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Aging affects both perceptual and lexical/semantic components of word stem priming: An event-related fMRI study

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Abstract

In this event-related fMRI study, brain activity patterns were compared in extensive groups of young ($N = 25$) and older ($N = 38$) adults, while they were performing a word stem completion priming task. Based on behavioral findings, we tested the hypothesis that aging affects only the lexical/semantic, but not the perceptual component of word stem priming. To this end, we distinguished between priming-related activity reductions in posterior regions involved in visual processing, and regions associated with lexical/semantic retrieval processes, i.e., left lateral temporal and left prefrontal regions. Both groups revealed significant priming-related response time reductions. However, in accordance with earlier findings, a larger priming effect was found in the group of young participants. In line with previous imaging studies, the groups showed common priming-related activity reductions in the anterior cingulate, and the left inferior prefrontal cortex extending into the anterior portion of the left superior temporal gyrus, and at lower thresholds also in the right occipital lobe. However, when directly comparing the groups, greater priming-related reductions were found for the young group in the left anterior superior temporal gyrus and the right posterior occipital lobe. These findings suggest that, converse to current psychological views, aging affects both perceptual and lexical/semantic components of repetition priming.

1. Introduction

Aging is accompanied by marked deficits in declarative memory, the conscious and intentional recollection of episodes and facts (Cabeza, Nyberg, & Park, 2005). Although the precise relationship between brain atrophy and functional decline remains unclear (e.g., Johnson et al., 2000), these deficits are thought to be related to age-related volume reductions in structures that are assumed to be critical to declarative memory function, including the medial temporal and frontal lobes (Golomb et al., 1993; Haug et al., 1983; Raz et al., 1997; Tisserand, Visser, van Boxtel, & Jolles, 2000). Interestingly, aging effects on nondeclarative types of learning and memory, such as repetition priming, appear to be less pronounced (Cabeza et al., 2005). This suggests that the structures responsible for these types of learning are relatively spared by the aging process, and that brain regions that mediate declarative memory are not contributing to priming effects.

Repetition priming refers to the phenomenon that response to a stimulus is faster, more accurate, and/or biased when this stimulus has been processed previously. The most widely used priming test has been the word stem completion (WSC) task, which is composed of a

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study and a test phase. At study, participants are presented with a list of target words, usually incorporated in a particular encoding task to be performed. Then, at test, the participants are visually presented with two or three letter word stems under the instruction to complete these stems with the first word that comes to mind. In general, half of the word stems are taken from the study list, the other half are extracted from a control list not presented at study. Implicit learning is indicated by the difference between the number of stems completed with target words relative to control words.

Neuroimaging studies on word stem priming have reported priming-related activity changes, typically reductions, in visual brain regions (Backman, Almkvist, Andersson, & Nordberg, 1997; Badgaiyan & Posner, 1997; Buckner, Koutstaal, Schacter, & Rosen, 2000; Buckner & Miezin, 1995; Thiel, Henson, Morris, Friston, & Dolan, 2001), and in regions generally assumed to be involved in lexical/semantic retrieval processes, i.e., the left lateral temporal and left prefrontal cortex (Buckner et al., 2000; Thiel et al., 2001). These activity reductions are assumed to reflect enhanced efficiency of repeated processing resulting in diminished computational demands. Interestingly, Buckner and colleagues did not observe reductions in posterior visual areas (BA 17/18) when the word stems were aurally cued, whereas the priming reductions in the temporal and prefrontal cortex were still present. These findings suggest that word stem completion priming consists of a perceptual, modality-specific component and a lexical/semantic component, independent of stimulus modality (Buckner et al., 2000). Other evidence for the involvement of lexical/semantic processes in word stem priming has come from studies showing a greater priming effect with additional lexical or semantic processing during the study phase (Challis & Brodbeck, 1992).

Behavioral studies have generally indicated a modest age-related reduction in WSC priming (Chiarello & Hoyer, 1988; Hultsch, Masson, & Small, 1991; Winocur, Moscovitch, & Stuss, 1996). It has been suggested that aging affects only the lexical/semantic component of word stem priming and that perceptual priming is still intact (Rybash, 1996). Several findings concur with this hypothesis. Winocur et al. found a correlation between priming magnitude on the WSC task and frontal lobe test performance in both community-dwelling and institutionalized elderly adults. This finding indicates that frontal lobe dysfunction is a factor in reduced priming on the WSC test (Winocur et al., 1996). In addition, age-related volume decreases are generally greater in frontal and temporal lobes compared to perceptual regions (Golomb et al., 1993; Good et al., 2001; Haug et al., 1983; Tisserand et al., 2000). Finally, age differences in priming are more reliably observed on priming tests that are viewed as mainly conceptual (e.g., word association priming) than on tests that are regarded as mostly perceptual (e.g., perceptual identification priming) (Rybash, 1996). Still, it has been difficult to distinguish between perceptual and lexical/semantic priming components using behavioral paradigms.

In the present functional MRI study (fMRI), we examined to what extent aging affects perceptual and lexical/semantic components of WSC priming by comparing brain activity patterns in extensive groups of young and elderly adults while they were performing an adapted version of the WSC task. We used (self-paced) event-related fMRI, which permits randomization of the presentation order of primed and control word stems, thereby preserving the implicit nature of the task. We tested the hypothesis, based on behavioral findings, that young compared to old participants will show greater priming-related activity reductions in regions associated with lexical/semantic retrieval, but a similar reduction in modality-specific visual regions, reflecting spared perceptual priming in the elderly group.

2. Methods

2.1. Participants

Twenty-five right-handed males between the ages of 30 and 35 and 38 right-handed males between the ages of 63 and 71 participated. They were recruited by means of advertisements in local newspapers. None of the participants were taking psychoactive medication and they did not report any neurological or psychiatric impairment on a general health questionnaire. We used a cut-off of 25 (out of 30) or higher on the Mini Mental Status Examination (MMSE; (Folstein, Folstein, & McHugh, 1975), a common test for assessing cognitive competence. Mean MMSE score was 27.8 [$SD = 1.5$]) with only two older adults having a score of 25. In addition, structural MR images (MPRAGE: inversion time: 300 ms, TR = 15 ms, TE = 7 ms, flip angle = 8°), which were acquired previous to this study, did not reveal indications for anatomical deviations that were uncharacteristic for this age group. All participants had completed at least the lowest level of high school in the Netherlands, which corresponds to level 4 on a 7-point Dutch educational scale (1 = "no education," 7 = "university level"). All elderly participants, and most of the young participants (19 out of 25) had participated in a previous fMRI study of memory (Daselaar, Rombouts, Veltman, Raaijmakers, & Jonker, 2003a) and visited the outpatient clinic for the second time. The participants' informed consent was obtained according to the declaration of Helsinki and approved by the ethical committee of the "Vrije Universiteit" Medical Center. Demographic data and self-rated health measures are shown in Table 1 for the different groups.

Table 1
Demographic data and self-rated health

[*SD*]	Young ($N = 25$)	Elderly ($N = 38$)
Age	32.3 [1.8]	66.4 [2.0]
Education (7-point scale)	6.0 [1.0]	5.5 [0.8]
Self-rated physical health (1 = bad, 5 = excellent)	4.0 [0.6]	4.0 [0.6]
Self-rated psychological health (1 = bad, 5 = excellent)	4.1 [0.7]	4.3 [0.7]

2.2. Magnetic resonance procedures

Imaging was performed on a 1.5 T Siemens Sonata (Siemens, Erlangen, Germany) scanner using a standard circularly polarized head coil. Stimuli were generated by a Pentium PC and projected on a screen at the back end of the scanner table. The projected image was seen via a mirror placed above the subject's head. Two magnet-compatible four-key response boxes were used to record the subject's responses and reaction times. The subject's head was immobilized using foam pads to reduce motion artifact and earplugs were used to moderate scanner noise. For each subject, a series of echo planar images (EPI) was acquired sensitive to BOLD contrast, involving a T2*-weighted gradient echo sequence (Repetition Time = 2.1 s, Echo Time = 60 ms, flip angle = 90°) consisting of 293 transversal whole-brain acquisitions (20 slices, $3 \times 3\,\text{mm}^2$ in-plane resolution, 5 mm slice thickness, 1 mm interslice gap).

2.3. Word stem completion task

Two lists of 80 nouns were drawn from a standard Dutch dictionary with word lengths ranging from five to nine letters. One set of nouns represented animate objects (e.g., "chicken," "barber," "begonia"), the other set referred to inanimate objects (e.g., "pencil," "costume," "bumper"). Word stems were constructed by extracting the first three letters of these nouns. We made sure that at least five and at most 10 alternative words could be created by completing the stems as indicated in the dictionary. Next, the nouns from the two lists were randomly assigned to be used either as primes or control words, yielding different stimulus sets for each individual subject (see below).

In view of possible motion artifacts, we used an adapted version of the WSC task in which the word stems were completed in silence followed by a button-press. The WSC task included eight study blocks, consisting of 10 trials, and eight WSC blocks, consisting of 20 trials, which alternated throughout the scan session. At study, participants were presented with a noun in the middle of the screen. They were instructed to indicate whether the word represented a living (left-handed press) or a nonliving object (right-handed press) using their index fingers. On each trial, response options were indicated at the bottom of the screen by two cursors pointing to the left ("living") and right ("nonliving").

During a subsequent word stem completion block, participants were randomly presented with three letter word stems. They were instructed to *silently* complete the stems with the first word that came to mind, and subsequently, to press a right-hand button as fast as possible using their index finger as soon as the word stem was successfully completed. Half of the word stems came from the previous study block; the other half were taken from the control list. A measure of implicit learning was obtained by comparing the response times for primed and control word stems, expecting the first to be reduced relative to the latter. However, as an additional manipulation check, the group of young participants was required to complete the entire list of word stems again in writing immediately after the scan session had ended.

The study and test blocks were separated by a 2-s instruction screen (i.e., "LIVING/NONLIVING"; "WORD STEM COMPLETION"). Stimuli were presented in a self-paced fashion, although a time limit of 5 s was applied in case of nonresponses. For the study blocks, the response-stimulus interval (RSI) was fixed at 1 s, for the WSC blocks, at 2 s. Hence, the intertrial intervals for the WSC blocks constituted 2 s RSI + the response time. Trials were only included when participants responded within the 5-s time limit. The number of functional scans was fixed at 293 in order to meet the equal variance assumption intrinsic to random effects analyses (see the following section).

2.4. Data analysis

Data were analyzed using SPM99 (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm). After discarding the first three volumes, time-series were corrected for differences in slice acquisition times, and realigned. Next, the EPI volumes were spatially normalized into approximate Talairach and Tournoux space (Talairach & Tournoux, 1988) defined by a standard SPM EPI template and resliced to a resolution of $3 \times 3 \times 3$ mm voxels. Data were spatially smoothed using a Gaussian kernel of 8 mm and normalized for global effects using proportional scaling.

The event-related fMRI analysis was based upon the assumption that individual hemodynamic responses summate in a practically linear fashion over time (Boynton, Engel, Glover, & Heeger, 1996; Buckner, 1998; Dale & Buckner, 1997). First, the response times (RT) of each individual subject were checked for outliers. The WSC trials which resulted in a RT exceeding the set cut-off ($= \text{percentile}[75] - 1.5 \times \text{percentile}[25] + \text{percentile}[50]$), were excluded from the analyses. In the young participants, this resulted on average in exclusion of 9.97% ($SD = 4.50$) and 9.70% ($SD = 3.33$) of the primed and control trials, respectively. In the older group, this resulted in exclusion of 9.98% ($SD = 4.39$) of the primed trials and 8.09% ($SD = 3.91$) of the control trials. Next, after applying a 40-s high-pass filter, evoked hemodynamic responses to the WSC events and the study blocks were modeled, respectively, as delta functions and box car functions (mixed epoch/event-related design), which were convolved with a synthetic hemodynamic response function in the context of the general linear model (Josephs, Turner, & Friston, 1997). We assessed average activations across participants by carrying out a two-step random effects analysis (Woods, 1996). The number of scans, and thereby the number of degrees of freedom, was held equal across participants, because this type of analysis assumes approximately equal within-subject variances. Hence, the number of trials completed varied across participants due to the self-paced design. The feasibility of using self-paced event-related fMRI designs has been discussed in previous papers (Daselaar et al., 2001; Josephs et al., 1997; Maccotta, Zacks, & Buckner, 2001).

As a first step, specific effects were tested by applying appropriate contrasts to the parameter estimates for each event, giving a t statistic for every voxel. In this way, SPMs (Statistical Parametric Maps; Friston, Frith, Frackowiak, & Turner, 1995) were assessed for each individual subject. During the second step, we carried out a one-sample t test upon the resulting contrast images in order to assess the main effects for each group. Group comparisons were carried out by means of a two-sample t test without constant term, which allows inclusive masking of the main effects of either one of the groups, thereby controlling for possible deactivations associated with the opposite main effects (see below).

Based on the results of previous neuroimaging studies (Backman et al., 1997), we only tested for significant priming-related activity reductions, i.e., control vs. primed word stems. Furthermore, the groups were directly compared to each other on this contrast. We applied an FDR-corrected (Genovese, Nichols, & Lazar, 2002) threshold of $p < .05$ with a minimum cluster size of 5 voxels for the assessment of group averages. The areas surviving this threshold in either one of the groups were subsequently identified as regions of interest for the regression analysis described below. In order to increase the sensitivity for detecting group differences, we applied a slightly lower threshold ($p < .001$ uncorrected, with a cluster size = 10) for the assessment of group interactions, which were masked inclusively by the main effect (control vs. primed; $p < .005$, uncorrected) of the respective groups.

Additionally, we applied a simple regression model to the data for each group using percent response time reductions of the individual participants as a covariate. This analysis was also set at a lower threshold of $p < .001$, uncorrected with a minimum cluster size of 10 adjacent voxels. The rationale for the regression analysis was twofold; first, we wanted to examine the extent to which behavioral and neurofunctional measures were correlating in general, and second, whether perceptual and lexical/semantic regions were differentially contributing to the magnitude of the priming effect in the young and elderly groups.

3. Results

3.1. Behavioral results

The performance measures on the word stem completion task are summarized in Table 2. Both the young ($t(24) = 8.5$; $p < .001$) and the elderly group ($t(37) = 7.9$; $p < .001$) showed a significant priming effect as reflected in the percent reduction in RTs for primed vs. control word stems. However, the priming effect was larger for the young participants ($t(61) = 4.7$; $p < .001$). Surprisingly, the elderly participants were significantly faster than the young participants in completing the control word stems ($t(61) = 2.124$, $p = .038$). Consequently, the number of completed word stems was significantly higher (primed: $t(61) = 2.995$, $p = .004$; control: $t(61) = 2.482$, $p = .016$) for the old (primed = 64.0, $SD = 6.6$; control = 64.0, $SD = 6.7$) than for the young adults (primed = 59.2, $SD = 5.6$; control = 59.7; $SD = 5.7$).

The faster performance in the older participants may indicate that they had a larger vocabulary at their disposal. Alternatively, though, this pattern of results could imply that the elderly were performing the covert completion task differently than the young participants, which could also have contributed to the observed group difference in the priming effect. For instance, some elderly may have simply pressed a button without generating a word on some trials. However, such a response pattern would predict either greater variability in the old group, in the case that only a subset of the older participants were button-pressing without generation, or greater within-subject variance in the older adults in the case that in most participants only some of the trials were button-pressed without generation.

In order to test the first possibility, we calculated the variance ratio, which indicated significantly greater variance in the priming effect (i.e., % RT reductions) for the young participants (variance ratio [young/old] = 2.97, $F(24,37) = 3.09$; $p = .004$), indicating greater similarity in

Table 2
Behavioral results

[*SD*]	Young	Elderly
RT primed word stems (s)	1.31 [.40]	1.22 [.44]
RT control word stems (s)	1.61 [.43]	1.35 [.49]
Priming effect: % RT	18.7 [11.2]	8.3 [6.5]

the response patterns of the older adults. In order to test the second alternative, we assessed the coefficient of variance (COV = average/standard deviation) in the RTs for each subject, which is a measure of within-subject variability. Again, the COV was found to be greater for the young participants both for the primed (COV-young = 0.430, $SD = 0.099$; COV-old = 0.344, $SD = 0.131$; $t(61) = 2.961$; $p = .004$) and the control word stems (COV-young = 0.459, $SD = 0.339$; COV-old = 0.344, $SD = 0.131$; $t(61) = 3.994$; $p < .001$), indicating that the elderly actually showed a more consistent, rather than a more variable, response pattern. In sum, the fact that the older adults showed clear priming effects as reflected in a clear reduction in the RTs, together with the finding of smaller variability in the old group's response patterns, does not indicate that the older adults were performing the task inappropriately.

Still, the difference in baseline completion times combined with the observed difference in RT reductions could imply that the priming effects were nonlinear, for instance, as a result of a ceiling effect. However, in that case, one would expect the slowest participants to show the greatest priming effects and vice versa. We tested this possibility by calculating the correlation between baseline completion times and percentage RT reductions across all participants. The results were clearly nonsignificant ($R(\mathrm{rt}[\mathrm{baseline}], \mathrm{rt}[\%\mathrm{reduction}]) = 0.079$; $p = .542$). As a final check, we reanalyzed the behavioral and imaging data after creating an old and a young group with similar baseline completion times using the young participants' normal score (means ± SD) as a cut-off (RT between 1.18 and 2.04 s). The resulting groups (17 young, 16 old participants) did not differ significantly ($t(31) = 1.075$; $p = .29$) in completion times for control word stems (young = 1.59 s, $SD = 0.26$; old = 1.49 s, $SD = 0.27$). Comparison of these two groups revealed similar age differences in priming magnitude (young = 18.8%, $SD = 10.4$; old = 10.0%, $SD = 6.7$; $t = 2.86$; $p = .008$) and priming-related activity (see Section 3.2). Hence, collectively, the current findings indicate that the age differences we observed cannot be accounted for by differences in task execution or baseline completion times. Instead, results suggest that, although priming was reduced in the older adults, they were more proficient in the completion of control word stems than the young participants.

As an additional manipulation check, the entire list of word stems that had been presented in the scanner was completed again in writing by the young participants. The primed word stems were completed with study words in 42.1% [$SD = 4.8$] of the cases, and the control word stems with control words in 22.1% [$SD = 10.0$] of the cases, which was a highly significant difference [$t(24) = 10.2$; $p < .001$]. In addition, a significant correlation was found between the primed vs. control ratio and the percent reduction in response times ($r = .44$; $p = .026$), indicating the validity of the use of response time reductions as a measure of priming.

3.2. Imaging results

Both groups showed priming-related activity reductions in the left inferior frontal cortex, and the anterior cingulate. However, the young group revealed additional reductions in the anterior part of the left superior temporal gyrus and the cerebellum (Table 3, Fig. 1A). These differences were found to be significant as determined by a direct group comparison (Table 4). The older participants revealed an additional reduction in the right inferior prefrontal cortex, whereas the young participants did not. However, this difference was not significant as indicated by a direct group comparison, which was related to the fact that the young participants showed similar reductions at a slightly lower threshold (Table 3, Fig. 1A).

An additional region in the right posterior occipital lobe (BA 17/18) also showed a larger activity decrease in young relative to old participants. However, at the set threshold (= $p < .05$; FDR-corrected), no evidence was found for activity reductions in this area in the young participants' group average (Table 3). Still, at a slightly lower threshold ($p < .001$, uncorrected) we did observe reduced activity in this region (Figs. 1A and B; Talairach coordinates [x, y, z]: 27, −96, 5; $z = 3.68$). Only when we

Table 3
Maxima of regions showing significant BOLD signal reductions ($p < .05$, FDR-corrected; cluster = 5; unless indicated otherwise by asterisk) in comparison of primed vs. control word stems

Region of activation	Left/right	Brodmann area	Talairach coordinates x, y, z {mm}			Z value
Young						
Inferior frontal gyrus	L	44/45	−48	41	1	5.26
	R	47	53	12	10	3.40*
Anterior cingulate gyrus	L	32	−3	25	40	4.30
Superior temporal gyrus	L	22	−53	15	5	4.97
Cerebellum	L	—	−9	−45	−23	4.97
Elderly						
Inferior frontal gyrus	L	47	−45	17	−6	5.33
	R	47	45	20	−6	4.36
Anterior cingulate gyrus	R	24/32	3	19	32	5.11

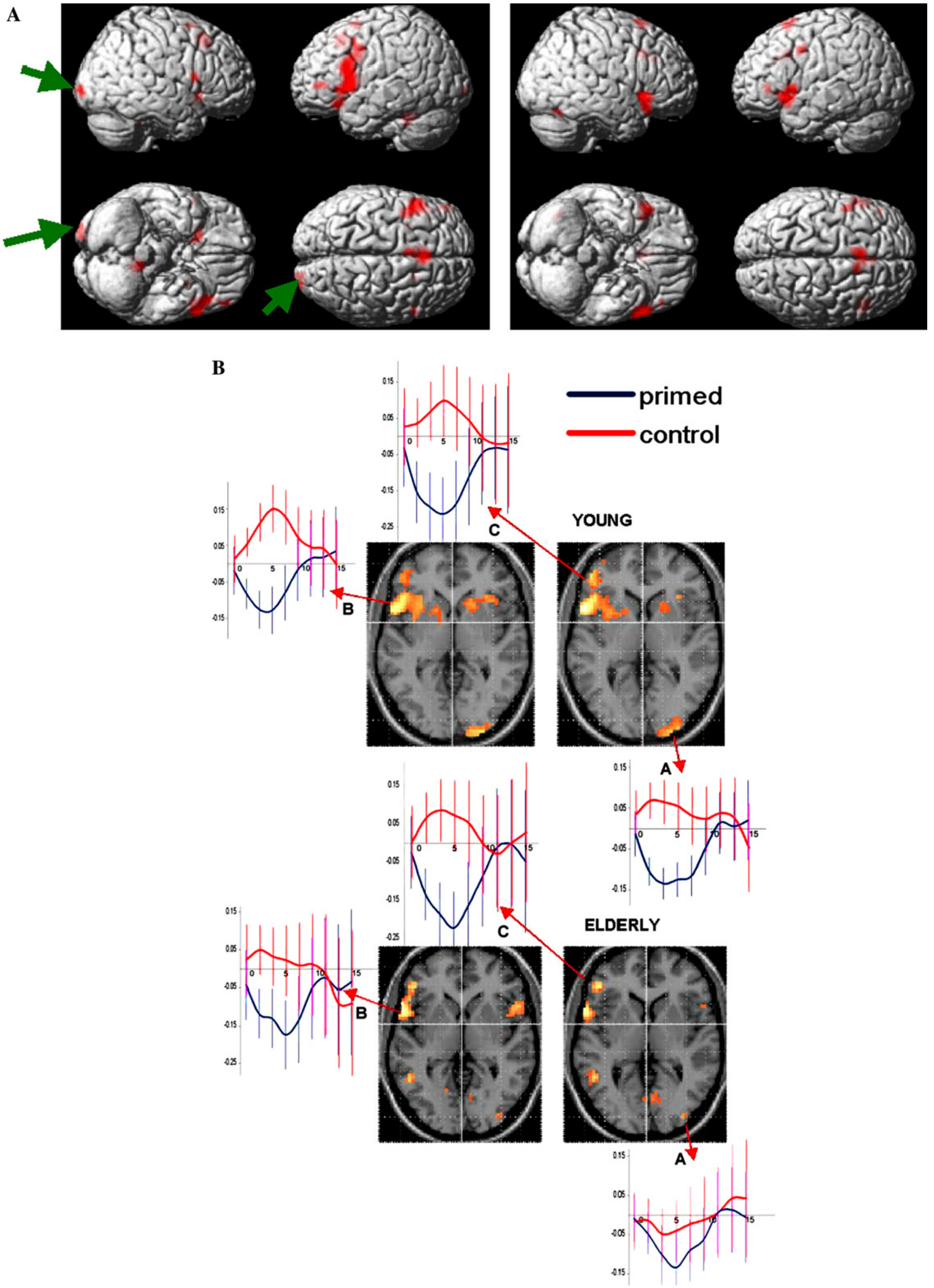

Fig. 1. (A) Normalized 3-D renderings, showing regions of the brain that showed reduced activity (for the purpose of illustration: $p < .001$; uncorrected; cluster = 10) during presentation of primed compared to control word stems. Group averages for the young participants are shown on the left, for the elderly participants on the right. The green arrows indicate a cluster of reduced activity in the right posterior occipital lobe (BA 17/18) in the group of young participants. (B) Normalized axial T1-images, showing reduced activity (for the purpose of illustration: $p < .01$; uncorrected) in the right posterior occipital lobe (A), the left anterior superior temporal gyrus (B), and the left inferior frontal gyrus (C) in comparison of primed versus control word stems. Plots for the local maxima in the young (A[x, y, z]: $27, -96, 5$; B[x, y, z]: $-53, 15, 5$; and C[x, y, z]: $-48, 17, -6$) and old (A[x, y, z]: $36, -87, 7$; B[x, y, z]: $-53, 12, 2$; and C[x, y, z]: $-45, 17, -6$) groups indicate event-related data in terms of the percentage signal change averaged across participants (relative to the global mean over voxels and scans) against peri-stimulus time (s), adjusted for confounds and binned every 2 s. The vertical bars indicate mean standard errors.

Table 4
Maxima of regions showing significant priming-related BOLD signal reductions ($p < .001$, uncorrected; extent threshold = 10) in comparison of the young and elderly groups

Region of activation	Left/right	Brodmann area	Talairach coordinates x, y, z {mm}			Z value
Young—Elderly						
Superior temporal gyrus	L	22	−53	12	2	3.38
Primary visual cortex	R	17/18	15	−99	0	3.49
Cerebellum	L	—	−9	−45	−23	4.78
Elderly—Young						
No significant differences						

Table 5
Maxima of regions showing correlations ($p < .001$, uncorrected; extent threshold = 10; unless indicated otherwise by asterisk) between activity reductions and priming effect (percent reduction in response times) for the young and elderly groups

Region of activation	Left/right	Brodmann area	Talairach coordinates x, y, z {mm}			Z value
Young						
Inferior frontal gyrus	L	47	−53	20	2	2.29*
	L	44	−50	13	19	2.46*
	L	10	−45	44	−2	2.28*
Superior frontal gyrus	L	8	−3	20	43	2.76*
Elderly						
Inferior frontal gyrus	L	47	−50	23	−11	4.42
	R	47	50	20	−6	4.24
Superior frontal gyrus	R	8	3	23	51	3.77

lowered the threshold to $p < .005$, uncorrected, some reduced activity was observed in this area in the old group as well (Fig. 1B; Talairach coordinates [x,y,z]: 36, −87, 7; $z = 2.87$). In Fig. 1B, BOLD signal time courses are included for the primed and control conditions in the left inferior frontal gyrus, the left anterior superior temporal gyrus, and the right posterior occipital lobe (BA 17/18). The error bars indicate comparable within-subject variance in the imaging data for the two groups.

As shown in Table 5, the regression analysis identified four regions in the group of older participants in which the amount of activity reduction correlated significantly with the degree of priming as indicated by the percent RT reduction. These regions included the left and right inferior prefrontal cortex, superior frontal gyrus and right middle temporal gyrus. Only the areas in the left and right inferior prefrontal cortex were also identified in the general group analysis, but at a slightly lower threshold of $p < .001$, uncorrected, the other regions also showed a reduction based on the general group analysis (Fig. 1A, Table 3).

At the set threshold, the young group did not show any significant correlations with priming magnitude. However, when we lowered the threshold to $p < .05$, cluster extent = 5, similar correlations could be observed in left inferior frontal regions and the anterior cingulate/superior frontal gyrus.

The right occipital region was not part of our regions-of-interest, because it did not reach the set threshold in the within-group analysis. Nevertheless, this region was included in the regression analysis, because, as noted, priming-related reductions have been reported consistently in this region, and because it was part of our research question. However, in both groups activity within the right occipital lobe was not correlated with priming magnitude even when the threshold was lowered to $p < .05$, uncorrected, cluster extent = 5. Resuming, at the set threshold, behavioral measures of priming correlated significantly with neurofunctional measures only in the elderly group. However, at a more lenient threshold ($p < .05$, uncorrected), similar correlations were observed in the young group.

Since our screening procedure may have missed some older participants with more subtle brain atrophy, we performed an additional ANCOVA analysis upon the older adults' imaging data using MMSE scores as a confounding factor. Inclusion of this factor did not meaningfully change the results (data not shown). Hence, these findings indicate that age-related pathology did not play a major role in the present study.

Finally, in order to address a possible confound presented by group differences in baseline completion times (see Section 3.1), we redid the fMRI group comparison using young and old groups with comparable RTs for the control word stems. Again, age differences were observed in the left superior temporal gyrus (Talairach coordinates [x,y,z] = −54, 15, 3; $z = 2.68$), right posterior occipital lobe (Talairach coordinates [x,y,z] = 30, −96, −3; $z = 3.27$), and cerebellum (Talairach coordinates [x,y,z] = −9, −42, −30; $z = 4.23$). This demonstrates that the differences in priming-related activity we observed cannot be explained by age differences in baseline completion times only.

4. Discussion

In this fMRI study, brain activity patterns were compared in young and elderly adults, while they were performing an adapted version of the word stem completion (WSC) priming task. We tested the hypothesis that elderly relative to young participants show intact perceptual priming, but impaired lexical/semantic priming. To this end, we distinguished between priming-related activity reductions in modality-specific regions involved in visual processing, and regions associated with lexical/semantic retrieval processes, i.e., left lateral temporal and left prefrontal regions.

In view of possible motion artifacts, we used an adapted version of the WSC task in which the word stems were completed in silence followed by a button-press. The percent response time (RT) reduction for primed relative to control word stems was used as a behavioral measure of priming. The validity of this measure was indicated in the young group by a positive correlation with the proportion of word stems completed (in writing) with targets relative to control words. Both groups revealed significant RT reductions for the primed compared to the control word stems. However, in accordance with earlier findings, a larger priming effect was found in the group of young participants (Chiarello & Hoyer, 1988; Hultsch et al., 1991).

Contrary to our expectations, the elderly participants were significantly faster than the young adults to complete the control word stems. This difference in task performance could account, at least to some extent, for the group difference in priming magnitude that was observed in the present study. However, we ruled out this possibility based on a series of follow-up statistical tests, which indicated that the age difference in priming magnitude was not related to a ceiling effect, inappropriate task performance, or differences in baseline completion times. We believe that the faster completion times in the elderly reflected greater proficiency in stem completion in the older adults. One reason for this may be that older adults have a larger vocabulary at their disposal. Such an explanation fits well with studies showing that crystallized verbal skills continue to show an improvement across the life span, while other cognitive functions show a consistent decline (e.g., Park et al., 2002). Moreover, a positive relation between age and vocabulary scores has been reported many times. Based on an extensive meta-analysis of 210 articles, Verhaeghen (2003) recently reported significantly higher scores in old relative to younger adults on vocabulary tests including those that require production of verbal information, such as word stem completion tasks.

Priming effects were also observed on a neuroanatomical level. In line with previous imaging studies, the groups showed common activity reductions in the anterior cingulate, and the left inferior prefrontal cortex extending into the anterior portion of the left superior temporal gyrus, and at lower thresholds also in the right occipital lobe (Backman et al., 1997; Badgaiyan & Posner, 1997; Buckner & Miezin, 1995; Buckner et al., 2000; Thiel et al., 2001). However, activity reductions in the cerebellum and the anterior part of the left superior temporal gyrus were found to be greater in the young participants, when directly comparing the groups. Activity in the cerebellum has previously been found to be reduced in association with covert visual word stem priming (Buckner et al., 2000). Since this region has been associated with speech production, this could reflect priming of motor components of speech, although the task was silent (Ackermann & Hertrich, 2000; Fiez, 2001). As noted, the left anterior temporal lobe has been implicated in lexical/semantic retrieval processes (Mummery et al., 1999a, Mummery, Shallice, & Price, 1999b; Tyler, Russell, Fadili, & Moss, 2001; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996). In addition, several studies have reported activity reductions in this region specifically associated with lexical/semantic priming (Buckner et al., 2000; Dhond, Buckner, Dale, Marinkovic, & Halgren, 2001; Mummery et al., 1999a). Hence, the smaller reduction seen in this region for the older group supports the view that aging affects the lexical/semantic component of word stem priming.

A recent fMRI study by Lustig and Buckner (2004) also reported subtle age difference in semantic priming. They compared groups of young adults, healthy elderly, and Alzheimer dementia (AD) patients using a semantic (living vs. nonliving classifications) repetition priming paradigm. Post hoc analyses on the time course data for repeated items revealed a slight but significant reduction of the priming effect in left inferior PFC (BA 45/47) in both the older adults and the AD group.

Several neuroimaging studies have shown that word stem completion and word stem priming are subserved by the same neuroanatomical substrates (e.g., Buckner et al., 2000; Thiel et al., 2001). Therefore, it may seem counterintuitive, that, in the present study, older adults were more proficient in word stem completion, while, at the same time, they showed a reduced priming effect. However, even though the relation between priming and decreased neural activity is well established (Henson & Rugg, 2003), the specific neural mechanisms underlying this reduction remain unclear. Accordingly, it is possible that, on the cellular level, the initial activation of the stimulus representation involves a different mechanism than the one supporting repetition priming. If this is the case, the current results would suggest that, despite the overlap in brain regions, these mechanisms operate relatively independently from each other, and are differentially sensitive to effects of aging.

Another region that showed a significant group interaction was the right occipital lobe. The young participants again showed a larger priming-related decrease in this region than the old participants. This seems to indicate that, contrary to our expectations, aging also has an effect on visual/perceptual components of repetition priming. It is important to note, though, that previous neuroimaging studies of WSC priming provided indications that occipital reductions do not necessarily reflect visual priming. Badgaiyan, Schacter, and Alpert (1999) and Buckner et al. (2000) also found decreases in the inferior temporal/extrastriate cortex when the study words were presented auditorily. Furthermore, Badgaiyan, Schacter, and Alpert (2001) found no evidence that extrastriate decreases are sensitive to a voice change, and Buckner and Miezin (1995) found no evidence that they are sensitive to a case-change, suggesting that the region is not sensitive to low-level perceptual details. However, neither Badgaiyan et al. (1999) nor Schacter, Badgaiyan, and Alpert (1999) found occipital decreases for cross-modal priming, suggesting that such decreases are not completely amodal either.

Nevertheless, it is important to distinguish between more anteriorly situated extrastriate regions and the reduced activity we observed at or near the primary visual cortex (BA 17/18). In the Buckner et al. (2000) study, similar to our study, an additional region near the primary visual cortex showed a reduction in activity, which was found to be specific to visual priming. They suggested, though, that this finding did not reflect perceptual priming per se, but might have been related to the blocked presentation of primed and control word stems in that study. They further suggested that the participants might have become aware that all of the items would be new or that all would be repetitions. According to the authors this awareness could have altered attentional aspects of processing during presentation of the priming blocks resulting in these reductions near the primary visual cortex. However, we replicated this finding on an item-by-item basis using an event-related paradigm, indicating that it is not reflecting a block or "state-related" change. Furthermore, the finding of priming-related reductions near the primary visual cortex is not unusual, since it has been reported in other studies (Koutstaal et al., 1999: visual object priming). This finding by Buckner et al., in addition to the early position of this region in the ventral processing stream, substantiates our view that the activity decreases that we observed in the posterior occipital lobe reflect a change in modality-specific, perceptual processes.

The finding of a smaller priming effect in the visual cortex for the older adults was surprising to us, since a large number of behavioral studies of perceptual priming did not report any age differences (for a review, see Rybash, 1996), with the exception of only a few (Abbenhuis, Raaijmakers, Raaijmakers, & Vanwoerden, 1990; Prull, Light, Collett, & Kennison, 1998; Schacter, Church, & Osowiecki, 1994). Nevertheless, according to one account of cognitive aging, a reduction in sensory processing is one of the main determinants of age-related cognitive decline (Lindenberger & Baltes, 1994). In a recent fMRI study, Cabeza et al. (2004) investigated this idea by comparing young and old adults on three different cognitive tasks. In line with this account, they observed an age-related decrease in visual activity, which was independent of the specific task being performed. Moreover, age-related reductions in visual activation have been observed in several other neuroimaging studies covering different cognitive domains (for a review, see Cabeza, 2001). Hence, in view of these neuroimaging findings, it is not surprising that we also observed age differences in visual regions during word stem priming. The discrepancy between behavioral and functional neuroimaging measures may reflect a difference in sensitivity to detect subtle neurobiological changes (Wilkinson & Halligan, 2004). Also, priming tasks generally have low reliability, making it difficult to detect small differences between groups and conditions (Meier & Perrig, 2000).

Our results are not consistent with a previous imaging study on the effects of aging on word stem priming by Backman et al. (1997), in which a similar priming-related reduction was found in the right extrastriate cortex in young and elderly participants. In addition, this study reported no activity reductions in lexical/semantic regions, even though they used a semantic encoding condition (i.e., pleasantness ratings). However, Backman et al. used a different scanning modality, i.e., Positron Emission Tomography, with very small sample sizes. Furthermore, they used a blocked presentation design, and consequently, they could not make a pure primed vs. control comparison. Instead, they used an equal presentation ratio of primed vs. control word stems for the priming condition, relative to no primed word stems for the baseline. Hence, an explanation for these inconsistent results could reside in methodological differences.

To examine whether perceptual and lexical/semantic regions were differentially contributing to the amount of priming in the young and old adults, we carried out a regression analysis upon the imaging data using the percent RT reductions as a covariate. In the old group, significant correlations were observed in the same regions that were indicated by the main effect, but not in the right posterior occipital lobe, even at more liberal thresholds. Surprisingly, no region reached significance in the group of young participants. Only when we applied a more lenient threshold similar correlations were observed between priming magnitude and activity in left inferior prefrontal cortex and superior frontal gyrus. One reason for the lack of significant correlations may be that the young participants' behavioral data were somewhat noisier than that of the elderly participants, as reflected in the greater within-subject variability. Importantly, similar to the old group, no correlations were seen in the visual cortex. Contrary to our expectations, these results indicate that, at least, in our version of the word stem completion task priming is more dependent on lexical/semantic than on perceptual processes. One likely reason for this is that we used a semantic encoding task in order to boost lexical/semantic priming. Two previous fMRI studies, which also used a semantic encoding paradigm, either by mere repetition of the word stems (Buckner et al., 2000) or by pleasantness ratings about the target words (Thiel et al., 2001), similarly reported more prominent activity reductions in lexical/semantic regions than in visual regions.

There is another account of priming deficits in elderly and demented participants that distinguishes between identification and production forms of priming (Gabrieli et al., 1994). According to this view, identification priming relies on perceptual overlap at study and test and occurs when participants are instructed to identify previously presented stimuli. In contrast, production priming occurs during tasks in which participants are instructed to use a presented cue to guide retrieval of a response, such as during word stem priming. It has been suggested that it is this retrieval component that determines impaired priming in elderly and demented participants on WSC tasks (Fleischman & Gabrieli, 1998; Gabrieli et al., 1999). However, our findings suggest that aging also affects the perceptual component, which is thought to underlie visual identification priming.

It should be stated, though, that some caution in the interpretation of the group difference we observed in the occipital lobe would be appropriate since, as mentioned, the reduction in this region did not meet the criterion we applied for the within-group analyses in neither one of the groups. Consequently, strictly speaking, it was not part of the regions of interest that we identified for the group comparison and regression analysis. Other grounds for caution in interpreting our data may be that indications have been provided that the signal-to-noise ratio of the BOLD fMRI signal is somewhat greater in young than in elderly adults (D'Esposito, Zarahn, Aguirre, & Rypma, 1999a, 1999b). Hence, this could have influenced the results reported in this study. However, this aspect appears to affect the extent of activated clusters rather than the peak activation, and accordingly, this is not likely to have influenced the group differences in brain activity observed in this study, which were all found at or near the local maxima of the young participants (Huettel, Singerman, & McCarthy, 2001). Furthermore, the plots of the percent signal change across peristimulus time for the various regions of interest indicated comparable variance for the young and the old groups in our study. Moreover, most of the young and old participants participated in three other fMRI studies, in which we observed either equivalent levels of activity or regionally specific differences, indicating that, at least for the sample of old participants that we used, reductions in BOLD signal changes are not aspecific (Daselaar et al., 2003a; Daselaar, Veltman, Rombouts, Raaijmakers, & Jonker, 2003b, 2003c).

A final issue is that we cannot exclude the possibility that the participants gradually became aware of the nature of the priming task, since we used a multiple study-test block design. It is, therefore, conceivable that, despite the indirect task instructions, our results have been contaminated with intentional retrieval strategies. Accordingly, the reduced priming effects observed in the elderly group could reflect differential contributions of explicit memory strategies in the young and elderly participants. However, we believe the specific instruction to respond as fast as possible prevented the use of an explicit strategy. Another issue may be that the validity of using response time reductions as a priming measure was not tested in the elderly participants. The reason for the lack of post-scan priming measures in the elderly group stemmed from the expectation that scanning session to be rather strenuous for the old participants and that factors related to fatigue and physical exertion would affect the manipulation check, which involved another 15–20 min of testing. However, as noted, a positive correlation was found between post-scan priming measures and RT reductions in the young participants. Moreover, in both groups the priming condition yielded reduced activity in various regions that have been associated with word stem completion priming in previous imaging studies. Finally, both groups showed a positive correlation between response time reductions and brain activity. In sum, a relation between RT reductions and behavioral priming was indicated in the young participants, whereas a relation between reduced RT and reductions in brain activity was observed in both young and older adults. Together, these findings indicate the validity of using RT reductions as a measure of word stem priming in the older adults.

In sum, despite faster baseline completion times, the older participants showed a reduced priming effect as measured with an adapted version of the word stem completion task. In both groups, the same brain regions were found to be involved in word stem priming. However, greater priming-related reductions were found in the young group in both perceptual (right posterior occipital lobe) and lexical/semantic (left anterior superior temporal gyrus) regions. Converse to current psychological views, these findings suggest that aging affects both perceptual and lexical/semantic components of word stem priming.

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