manenti et al., 2011; Reuter-Lorenz et al., 1999), or as the consequence of an age-related cortical dedifferentiation process, leading to processing inefficiency (Morcom and Friston, 2012; Persson et al., 2006).

Very few studies have examined the effects of aging on the neural correlates of retrieval operations by dissociating recollection and familiarity processes. In the first fMRI study addressing this issue directly, Daselaar et al. (2006) isolated activity associated with recollection and familiarity by means of a recognition task with confidence judgments. They found that the neural correlates of recollection and familiarity were differentially affected by aging. While the recollection-related activity in the hippocampus and posterior cortical regions was reduced by aging, older adults showed enhanced familiarity-related activity in the rhinal cortex. This was interpreted as suggesting that older adults compensate for their recollection deficit by relying more than young adults on familiarity processes. This finding is of great interest since it suggests that older adults may sometimes implement alternative strategies to overcome their difficulties. Two fMRI studies explored age-related effects on recollection and familiarity processes using the Remember/Know paradigm (Duarte et al., 2010; Duarte et al., 2008). Deficits of recollection in older adults were associated with impaired activity in parietal and retrosplenial regions (Duarte et al., 2008) or in parieto-occipital regions (Duarte et al., 2010). In addition, familiarity-related activity in the frontal and temporal cortex was also reduced in older adults (Duarte et al., 2010). It should be noted that these older adults had impaired behavioral estimates of familiarity, which is inconsistent with the classic finding of intact familiarity in aging. As explained by the authors, that study also aimed to explore the neural correlates of false recognition, so participants were selected in order to provide enough false alarms, which may explain this particular behavioral pattern.

Overall, these data suggest age-related differences in neural activity associated with recollection and familiarity. However, the interpretation of these findings is ambiguous because of age-related differences in performance. Indeed, as in most previous neuroimaging studies of cognitive aging, between-group differences in the pattern of brain activation could be attributed to age but also to differential memory performance. Older adults may show reduced activations only because they experience greater difficulty executing the memory task. Consequently, findings of increased or decreased brain activity can be unambiguously interpreted only if performance is equated between age groups. Furthermore, equating overall memory performance is not sufficient, since the relative contribution of different processes (e.g. recollection and familiarity) may still differ between young and older groups. Two earlier studies have addressed this issue directly (Duverne et al., 2008; Morcom et al., 2007; see also Li et al., 2004 for a study using ERPs). In both experiments, recollection performance, as indexed by the ability to retrieve encoding contextual details (source memory paradigms), was matched between a young group and an older group by varying the number of presentations of items at study (from 1 to 3). Older adults showed enhanced recollection-related activity compared to young adults in a hippocampal region and in the extrastriate visual cortex in one study (Duverne et al., 2007), and in a large left-sided network including prefrontal regions, parietal, temporo-parietal, occipital cortices and the right temporal lobe and left anterior medial temporal lobe in the other (Morcom et al., 2007). However, these studies did not examine familiarity-related neural activity. Another potential issue concerning these studies is that both used source memory paradigms to assess the ability to recollect information. With this method, items associated with incorrect source judgments are used to index familiarity. However, they may also include a contribution of recollection processes for the retrieval of contextual attributes that are irrelevant for the source memory task. As acknowledged by the authors, another limitation of these studies is that the brain correlates of recollection processes were isolated by contrasting neural activity for items that were recognized with a correct source judgment and neural activity for correctly rejected items. In addition to recollection processes, this contrast is likely to reflect the involvement of familiarity.

The present study was designed to address all the above-mentioned issues. We used fMRI to investigate the effects of aging on the neural correlates of recollection and familiarity. First, participants encoded pictures incidentally with a semantic orienting task. In order to avoid the confounding effects of age with performance factors, task difficulty was manipulated by varying the number of presentations of items during study. Thus, pictures were presented either once or twice. This manipulation has been used successfully in several previous studies to equate the memory performance of young and older adults (Duverne et al., 2008; Morcom et al., 2007; see also Li et al., 2004 for a study using ERPs). This allowed the performance of young and older adults to be matched in an Easy condition (two presentations) for recollection and in a Hard condition (one presentation) for familiarity processes. The subsequent retrieval task was a recognition test using the Remember/Know paradigm. We used this task because it is less restricting than a source memory paradigm; because any retrieved contextual detail can lead to a Remember judgment, it should allow brain activity associated with recollection and familiarity to be clearly differentiated. Comparing the neural activity for correct Remember responses and for correct Know responses allowed recollection-related activity to be isolated. Familiarity-related activity was operationalized by contrasting activity elicited by Know responses and by correct rejections. First, we expected both age groups to show the classic networks associated with recollection and familiarity, including activations in medial temporal, frontal and parietal regions (see Skinner and Fernandes, 2007 for review; Spaniol et al., 2009). In addition, based on previous studies, we expected that aging would modify the neural correlates of recollection more than those of familiarity once performance of each process has been equated. These age-related reductions would be greater for recollection-related activations than familiarity-related activations. These reductions are mostly expected in or near regions activated in both age groups. These age-related decrements in brain activity are likely to reflect older adults' difficulty recruiting the same processes as young adults, particularly for recollection. We also hypothesized that there would be an age-related over-recruitment of some brain areas, presumably regions contralateral to those activated by both age groups (HAROLD model; Cabeza, 2002), reflecting older adults' tendency to compensate for their deficits by implementing alternative strategies (Daselaar et al., 2006). Any such additional recruitment should be more apparent for recollection than for familiarity-related activities, since recollection processes are thought to require greater cognitive resources (see Yonelinas, 2002 for review).

2. Material and methods

2.1. Participants

Insert Table 1 about here

Twenty young adults (eight males) aged 19 to 29 and twenty older adults (seven males) aged 60 to 78 participated in this experiment. Participants' characteristics for each age group are shown in Table 1. Older adults were recruited from senior clubs in Liège and most of the young participants were students at the University of Liège. All were right-handed, as assessed by the Edinburg laterality test (Oldfield, 1971). None reported any history of psychiatric or neurological disease or were taking medication likely to affect the central nervous system. All had normal or corrected-to-normal vision and none suffered from hearing problems. The two groups did not differ in years of education, or cultural level as assessed by the Mill Hill vocabulary test (Deltour, 1993), and had similar scores on the Beck Depression Inventory (BDI, Beck, 1961). All the older adults obtained a minimal score of 124 (range: 133-144) on the Mattis dementia rating scale (Mattis, 1976), reducing the risk of including anyone suffering from a neurodegenerative disease. The experimental procedures were approved by the Ethics committee of the University of Liege and were performed in accordance with the ethical standards laid down in the Declaration of Helsinki (1964). All participants gave their signed informed consent prior to the experiment and were paid twenty euros for their participation.

2.2. Material

The critical stimuli consisted of three hundred black-and-white line drawings of common objects selected from the Cycowicz et al. (1997) database and standardized for French-speaking subjects (Alario and Ferrand, 1999). These pictures were randomly divided into three lists of one hundred pictures, according to three possible versions. The lists were matched for name agreement, image agreement, complexity, familiarity, variability and age of acquisition (for a detailed description of each characteristic, please see Alario and Ferrand, 1999). Each subject was allocated one version of the stimulus lists. In each version, the three lists were used for: 1) study items presented once (Hard condition), 2) study items presented twice (Easy condition), and 3) new items presented only during the test phase. Fifteen additional items were selected to form practice lists for the study and test phases. We also included thirty scrambled pictures to serve as null events. Study lists were created by pseudo-arranging critical items and null events, with the constraint that two presentations of the same stimulus should be separated by at least ten stimuli. Two additional pictures were used at the beginning of the study phase to reduce the risk of primacy effects. Test lists consisted of items from the study lists, mixed with new items and null events, so that no more than three items of the same condition (studied, new or null events) should occur consecutively. Two filler items were added at the beginning of the block.

2.3. Procedure

The experiment included a study phase and a test phase, both performed in the fMRI scanner. Before entering the scanner, participants carried out a practice session for the study phase. Then, they were positioned in the scanner and the study phase began. The study phase consisted of 332 trials corresponding to the 100 items presented once (Hard condition), 100 items presented twice (Easy condition), 30 null events, and the two filler items. All stimuli appeared on a black screen that participants could see in an overhead mirror. For each trial, a fixation cross was displayed for 500 ms in white and for 500 ms in red. Then, the item appeared for 3000 ms, with a jitter from 0 to 750 ms. Participants were not informed of the subsequent memory task. However, to encourage incidental encoding of the item and to reduce between-group variability in encoding strategies, a semantic task was introduced in which participants had to decide whether the depicted object would fit into a shoebox. They answered using a response box held in their right hand. There was a short break (30 s) after every 110 items. After the study phase, participants left the scanner for a break (5 minutes) and performed a practice session for the test phase. The test phase included 332 trials, with the 100 items studied in the Easy condition, the 100 items studied in the Hard condition, 100 unstudied items, 30 null events and two filler items. Each test trial began with a white fixation cross for 500 ms that then became red for 500 ms. The item was displayed until the subject responded, with a maximum of 4000 ms. Depending on response speed, a black screen sometimes appeared after the item to ensure inter-trial intervals of 3000 ms minimum, with a jitter from 0 to 750 ms. For each item, participants were instructed to choose between three possible answers: Remember (studied item associated with the recollection of some contextual detail), Know (studied item recognized as old but without any contextual information), New (unstudied item). The answer was given by pressing one of the buttons of the response box. There was a short break (30 s) after every 110 items. After the test phase, participants were debriefed about the experiment, outside the scanner. In particular, correct use of the Remember/Know categories was checked by asking them to explain the basis of their Remember responses to ten items.

2.4. fMRI acquisition

Functional MRI time series were acquired on a 3T head-only scanner (Magnetom Allegra, Siemens Medical Solutions, Erlangen, Germany) operated with the standard transmit-receive quadrature head coil. Multislice T2*-weighted functional images were acquired with a gradient echo-planar imaging sequence using axial slice orientation and covering the whole brain (34 slices, FoV = 192x192 mm^2, voxel size 3x3x3 mm^3, 25% interslice gap, matrix size 64x64x34, TR = 2040 ms, TE = 30 ms, FA = 90°). The three initial volumes were discarded to avoid T1 saturation effects. Gradient-recalled sequences were applied directly after the study and test phases to acquire two complex images with different echo times (TE = 4.92 and 7.38 ms respectively) and to generate field maps for distortion correction of the echo-planar images (EPI). The other acquisition parameters were TR = 367 ms, FoV = 230x230 mm^2, 64x64 matrix, 34 transverse slices (3 mm thickness, 25% inter-slice gap), flip angle = 90°, bandwidth = 260 Hz/pixel. For anatomical reference, a high-resolution T1-weighted image was acquired for each subject (T1-weighted 3D magnetization-prepared rapid gradient echo

(MPRAGE) sequence, TR = 1960 ms, TE = 4.43 ms, inversion time (TI) = 1100 ms, FoV = 230x173 mm^2, matrix size = 256x192x176, voxel size = 0.9x0.9x0.9 mm^3).

2.5. Data analysis

Only data from the retrieval session were analyzed and are included here. fMRI data were preprocessed and analyzed using SPM8 (Wellcome Department of Imaging Neuroscience, http//www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB (Mathworks Inc., Sherborn, MA). For each subject, EPI time series were corrected for motion and distortion using Realign and Unwarp (Andersson et al., 2001) together with the FieldMap toolbox (Hutton et al., 2002) in SPM. Next, functional scans were realigned using rigid body transformations, iteratively optimized to minimize the residual sum of squares between the first and each subsequent image separately, and a mean realigned image was created. The structural T1-image was coregistered to this mean functional image using a rigid body transformation optimized to maximize the normalized mutual information between the two images. The mapping from subject to MNI space was estimated from the structural image with the “unified segmentation” approach (Ashburner and Friston, 2005). The warping parameters were then separately applied to the functional and structural images to produce normalized images of resolution 2 x 2 x 2 mm^3 and 1 x 1 x 1 mm^3 respectively. Finally, the warped functional images were spatially smoothed with a Gaussian kernel of 8 mm full-width at half maximum (FWHM).

Neural activity was modeled at each voxel with a general linear model, using event types as regressors. These events were sorted by item status (Old, New, Null event), encoding condition (Easy vs. Hard) and participants’ response in the test phase (Remember, Know, New, No response). Consequently, the design matrix included eleven events: 1) Hits-Remember in the Easy condition, 2) Hits-Remember in the Hard condition, 3) Hits-Know in the Easy condition, 4) Hits-Know in the Hard condition, 5) Correct rejections, 6) Misses in the Easy condition, 7) Misses in the Hard condition, 8) False alarms-Remember, 9) False alarms-Know, 10) Null events, 11) No responses. The onset vector of each event type was convolved with a canonical hemodynamic response function. The design matrix also included the realignment parameters to account for any residual movement-related effect. A high-pass filter was implemented using a cut-off period of 128 s in order to remove low-frequency drifts from the time series. Serial autocorrelations were estimated with a restricted maximum likelihood algorithm with an autoregressive model of order one (plus white noise).

To explore the neural correlates of recollection and familiarity processes, a series of linear contrasts was performed at the individual subject level. First, brain areas associated with recollection were isolated by comparing changes in brain activity for Hits-Remember and Hits-Know. This contrast was performed for the Easy and the Hard conditions separately. Next, contrasts were performed to determine the neural substrates of familiarity in the Easy and Hard conditions separately, by comparing the brain activity associated with Hits-Know and with Correct rejections. Statistical analysis was performed in two stages, using these contrasts of interest.

Individual contrast images were further smoothed (8 mm) and submitted to a second-level analysis corresponding to a random effects model in which subjects are considered as random variables. These individual contrast images were used to analyze: 1) neural activity common to both age groups, and 2) between-group differences. First, to identify the effects common to the two age groups for recollection and familiarity, the effects observed in the young group (collapsed across the two difficulty conditions) were inclusively masked with the effects observed in the older group. These statistical maps were thresholded at $p<.05$ corrected for multiple comparisons. All inclusive masks were applied at an uncorrected threshold of $p<.001$. Secondly, we focused on age-related differences in the neural correlates of recollection and familiarity in the conditions where performance was matched.

Anticipating the behavioral results, the young and older groups showed similar accuracy in the Easy condition for recollection processes and in the Hard condition for familiarity processes. We performed t-test comparisons between young and older participants for the Recollection-Easy and Familiarity-Hard contrasts, thresholded at p <.001 uncorrected for multiple comparisons. These contrasts were inclusively masked with the simple effects of each group, with an uncorrected threshold of p<.001.

3. Results

3.1. Behavioral results

Insert Table 2 about here

The behavioral performance (accuracy and reaction times) of the young and older groups is summarized in Table 2. More correct rejections were made by the young than by the older group [$t(38) = 3.73$, $p<.001$]. Older adults produced more Remember responses to unstudied items (false alarms) than young adults [$t(38) = -3.04$, $p<.01$] but the rate of false alarms with Know responses did not significantly differ between age groups [$t(38) = -0.75$]. To examine this potential bias, memory accuracy was estimated using the discrimination index (*Pr*), computed as the difference between the probability of hits and the probability of false alarms, for both Remember and Know responses (Snodgrass and Corwin, 1988). According to independence models of recollection and familiarity (Yonelinas and Jacoby, 1995), probabilities for correct Know judgments and false alarms with Know responses were estimated respectively using the following formulae: *pc*(Hits-Know) = *p*(Hits-Know) / (1 - *p*(Hits-Remember)) and *pc*(False alarms-Know) = *p*(False alarms-Know) / (1 - *p*(False alarms-Remember)) (Stanislaw and Todorov, 1999).

All groups showed *Pr* values that differed reliably from 0, as assessed by one-sample *t*-tests. An ANOVA with factors of Age (Young vs. Old) and Difficulty (Easy vs. Hard) was conducted on each discrimination index (*Pr*(R) and *Pr*(K)) separately, given that R and K judgments are assumed to depend on independent processes (Yonelinas and Jacoby, 1995). The ANOVA on Remember responses revealed a main effect of group [$F(1,38) = 5.97$; $p<.05$], a main effect of difficulty [$F(1,38) = 145.49$; $p<.001$] and a significant interaction between these factors [$F(1,38) = 4.25$; $p<.05$]. Planned comparisons showed that older adults made fewer recollection-based responses than the young adults in the Hard condition [$F(1,38) = 11.28$; $p<.01$], but that the two groups had the same level of accuracy as the young adults in the Easy condition [$F(1,38) = 1.96$]. A similar analysis of the discrimination index for Know responses indicated that the main effect of age was not significant [$F(1,38) = 1.12$], but the main effect of difficulty [$F(1,38) = 94.28$, $p<.001$] and the interaction between age group and difficulty level [$F(1,38) = 6.47$; $p<.05$] were significant. Follow-up contrasts revealed that the estimate of familiarity did not differ reliably between the two age groups in the Hard condition [$F(1,38) = 0.12$]. In the Easy condition, older adults outperformed young adults in this familiarity-based responding [$F(1,38) = 5.01$; $p<.05$].

Additionally, in order to determine whether the higher false alarm rates for remember responses in the older group could be due to differences in decision criteria, we also performed analyses on response bias estimates (*Br*) for Remember and Know responses, which differed significantly from 0 for both young and older adults, with the exception of the *Br*(K) for young adults in the Easy condition which was only marginally different from 0. A mixed ANOVA with factors of age and difficulty on the *Br* for Remember judgments yielded a main effect of group [$F(1,38) = 7.05$; $p<.05$], a main effect of difficulty [$F(1,38) = 8.32$; $p<.01$] and a significant group by difficulty interaction [$F(1,38) = 4.3$; $p<.05$]. Older adults showed a more liberal decision criterion to produce Remember responses than young adults, and this response bias was greater in the Easy condition. This finding suggests that the higher false alarm rate in the older group may be due to their more liberal response bias. By contrast, for the response bias for Know responses, the main effect of age [$F(1,38) = 2.03$], the main effect of difficulty [$F(1,38) = 2.71$] and the interaction between these two factors [$F(1,38) = 0.74$] were not significant.

Finally, we analyzed whether reaction times differed as a function of age and difficulty. Reaction times for correct rejections did not differ reliably between the two age groups [$t(38) = -0.60$]. A mixed ANOVA showed that participants produced Remember responses faster in the Easy than in the Hard condition [$F(1,38) = 42.09$; $p<.001$]. The main effect of group [$F(1,38) = 1.08$] and the interaction between group and difficulty [$F(1,38) = 1.82$] on Remember responses were not significant. Analyses of reaction times for Know responses revealed a significant interaction between group and difficulty [$F(1,38) = 5.03$; $p<.05$] although the main effects of group [$F(1,38) = 1.63$] and difficulty [$F(1,38) = 1.42$] were not significant. In the Hard condition, young adults were slower than older adults in producing Know responses [$F(1,38) = 6.77$; $p< .05$].

To sum up, these behavioral results show that performance was closely matched across age groups in the Easy condition for recollection and in the Hard condition for familiarity.

3.2. fMRI results

As described above, we examined: (1) recollection-related and familiarity-related effects (collapsed across the two difficulty conditions) common to young and older groups; (2) age-related differences in the recollection-related and familiarity-related effects when performance is matched.

Effects common to both groups

Insert Table 3 about here

Insert Figure 1 about here

Recollection: Analyses revealed a large network of brain regions, more extensive in the left than in the right hemisphere, exhibiting greater activity for Hits-Remember than Hits-Know for both young and older adults (see Table 3 and Fig. 1). These recollection-related areas included regions in the inferior frontal gyrus bilaterally, left middle and superior frontal gyri, medial frontal gyrus, left parietal (supramarginal and angular gyri, posterior cingulate gyrus and precuneus), left middle temporal areas and left parahippocampal gyrus. No region demonstrated greater activity for Hits-Know than Hits-Remember.

Insert Table 4 about here

Insert Figure 2 about here

Familiarity: A wide network of regions showed familiarity-related activity common to young and older groups (see Table 4 and Fig. 2). Some regions manifested greater activity for Hits-Know than for Correct rejections, including bilateral frontal areas (left medial and inferior frontal gyri, left anterior cingulate gyrus, right superior frontal gyrus and middle frontal gyrus bilaterally), the left precuneus, the inferior parietal lobule bilaterally and the left insula. In addition, the reverse contrast revealed a pattern of reduced activity for Hits-Know relative to Correct rejections in the left post-central gyrus and in the right anterior parahippocampus.

Age-related differences

Insert Table 5 about here

Insert Figure 3 about here

Recollection (in the Easy condition): The comparison of recollection effects between age groups revealed differences in several regions, as shown in Table 5 and Fig. 3. Numerous regions showed greater activity for Hits-Remember than Hits-Know in the young group but little differential activity in the older group (Figure 3A). These activations specific to young adults were mainly left-sided, including regions in the frontal (left medial and superior gyri, the temporal (middle, superior, fusiform) cortices and in the left parahippocampus. Greater activity was also found in the right angular gyrus and right caudate nucleus. In addition, greater activity was found in the right middle frontal gyrus for Hits-Know than Hits-Remember, but only in the young group (Figure 3B). Notably, one region in the right precuneus demonstrated a reliable recollection effect in the older group, with greater activity for Hits-Remember than Hits-Know, whereas no significant effect was observed in the young group (Figure 3C). To explore the significance of this additional recollection-related activity in the older group, we computed the correlation between the activity in this region of the right precuneus and the *Pr*(Remember) in this condition. We found that accuracy of Remember responses was positively correlated to activity in the right precuneus, in the older group only (see Fig. 4). It should be noted that no other region correlated significantly with memory performance.

Insert Figure 4 about here

Insert Table 6 about here

Insert Figure 5 about here

Familiarity (in the Hard condition): A few regions demonstrated familiarity effects only in the young group, with greater activity for Hits-Know than Correct rejections. This pattern was found in several frontal regions (the right inferior frontal gyrus, left cingulate gyrus, anterior cingulate gyrus bilaterally), the left superior temporal gyrus, left insula and right culmen. No region showed greater effects or specific familiarity effects in the older group.

4. Discussion

This study aimed to examine the effects of age on the neural correlates of recollection and familiarity processes, unbiased by age-related differences in task performance thanks to a manipulation of task difficulty. Several noteworthy findings emerged from this experiment. First, we found the classic network of regions associated with recollection and familiarity processes in both the young and the older groups. Second, we observed reduced recollection-related and familiarity-related activations in older adults compared to young adults in several regions. Finally, a recollection-based activity in the right precuneus was found only in the older group. These findings and their implications for cognitive aging are discussed in more detail below.

4.1. Behavioral findings

Our behavioral results indicate that when the two difficulty conditions were collapsed together, older adults demonstrated a deficit in accuracy compared to young adults for recollection but not familiarity processes. This finding adds support to the wealth of studies suggesting that recollection processes are more strongly impaired by aging than familiarity processes (Bastin and Van der Linden, 2003; Bugaiska et al., 2007; see Davidson and Glisky, 2002 for review). Our main methodological aim in this experiment was to compare the fMRI patterns of young and older adults in conditions where the two components of retrieval success (recollection and familiarity) were matched as much as possible across groups. To achieve this, the number of presentations of items during encoding was varied from one (Hard condition) to two (Easy condition). While recollection performance was poorer for older than young adults in the Hard condition, accuracy and reaction times for Hits-Remember were equivalent between the two age groups in the Easy condition. Remember judgments for unstudied items were made more often by older than young adults. This high rate of false alarms was attributed to more liberal decision criteria. By contrast, older adults produced more Know responses than young adults in the Easy condition, whereas familiarity accuracy did not differ between the two age groups in the Hard condition. However, in this condition, reaction times for familiarity-based responses were slightly longer for the young than for the older group. This difference in reaction times, favoring the older group, will be considered in the fMRI findings part. Age differences in the neuroimaging data described below cannot therefore be attributed to differences in performance, given that recollection and familiarity performance was closely matched across groups.

4.2. fMRI findings

Common effects

We observed a large network of regions, strongly left-lateralized, that were associated with recollection processes in each age group. This network encompassed regions in the left superior, middle and medial frontal gyri and in bilateral inferior frontal gyri. Recollection-related activity was also reported in left parietal regions (supramarginal, angular and posterior cingulate gyri, precuneus) as well as in the left middle temporal gyrus and in the left anterior and posterior parahippocampus. The level of activity in these regions did not differ reliably between groups. These regions were broadly consistent with the recollection-related network typically reported by previous studies (see Skinner and Fernandes, 2007 for review; Spaniol et al., 2009). We did not observe any reliable recollection-based activity in the hippocampus; while this region has been strongly associated with recollection processes (Eichenbaum et al., 2007), numerous studies have also failed to observe any such activity (e.g., Vilberg and Rugg, 2008; see Spaniol et al., 2009 for a meta-analysis).

With regard to familiarity, both groups showed greater activity for Hits-Know than for Correct rejections in the left medial and inferior frontal gyri, left cingulate gyrus, right superior frontal gyrus and bilateral regions of the middle frontal gyrus. These activations support previous studies suggesting that some frontal regions, in particular inferior frontal regions and dorsolateral frontal regions, may contribute to familiarity (Aly et al., 2011;

Skinner and Fernandes, 2007). The most likely hypothesis is that at least some of these regions are not directly related to familiarity but rather to cognitive control processes (Fletcher and Henson, 2001). For instance, the inferior frontal cortex may be involved in monitoring processes used to resolve response competition (Badre and Wagner, 2007). Brain activity associated with familiarity was also found in the left precuneus, the inferior parietal lobule bilaterally and the left insula. Numerous studies examining the neural correlates of familiarity have demonstrated an involvement of parietal regions including the left precuneus and inferior parietal regions, even though they have been more often found for recollection than familiarity (Skinner and Fernandes, 2007). In addition, two regions (the right anterior parahippocampus and the left post-central gyrus) showed reduced activity for Know-hits compared to correct rejections. Our findings thus confirm the differential involvement of medial temporal regions in recollection and familiarity (Skinner and Fernandes, 2007); recollection is associated more with increased activity in left parahippocampal regions, whereas familiarity is associated with decreased activity in the right anterior parahippocampal gyrus (Henson et al., 2003).

Age differences in recollection effects

By manipulating task difficulty, we were able to compare recollection effects between young and older adults in the Easy condition in which recollection performance was equated across groups. Age-related differences were observed in several brain areas. Many regions showed recollection-related activity in young but not in older adults, with Hits-Remember exhibiting greater activity than Hits-Know. These regions were located in the left superior and medial frontal gyri, the right middle frontal gyrus, and in the left superior and middle temporal gyri, left angular gyrus, left fusiform gyrus and in the left parahippocampus. We also observed less activity for Hits-Remember than Hits-Know in two regions of the right middle frontal gyrus in the young group only. Thus, the areas showing specific activity in the young group were very close to the recollection-related network common to the two age groups. This finding is in agreement with our predictions and with previous evidence of impaired recollection-related activity in older adults (Daselaar et al., 2006; Duarte et al., 2008, 2010). If activity in frontal areas reflects the involvement of an executive control system in retrieval success, then the age-related reduction of activation within these regions suggests that older adults may have difficulty engaging control processes, for instance post-retrieval monitoring processes (Dulas and Duarte, 2011; Luo and Craik, 2009; McDonough et al., 2012). This explanation is consistent with the observation that older adults produced more Remember-false alarms that young adults. The attenuation of recollection effects in the left parahippocampus is also in agreement with findings of reduced activity in the mediotemporal lobe in older adults (Daselaar et al., 2006).

However, one region, the right precuneus, was exclusively recruited by the older group to support successful recollection. This finding is consistent with numerous studies showing overactivation or additional recruitment of specific brain regions in older adults (Duarte et al., 2008; Grady et al., 2005; Morcom et al., 2007). More specifically, it supports the idea of reduced hemispheric asymmetry in old age (HAROLD model, Cabeza, 2002). While young adults recruited only the left precuneus, older adults recruited both left and right portions of the precuneus. Interestingly, we found that this additional recollection-related recruitment in older adults was strongly correlated to the accuracy of their recollection judgments. This suggests that this age-related contralateral parietal recruitment compensated for neural decline and allowed older adults to reach the young adults' level of performance in the Easy condition. This finding is interesting as most previous studies have found overactivations in frontal areas. It shows that compensatory recruitment in older participants is not restricted to the prefrontal cortex, but may also exist in the parietal cortex (Huang et al., 2012). The question that arises then is to determine the cognitive mechanisms underlying this age-related additional recruitment. One tentative interpretation is based on the AtoM model of the role of the parietal lobe in memory (*Attention To Memory*, Cabeza et al., 2008; Ciaramelli et al., 2008). According to this model, inferior parietal areas, for instance the angular gyrus, are involved in bottom-up attention to retrieved contents, whereas superior parietal areas, such as the precuneus, support top-down attention processes. This suggests that our older adults may have a deficit in bottom-up attention compared to young adults (reduced activity in the left angular gyrus) which may impose a heavier involvement of top-down controlled processes (enhanced precuneus activity). This may appear to contradict the previous idea that the reduced recollection-related activity reflects older adults' difficulty engaging control processes. In fact, older adults may have difficulty implementing the same control processes as young adults but they could compensate by increasing recruitment in other brain regions involved in executive functions such as the right precuneus. This interpretation is consistent with evidence that executive functions depend not only on distributed frontal and parietal regions (see Collette et al., 2006 for review). Another possibility is that older adults rely more than young adults on visually based processing to support their recollection judgments, as the precuneus has been associated with retrieval of visual information (Woodruff et al., 2005). This is consistent with the fact that the age-related overrecruitment of the precuneus was observed in the Easy condition, in which items were presented twice at study, but not in the Hard condition. Further knowledge about the cognitive operations implemented by young and older adults might be gained using paradigms allowing the verbalization of strategies.

Age differences in familiarity effects

With regard to familiarity, accuracy was closely matched across age groups in the Hard condition. Consequently, age-related differences in the neural correlates of familiarity could be analyzed, for the first time, without the confounding effect of performance. We observed that in some regions, familiarity-based activity was significant only in the young group. This result is in agreement with a recent finding suggesting an age-related impairment of the familiarity network (Duarte et al., 2010). However, it contradicts another study (Daselaar et al., 2006) which found that activity in regions associated with familiarity processes was preserved or enhanced in older adults compared to young participants. This discrepancy between studies may be due to methodological differences. For instance, unlike the other studies, we tried to match familiarity performance as much as possible. Only a few regions exhibited a familiarity effect specifically in the young group (bilateral anterior cingulate gyri, left superior temporal gyrus and right inferior frontal gyrus), whereas the network of recollection-based regions that were affected by aging was much broader. The recollection network thus seems to be more widely impaired by aging than the familiarity network. The activity in the inferior frontal gyrus in the young group is of particular interest, since, as discussed above, frontal regions may not directly support familiarity processes but may reflect the involvement of control processes. Thus, the fact that some frontal regions were activated specifically in the young group may suggest that young adults engaged additional monitoring processes for familiarity-based responding. This idea is supported by the finding that young adults had longer reaction times for familiarity-based responses in the Hard condition than the older group. Furthermore, no region demonstrated specific recruitment or over-recruitment in the older group. Older adults may only need to recruit additional areas for recollection processes, which are known to be more effortful and resource-dependent than familiarity.

In conclusion, this study provides the first direct evidence that the neural correlates of recollection and familiarity are modified during aging, by matching the level of performance of each process between groups. Neural activity related to recollection and familiarity was reduced in older adults compared to young adults. However, for recollection processes only, older adults recruited an additional region (right precuneus), possibly to compensate for their difficulties. An important challenge for future studies will be to investigate the conditions under which neural activity is increased or decreased during aging. Another promising line of research is to develop paradigms providing more information about the strategies implemented by participants. This would improve our understanding of the significance of age differences in memory-related brain activity.

5. Acknowledgments

This work was supported by the National Fund for Scientific Research (FRS-FNRS) in Belgium, the University of Liège, the King Baudouin Fondation and a Belgian InterUniversity Attraction Pole. SG is a research fellow, CP a research associate, PM a research director, and FC a senior research associate at the FRS-FNRS.

Disclosure statement: There are no current or potential conflicts of interest.

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Table 1: Participants' characteristics in each age group (mean and standard deviations)

	Young (N=20)	Older (N=20)	t(38)
Age	25.4 (2.98)	67.8 (5.29)	***
Education (Number of years)	16.3 (2.45)	14.7 (2.99)	NS
Vocabulary (Mill Hill)	27.16 (3.00)	28.95 (4.19)	NS
Depression (BDI)	5.25 (3.95)	7.75 (5.9)	NS

Note : *** Significant difference between the young and the older group at p<.001; NS: Unsignificant

Standard deviations in parentheses

Table 2: Behavioral performance of young and older groups in the memory task

Note : Standard deviations in parentheses

Pr (Remember) = *p*(Hits-Remember) – *p*(False alarms-Remember)

Pr (Know) = *pc*(Hits-Know) - *pc*(False alarms-Know)

Br(Remember) = *p*(False alarms-Remember) / (1-(*p*(Hits-Remember) – *p*(False alarms-Remember)))

Br(Know) = *p*(False alarms-Know) / (1-(*p*(Hits-Know) – p(False alarms-Know)))

*p <.05; ** p < .01; *** p< .001

	Young		Older		ANOVA results		
	Easy condition	**Hard condition**	**Easy condition**	**Hard condition**	**Age effect**	**Difficulty effect**	**Age × Difficulty interaction**
Response rates							
Studied items							
Remember	0.49 (0.15)	0.33 (0.14)	0.45 (0.15)	0.23 (0.11)			
Know	0.38 (0.15)	0.38 (0.13)	0.52 (0.16)	0.43 (0.13)			
New	0.13 (0.05)	0.29 (0.08)	0.03 (0.05)	0.34 (0.06)			
Unstudied items							
Remember (False alarms)	0.01 (0.01)		0.03 (0.04)				
Know (False alarms)	0.09 (0.11)		0.11 (0.05)				
New (Correct rejections)	0.90 (0.047)		0.86 (0.08)				
Performance indices							
Discrimination index							
Pr (Remember)	0.48 (0.15)	0.32 (0.14)	0.42 (0.14)	0.19 (0.10)	*	***	*
Pr (Know)	0.62 (0.16)	0.47 (0.15)	0.71 (0.08)	0.45 (0.12)	NS	***	*
Response bias							
Br (Remember)	0.02 (0.02)	0.01 (0.01)	0.08 (0.10)	0.05 (0.06)	*	**	*
Br (Know)	0.26 (0.56)	0.13 (0.12)	0.36 (0.29)	0.28 (0.19)	NS	NS	**NS**
Reaction times (ms)							
Studied items							
Remember	1392.80 (191.76)	1518.20 (241.02)	1518.45 (379.54)	1600.65 (416.16)	NS	***	NS
Know	1614.60 (225.75)	1772.35 (223.85)	1617.35 (397.31)	1569.10 (268.11)	NS	NS	*
New	1751.11 (432.95)	1610.70 (304.52)	1711.20 (504.39)	1616.00 (398.18)	NS	*	NS
Unstudied items							
Remember (False alarms)	1454.67 (388.21)		1724.33 (738.80)				
Know (False alarms)	1867.80 (464.61)		1839.50 (529.40)				
New (Correct rejections)	1338.05 (243.22)		1388.05 (279.50)				

Table 3: Regions showing recollection effects common to both age groups (collapsed across the two difficulty conditions)

Region	L/R	Location (MNI coordinates, x, y, z)	T score
Hits-R > Hits-K			
Superior frontal gyrus	Left	-14, 54, 28	7.40
	Left	-12, 46, 38	6.24
Middle frontal gyrus	Left	-40, 10, 50	6.89
Medial frontal gyrus	Left	-6, 60, 12	6.91
Inferior frontal gyrus	Left	-46, 28, -8	9.63
		-42, 22, -16	9.52
		-48, 32, 2	9.04
Inferior frontal gyrus	Right	58, 30, 8	7.01
	Right	54, 32, -2	5.94
Supramarginal gyrus	Left	-48, -56, 22	9.55
Angular gyrus	Left	-46, -70, 32	9.35
Posterior cingulate gyrus	Left	-6, -48, 34	9.61
	Left	-6, -52, 10	8.40
Precuneus	Left	-2, -50, 30	7.28
Middle temporal gyrus	Left	-52, -68, 26	10.12
	Left	-60, -40, 0	8.07
Anterior parahippocampal gyrus	Left	-18, -2, -16	7.05
		-52, -34, -6	8.00
Posterior parahippocampal gyrus	Left	-10, -42, 0	5.81
	Left	-26, -28, -18	6.69

Note: Hits-R: Hits-Remember; Hits-K: Hits-Know, significant results at a statistical threshold of $p < .05$ FWE-corrected at the voxel level.

Table 4: Regions showing familiarity effects common to both age groups (collapsed across the two difficulty conditions)

Region	L/R	Location (MNI coordinates, x, y, z)	T score
Hits-K > CR			
Superior frontal gyrus	Right	14, 16, 64	5.96
Middle frontal gyrus	Left	-38, 54, 10	11.07
	Left	-46, 44, 0	10.66
	Left	-36, 44, -8	8.17
	Left	-44, 20, 36	10.12
	Left	-34, 2, 54	7.98
	Left	-46, 10, 42	7.61
Medial frontal gyrus	Left	-4, 24, 44	12.25
Inferior frontal gyrus	Left	-52, -16, -4	6.86
Cingulate anterior gyrus	Left	-6, 28, 32	9.77
Cingulate gyrus	Left	-2, -26, 28	8.33
Middle frontal gyrus	Right	40, 8, 56	6.87
	Right	34, 8, 50	5.99
	Right	46, 34, 30	6.62
Precuneus	Left	-28, -64, 36	5.89
Inferior parietal lobule	Left	-44, -50, 44	10.39
	Left	-44, -58, 50	9.78
	Right	50, -48, 42	5.95
Insula	Left	-40, 16, 2	8.50
CR > Hits-K			
Postcentral gyrus	Left	-62, -30, 20	6.64
Anterior parahippocampal gyrus	Right	22, -8, -18	7.57

Note: Hits-K: Hits-Know; CR: Correct rejections, significant results at a statistical threshold of $p < .05$ FWE-corrected at the voxel level.

Table 5: Regions showing age-related differences in recollection effects (Easy condition)

Region	L/R	Location (MNI coordinates, x, y, z)	T score	Cluster size
Young>Older				
Superior frontal gyrus [1]	Left	-12, 56, 30	5.28	164
	Left	-22, 28, 50	4.45	195
	Left	-16, 32, 54	4.17	
Medial frontal gyrus [1]	Left	-8, 48, 40	4.13	
Middle frontal gyrus [2]	Right	42, 52, -8	4.29	90
	Right	34, 48, 0	4.16	
Angulate gyrus [1]	Left	-48, -68, 32	3.88	20
Superior temporal gyrus [1]	Left	-42, 10, -24	4.10	
Middle temporal gyrus [1]	Left	-42, 8, -32	3.99	
Fusiform gyrus [1]	Left	-30, -36, -18	4.11	47
Parahippocampal gyrus [1]	Left	-18, -16, -24	4.21	22
	Left	-32, 2, -24	4.10	166
Caudate [1]	Right	4, 10, -6	4.22	59
Cingulate gyrus [1]	Right	2, -10, 40	3.61	11
Older>Young				
Precuneus [3]	Right	12, -60, 28	3.77	11

[1]: Significant Recollection effect (Hits-Remember > Hits-Know) in the Young group, at a statistical threshold of $p < .05$ uncorrected.

[2]: Significant inversed Recollection effect (Hits-Know > Hits-Remember) in the Young group, at a statistical threshold of $p < .05$ uncorrected.

[3]: Significant Recollection effect (Hits-Remember > Hits-Know) in the Older group, at a statistical threshold of $p < .05$ uncorrected.

Table 6: Regions showing age-related differences in familiarity effects (Hard condition)

Region	L/R	Location (MNI coordinates, x, y, z)	T score	Cluster size
Young>Older				
Inferior frontal gyrus [1]	Right	30, 28, -4	3.84	51
	Right	38, 20,-8	3.67	
Anterior cingulate [1]	Left	-4, 28, 28	4.40	75
	Right	10, 24, 22	5.72	90
Cingulate gyrus [1]	Left	-6, 22, 42	3.72	25
Superior temporal gyrus [1]	Left	-48, 14, -8	3.75	
Insula [1]	Left	-30, 18, -2	5.17	238
Culmen [1]	Right	24, -40, -28	3.74	17
Older>Young				
		nihil		

[1]: Significant Familiarity effect (Hits-Know > Correct Rejections) in the Young group, at a statistical threshold of $p < .05$ uncorrected.

Figure 1:

Regions showing recollection effects (Hits-Remember > Hits-Know) common to both age groups (p<.05 corrected for multiple comparisons). The regions are displayed on the 3D rendered MNI reference brain.

Figure 2:

Regions showing familiarity effects (Red: Hits-Know > Correct rejections; Green: Correct rejections > Hits-Know) common to both age groups (p<.05 corrected for multiple comparisons). The regions are displayed on the 3D rendered MNI reference brain.

Figure 3:

Regions showing age-related differences in recollection effects, inclusively masked with the simple effects in each group (p<.001 uncorrected). 3A: Regions showing a significant recollection effect (Hits-R > Hits-K) in the young group only; 3B: Region showing a significant recollection effect (Hits-K > Hits-R) in the young group only; 3C: Region showing a significant recollection effect (Hits-R > Hits-K) in the older group only.

Figure 4:

Scatter plots showing the relationships between the recollection-related activity in the right precuneus (12, -60, 28) and *Pr*(Remember) in the Easy condition, for the young group (4A) and the older group (4B).

Figure 5:

Regions showing age-related differences in familiarity effects, inclusively masked with the simple effects in each group (p<.001 uncorrected).