Sex influences on material-sensitive functional lateralization in working and episodic memory: Men and women are not all that different

Kristen M. Haut[a],[*] and Deanna M. Barch[a,b]

[a]Department of Psychology, Washington University in St. Louis, MO 63150, USA
[b]Department of Psychiatry, Washington University in St. Louis, MO 63150, USA

Research investigating the effects of sex on the lateralization of language functions has produced mixed results to date, with some studies finding sex differences and others not (Shaywitz, B.A., Shaywitz, S.E., Pugh, K.R., Constable, R.T., Skudlarski, P., Fulbright, R.K., Bronen, R.A., Fletcher, J.M., Shankweiler, D.P., Katz, L., et al., 1995. Sex differences in the functional organization of the brain for language. *Nature* 373 607–609; Frost, J.A., Binder, J.R., Springer, J.A., Hammeke, T.A., Bellgowan, P.S., Rao, S.M., Cox, R.W., 1999. Language processing is strongly left lateralized in both sexes. Evidence from functional MRI. *Brain* 122 (Pt. 2) 199–208). Further, few studies have evaluated how any such sex effects extend to tasks involving cognitive functions that may utilize language processes such as working and episodic memory. This study examined sex difference in material-sensitive functional activation (using fMRI) in working memory and episodic memory that included either words and faces. We performed these analyses on two large groups of healthy subjects with the goal of attempting to replicate results across two independent data sets. The results indicated that both males and females showed strong and consistent evidence for material-sensitive lateralization for both working and episodic memory, such that word tasks resulted in greater left-sided activation and face tasks resulted in greater right-sided activation. Further, few of the sex differences in regions showing material specificity effects in at least one gender replicated across studies, providing little evidence for any differences in lateralization patterns between the sexes. In conclusion, our data suggest that males and females show a similar pattern of lateralized activation to material type during working memory and recognition tasks.
© 2006 Elsevier Inc. All rights reserved.

Keywords: Sex differences; Functional lateralization; Working memory; Recognition

 * Corresponding author. Department of Psychology, University of Minnesota, N218 Elliott Hall, 75 East River Rd., Minneapolis, MN 55406, USA.
 E-mail address: hautx005@umn.edu (K.M. Haut).
 Available online on ScienceDirect (www.sciencedirect.com).

Introduction

The influence of sex on cortical activation in language processing is unclear. It has been hypothesized that during language processing tasks, females show more bilateral activation of frontal and temporal regions than males, but the evidence for this general hypothesis has been contradictory. Several studies using a range of behavioral and neuroimaging methods have found evidence to support increased bilateral activation in females (Shaywitz et al., 1995; Kansaku et al., 2000). However, a number of other studies fail to find this effect (Buckner et al., 1995; Shaywitz et al., 1995; van der Kallen et al., 1998; Frost et al., 1999; Kansaku et al., 2000; Vikingstad et al., 2000; Baxter et al., 2003). In addition, few studies have examined whether females show more bilateral activation than males in other cognitive tasks that may involve language processing, such as verbal working memory (Speck et al., 2000). The goal of the current study is to investigate sex similarities and differences in brain activation during working memory and episodic memory tasks using both verbal and nonverbal stimuli. To address some of the limitation of past studies, we used large sample sizes and examined the extent to which results replicated across two separate studies.

The hypothesis that there are sex differences in functional organization of brain activity during language processing was generated in part by evidence from lesion studies showing that males had greater language impairment from left hemisphere lesions than women (McGlone, 1977). This finding has been interpreted to suggest that language function in females may be more resilient following traumatic insult because they had a more distributed (e.g., bilateral) system for language processing. However, these findings of sex differences in language impairment following lesions have not always replicated (De Renzi et al., 1980; Kertesz and Benke, 1989). Other anatomical studies have examined the size and asymmetry of language-related regions like the planum temporale in males and females, with some results indicating sex differences in the size and symmetry of the planum temporale showing males to have greater asymmetry than females

(Witelson and Kigar, 1992; Kulynych et al., 1994). However, subsequent research found that women showed proportionally larger planum temporale bilaterally, with no difference in symmetry between males and females (Harasty et al., 1997), and another study found no sex differences in either the size or symmetry of other language-related areas (Aboitiz et al., 1992).

Even without clear evidence of sex differences in morphometrical characteristics of language-related brain regions, there still could be sex differences in functional brain activation patterns. For example, there is evidence that women perform better than men on some verbal tasks, including verbal fluency and tasks involving verbal memory (Halpern, 1992; Kimura, 2000). However, differential performance on verbal fluency or verbal memory tasks does not provide evidence about the degree of lateralization of brain activity during the performance of such tasks.

More recently, researchers have begun to use functional neuroimaging as a method to investigate differences in brain activation patterns during language tasks in males and females. Shaywitz et al. (1995) found that females demonstrated more bilateral activation than males, especially in the inferior frontal gyrus, when making phonemic judgments of rhyming words. A further report of this same study indicated no additional laterality differences, though it provided evidence for other sex differences that suggest the functional networks used for phonological tasks and semantic tasks overlap more in women than in men (Pugh et al., 1996). Additional evidence of sex related lateralization differences in the inferior frontal gyrus has come from studies of past tense generation (Jaeger et al., 1998). Furthermore, females showed more bilateral activation than men in various inferior frontal and superior temporal regions during a forward listening task requiring global language comprehension (Kansaku et al., 2000; Phillips et al., 2001) and semantic decision tasks involving categorical knowledge (Baxter et al., 2003). In addition, silent verb generation elicited primarily left lateralized activity in males in the inferior and middle frontal gyri but only half the women showed bilateral activation of these regions (Vikingstad et al., 2000).

Although there have been several functional imaging studies indicating more bilateral activity in women than men during language tasks, the review above indicates that the exact nature and location of these sex differences have varied considerably across studies. In addition, a number of other studies have not found any evidence for sex differences in the degree of lateralization associated with language processing (Buckner et al., 1995; Price et al., 1996; van der Kallen et al., 1998; Frost et al., 1999; Szaflarski et al., in press). The lack of replication and consistency among imaging studies of language lateralization and sex may reflect in part the fact that many of the studies reviewed above used small sample sizes, which can contribute either to lower power to detect significant differences or to the detection of spurious differences that do not generalize to a larger population. In general, the studies finding lateralization differences between sexes had fewer participants than the studies that did not find sex differences. For examples, the studies finding sex differences had subject numbers ranging from 19 females and 19 males (Baxter et al., 2003) to 19 males and 19 males (Shaywitz et al., 1995; Pugh et al., 1996) and 22 males and 25 females (Kansaku et al., 2000). In the studies not finding sex differences, van der Kallen et al. (1998) used only 5 females and 9 males, but Buckner et al. (1995) had 37 females and 24 males, and Frost et al. (1999) included 50 females and 50 males. Given that larger samples sizes are generally better at detecting subtle differences between groups and eliminating

spurious findings (Price et al., 1996), the fact that the two largest imaging studies of sex differences in language function done so far found no lateralization differences raises questions about the robustness of some of the positive findings.

The hypothesis that functional lateralization for language processing differs by sex also raises the question of how such functional organization differences might influence other cognitive processes that depend in part upon language processing. If sex differences on language tasks reflect a global difference in language processing, then cognitive tasks that employ a language component should also illustrate these differences. One cognitive domain that has been examined for sex differences is working memory, using tasks such as 1-back and 2-back letter tasks and incremental number tasks (Speck et al., 2000). Speck and colleagues found that for all four tasks male subjects showed bilateral activation in regions commonly involved with working memory, while females showed activation primarily in the left hemisphere. As such, the results of this study actually suggest greater lateralization in verbal working memory tasks among women than men.

In contrast to the work on sex-related lateralization differences for verbal processing, there has been relatively little examination of sex differences in laterality or performance during face processing. Iaccino reviewed behavioral studies that suggest a left visual field advantages for men in spatial tasks, indicating that they may be more strongly lateralized (Iaccino, 1993). There is also limited behavioral evidence that males may have a stronger functional brain asymmetry in face recognition (Rizzolatti and Buchtel, 1977). Functional neuroimaging studies of face related lateralization differences between males and females have generally focused on processing of emotional faces (Killgore and Yurgelun-Todd, 2001). The findings of this study did suggest that males were more lateralized than females in the prefrontal cortex and amygdala. However, the authors interpreted this result as related to affect rather than basic face processing. Other studies of sex difference in activation to faces have not found lateralization differences (Voyer, 1998).

As reviewed above, the results in the existing literature on functional lateralization patterns across sexes in language and face processing tasks are mixed, and the data examining sex differences in lateralization in working memory and other cognitive tasks are sparse. The goal of the current study was to examine whether men and women show similar or different patterns of functional brain activation in response to stimulus type (i.e., verbal versus nonverbal). To do so, we examined data from both working memory and episodic retrieval tasks that used two different material types—words and faces. This allowed us to examine patterns of functional lateralization in response to both verbal and nonverbal materials in two different cognitive domains, permitting us to address the generality of any obtained sex differences. Further, we used data from two different studies, each of which had a large sample size. We attempted to replicate results obtained in one study with the other study in order to address potential confounds associated with using small samples sizes and varying methods across studies. We predicted that if sex differences in functional laterality of brain activation during language processing are a robust and reliable characteristic of human brain function, then such sex differences should extend to other cognitive domains that may also utilize language processing. Specifically, such a hypothesis would predict that females, as compared to males, should show more bilateral activation of regions such as inferior

frontal gyrus and superior temporal gyrus during both verbal working memory and verbal recognition. Further, such patterns should replicate across the two separate samples studied.

Methods

Participants

Participants in Study 1 were 49 healthy controls (26 females, 23 males), and participants in Study 2 were 61 healthy controls (37 females and 24 males). Group level data from the participants in Study 1 were presented in a prior report (Barch et al., 2002). In both studies, participants were recruited from the community using local advertisements, and informed consent was obtained following the procedures outlined by the Washington University IRB. Participants were excluded if they had a lifetime history of Axis I psychiatric disorders or any first order family member with a psychotic disorder (assessed using the Structured Clinical Interview for DSM-IV-nonpatient version (First et al., 2002)), administered by a Master's level clinician. Potential participants in both studies were also excluded for (1) meeting DSM-IV criteria for substance abuse (severe) or dependence (any type) at any time within the past 3 months; (2) the presence of any clinically unstable or severe medical disorder, or a medical disorder that would confound the assessment of psychiatric diagnosis, or make participation in the research protocol unsafe; (3) present or past head injury with documented neurological sequelae or causing loss of consciousness; and (4) meeting DSM-IV criteria for mental retardation. In both studies, handedness was assessed using the Edinburgh Inventory (Oldfield, 1971). Demographic information is shown in Table 1. In Study 1, the males and females differed slightly in age ($t(46) = 2.1$, $P = 0.04$) but did not differ significantly in either education ($t(47) = 0.61$, $P > 0.5$) handedness score ($t(47) = 0.17$, $P > 0.5$). In Study 2, the males and females did not differ significantly in either age ($t(59) = -0.06$, $P > 0.20$), education ($t(59) = 0.89$, $P > 0.20$), or handedness score ($t(59) = -1.1$ $P > 0.20$). In Study 1, a subset of 32 individuals were administered the Wechsler Adult Intelligence Scale—Third Edition (WAIS-III) Vocabulary subtest, and males and females did not differ significantly on vocabulary ($t(31) = -0.64$, $P > 0.5$). All participants in Study 2 were administered the WAIS-III vocabulary

subtest, and males and females again did not differ significantly ($t(59) = 0.92$, $P > 0.3$).

In both Study 1 and Study 2, all participants were scanned while performing three types of tasks: (1) episodic encoding; (2) working memory; and (3) yes/no recognition. Each task was performed twice, once with verbal stimuli and once with nonverbal stimuli (see below). In Study 1, the episodic encoding task was intentional encoding (try to remember these items for a later memory test), which did not generate any concurrent behavioral data that could be used to confirm attention to the task. In Study 2, participants did perform incidental encoding tasks (abstract/ concrete judgments for words, sex judgments for faces) that did generate such concurrent behavioral data. However, we chose not to analyze the data from these encoding tasks since they were not identical across studies and would not allow for replication analyses. In both studies, the task used to assess working memory was the "2-back" version of the "N-back" task. In this task, participants saw a sequence of stimuli presented in the center of a computer screen and were told to push one button (target) any time they saw a stimulus that was the same as the stimulus that they saw two trials back and to push a nontarget button otherwise. The stimuli for each task were presented in four blocks of trials, with each block containing 16 trials. Within each 16 trials, 1/3 were targets, and 2/3 were nontargets. The recognition task used a yes/ no format. Participants were presented with a series of stimuli and told to press one button if the stimulus had been seen during either of the two previous tasks (working memory or encoding) and another button if the stimulus was new. As with the working memory tasks, stimuli were presented in four blocks of 16 trials. Half of the stimuli were old and half were new, and of the old stimuli, half were seen during the working memory task, and half were seen during the encoding task.

Stimuli for the verbal tasks were concrete visually presented words, 3–10 letters in length, presented in 48-point Geneva font. Stimuli for the nonverbal tasks were nonnameable faces. These are the same stimuli used in a number of prior studies (Kelley et al., 1998; Braver et al., 2001; Barch et al., 2002; Logan et al., 2002). For both words and faces, stimuli were separated into lists, and the list used for the encoding versus the working memory task was counterbalanced so that half the participants received list 1 during encoding and list 2 during the working memory task, with the opposite order for the remaining participants. Tasks with the same stimulus type were grouped together, and the order in which participants received either the verbal or nonverbal tasks was counterbalanced across subjects. The encoding and working memory tasks were always performed before the recognition task. However, the order in which participants performed the working memory versus encoding task was counterbalanced across subjects. These counterbalancing procedures allowed us to control for any confounding effects of stimuli, time on task, head movement, scanner drift, etc.

In both studies, participants performed each task in a run lasting 255 s (6 runs total). Each run included 4 task blocks and 3 fixation blocks interleaved in alternating order with the task blocks. Task blocks lasted 40 s, and fixation blocks lasted 25 s. Each of the 16 items in a task block was presented for 2 s followed by a 500-ms interval. During fixation blocks, a cross-hair appeared continuously, and participants were told to fixate. Visual stimuli were generated by an Apple PowerMac and PsyScope (Cohen et al., 1993) and projected to participants with a Sharp LCD projector onto a screen positioned at the head end of the bore. Subjects viewed the screen through a mirror attached to the top of the MR head coil. A fiber-

Table 1
Demographic and clinical characteristics

| | Group | | | |
| | Males | | Females | |
	M	SD	M	SD
Study 1				
Age (in years)	33.1	10.8	39.7	10.8
Education (in years)	14.8	2.3	15.3	2.3
Handedness (laterality score)	90.4	26.9	82.3	55
WAIS-III vocabulary	10.5	4.4	11.6	3.8
Study 2				
Age (in years)	22.1	3.1	22.1	2.8
Education (in years)	13.9	1.8	14.3	2.1
Handedness (%right)	92%		100%	
WAIS-III vocabulary	13.21	2.9	12.6	2.3

Demographic data showing the age, education, and handedness of the male and female participants in each of the two included studies.

optic key press interfaced with the PsyScope Button box was used to record participant's behavioral performance.

Scanning

All scanning was performed on the 1.5-T Siemens VISION system at the Research Imaging Center of the Mallinkrodt Institute of Radiology at the Washington University Medical School. Two types of information were acquired in each scan session: functional and structural scans. The functional images were collected in runs using an asymmetric spin-echo echo-planar sequence sensitive to blood oxygenation level-dependent (BOLD) contrast (T2*) (TR = 2500 ms, TE = 50 ms, FOV = 24 cm, flip = 90°). During each functional run, 102 sets of axial images were acquired parallel to the anterior–posterior commissure plane (3.75 × 3.75 mm in plane resolution), allowing complete brain coverage at high signal-to-noise ratio (Conturo et al., 1996). In Study 1, 16 8-mm-thick slices were acquired in each image. In Study 2, 17 7-mm-thick slices were acquired in each image. Structural images were acquired using a coronal MP-RAGE 3D T1-weighted sequence (TR = 10 ms, TE = 4 ms, flip = 8°; voxel size = 1 × 1 × 1.2 mm). These structural images were used for between subject registration (as described below) and anatomic localization.

Data analysis

Functional magnetic resonance imaging data (fMRI)

fMRI preprocessing included (1) compensation for slice-dependent time shifts; (2) elimination of odd/even slice intensity differences due to interpolated acquisition; (3) realignment of all data acquired in each subject within and across runs to compensate for rigid body motion (Ojemann et al., 1997); (4) session-wise intensity normalization to a whole brain mode value of 1000; and (5) spatial smoothing with an 8-mm FWHM Gaussian kernel. The functional data were transformed into the stereotaxic atlas space (Talairach and Tournoux, 1988) by computing a sequence of affine transforms (first frame EPI to T2-weighted TSE to MP-RAGE to

atlas representative target) composed by matrix multiplication. Reslicing the functional data in conformity with the atlas then involved only one interpolation. All analyses described below were conducted on the basis of atlas transformed data resampled to 3-mm³ voxels and were performed using in-house software programmed in the Interactive Data Language (Research Systems).

For each participant, we estimated the magnitude of task-related activation in each voxel using a general linear model (GLM) using a boxcar function convolved with an estimated hemodynamic response to estimate task-related activation, with separate estimates for each task and material type (e.g., working memory–words, working memory–face, recognition words, recognition–face). These estimates were then entered in appropriately designed analysis of variance (ANOVA) and t tests (described in more detail below) that treated subjects as a random factor. The estimates were analyzed and reported as the percentage of change from fixation. Images were thresholded to control for false-positive rate using a cluster-size threshold of 9 contiguous voxels and a per-voxel alpha of 0.005, corresponding to a corrected whole brain false positive rate of approximately 0.05. The analyses presented below were conjunction analyses in which we required multiple effects to be significant simultaneously. When two or more effects were required to be significant, a P value threshold of 0.02 was required for each effect, leading to a combined significance of either 0.0004 (0.02*0.02) or 0.000008 (0.02*0.02*0.02).

We were interested in identifying regions that showed significant differences in the degree of material-sensitive brain activation as a function of sex. However, we wanted any such regions to be responsive to task demands in at least one of the tasks and to be regions that showed material-specific sensitivity in at least one of the sexes. Without such constraints, we might find regions showing sex differences that were not significantly responsive to any task and/or which did not show evidence of material-specific sensitivity, making it difficult to interpret the functional importance. To find such regions, we required voxels to show a conjunction of the following three effects, each at a significance of 0.02: (1) greater activity for task compared to fixation for at least

Table 2
Behavioral data

	Group							
	Study 1				Study 2			
	Males		Females		Males		Females	
	M	SD	M	SD	M	SD	M	SD
Working memory								
Accuracy								
Word	0.88	0.15	0.90	0.12	0.97	0.04	0.96	0.06
Face	0.88	0.15	0.83	0.15	0.96	0.04	0.94	0.06
Reaction time								
Word	901	328	814	173	792	204	753	146
Face	962	336	893	191	914	259	838	172
Recognition								
Accuracy								
Word	0.72	0.18	0.67	0.15	0.76	0.11	0.76	0.09
Face	0.68	0.17	0.65	0.16	0.72	0.09	0.70	0.10
Reaction time								
Word	980	307	907	155	1053	142	1009	183
Face	1118	283	1076	137	1133	141	1074	148

Accuracy and mean reaction times are reported for males and females during working memory and recognition tasks for each material type (words and faces). Behavioral data for each study are reported separately.

one material type (words or faces) for at least one sex (males or females), using dependent sample *t* tests comparing magnitude estimates for task versus fixation; (2) greater task-related activity for either words compared to faces, or for faces compared to words, in at least one sex, using ANOVAs with condition (task versus fixation) and material type (word versus face) as within-subject factors; and (3) significant sex differences in the material-sensitive task-related activation, using ANOVAs with sex (male versus female) as a between-subject factor and both condition (task versus fixation) and material type (word versus face) as within-subject factors. In other words, we considered a voxel to be "significant" if it showed (1) a three-way interactions between sex, material type, and condition; (2) a two-way interaction between material type and condition in at least one sex; and (3) a main effect of condition in at least one material type in at least one sex. We first conducted the above analyses in the data from just Study 1 and identified regions (groups of contiguous voxels) showing the conjunction of all three effects and applied these regions to the data from Study 2 to determine if the patterns for these ROIs replicate. We then did the identical procedure starting with the data from Study 2 and applying the obtained ROIs to Study 1. In addition, the same analyses were conducted just for right handed subjects, with the same findings as for the whole group. Thus, just the results for the total sample are reported here.

Behavioral data

Accuracy and median reaction times (RTs) were examined for the working memory tasks and the recognition tasks using SPSS statistical analysis software. For each study, the accuracy and RT data from the WM and the recognition tasks were analyzed using 2-factor ANOVAs, with sex (male versus female) as a between-subjects factor and material (verbal versus nonverbal) as a within-subjects factor.

Results

Behavioral data

Study 1

The means and standard deviations for all behavioral data are shown in Table 2. For Study 1, the accuracy ANOVA for working memory indicated a marginal main effect of material type ($F(1,45) = 3.7$, $P = 0.06$), but no main effect of sex ($F(1,45) = 0.18$, $P > 0.5$) or sex by material type interaction ($F(1,45) = 2.5$, $P > 0.1$). The RT ANOVA for working memory indicated a significant main effect of material type ($F(1,45) = 16.1$, $P < 0.01$), with RTs to faces overall slower than RTs to words. There was no significant main effect of sex ($F(1,45) = 1.1$, $P > 0.3$) or sex by material type interaction ($F(1,45) = 0.38$, $P > 0.5$). The accuracy ANOVA for recognition did not indicate significant effects of material type ($F(1,45) = 1.14$, $P > 0.29$), sex ($F(1,45) = -0.97$, $P > 0.3$), or a significant sex by material type interaction ($F(1,45) = 0.04$, $P > 0.8$). For recognition RT, the ANOVA indicated a significant main effect of material type ($F(1,45) = 76.1$, $P < 0.01$), with RTs to faces again slower than RTs to words. There was no significant main effect of sex ($F(1,45) =$
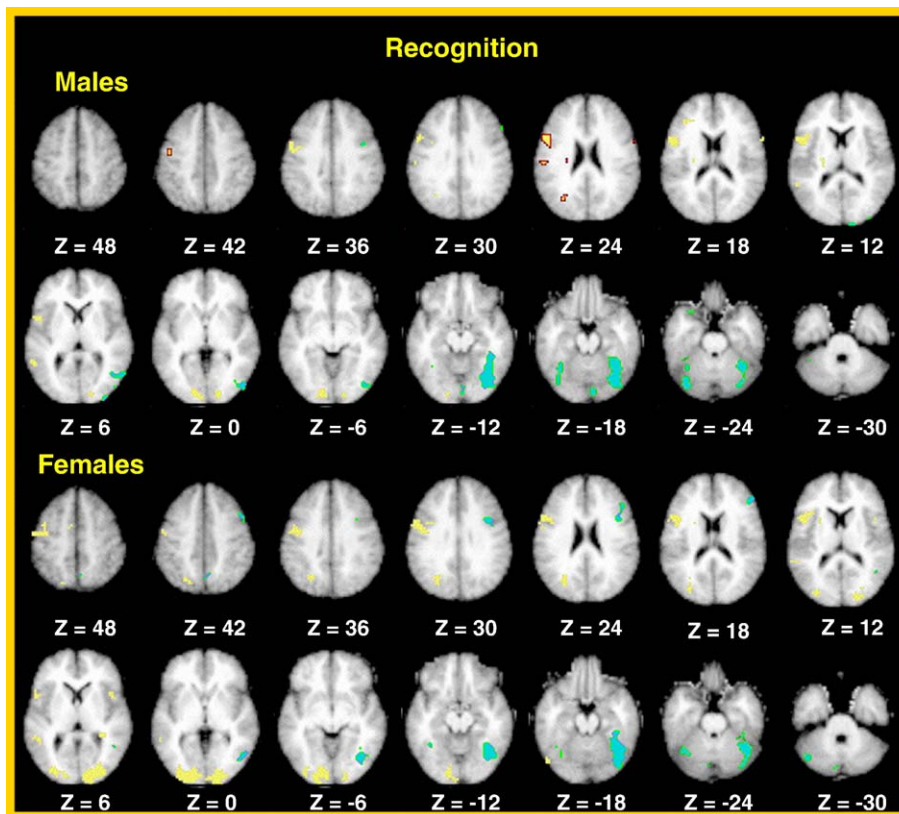

Fig. 1. Brain regions demonstrating significant material-specific activation during working memory in both Study 1 and Study 2, shown separately for males and females. The yellow regions represent regions where activity was greater to words than to faces. The blue regions represent regions where activity was greater to faces than to words. The right side of the image is the right side of the brain, and the left side of the image is the left side of the brain.

0.77, $P > 0.3$) or sex by material type interaction ($F(1,45) = 0.73$, $P > 0.3$).

Study 2

The behavioral results for Study 2 were similar to those for Study 1, although participants were overall more accurate and faster, potentially due to their younger age. The accuracy ANOVA for working memory indicated a significant main effect of material type ($F(1,59) = 7.9$, $P < 0.01$), with word more accurate than face. There was no significant main effect of sex ($F(1,59) = 1.8$, $P > 0.15$) or a significant sex by material type interaction ($F(1,59) = 0.4$, $P > 0.5$). The RT ANOVA for working memory again indicated a significant main effect of material type ($F(1,59) = 32.7$,

$P < 0.01$), with RTs to faces overall slower than RTs to words. There was no significant main effect of sex ($F(1,59) = 1.4$, $P > 0.2$) or sex by material type interaction ($F(1,59) = 1.04$, $P > 0.3$). The accuracy ANOVA for recognition indicated a significant main effect of material type ($F(1,59) = 10.6$, $P < 0.01$), with words recognized more accurately than faces. There was no significant main effect of sex ($F(1,59) = 0.17$, $P > 0.6$) or sex by material type interaction ($F(1,59) = 0.06$, $P > 0.8$). The RT ANOVA for recognition also indicated a significant main effect of material type ($F(1,59) = 23.0$, $P < 0.01$) with words responded to more quickly than faces. There was no significant main effect of sex ($F(1,59) = 01.71$, $P > 0.1$) or sex by material type interaction ($F(1,59) = 0.23$, $P > 0.6$). In summary, across both studies, performance of working

Table 3
Regions showing sex differences in material type effects in working memory

	Region coordinates (X, Y, Z)	Broadmann area	Volume (in voxels, each 3mm³)	Mean Z value for ROI	Pattern	Replication mean Z value	Replication pattern (if significant)
Study 1	+01, −47, −37	R cerebellum	64	3.3	♂:W > F, ♀:F > W	0.4	-----
	+33, −40, −28	R cerebellum	27	3.0	♂:W > F, ♀:F > W	0.1	-----
	−24, −60, −46	L cerebellum	22	3.2	♂:W > F, ♀:F > W	0.2	-----
	+24, −26, +25	Caudate nucleus	10	2.6	♂:W > F, ♀:F > W	2.1, P < 0.05	♂:F > W, ♀:W > F
	+10, −100, +09	R BA 18	47	3.9	♂:F > W. ♀:W > F	2.3, P < 0.05	♂:F > W, ♀:W > F
	+26, −94, −07	R BA 18	74	4.0	♂:F > W, ♀:W > F	1.5	-----
	−34, −96, −04	L BA 18	48	3.8	♂:F > W, ♀:W > F	1.2	-----
	+00, −86, −13	BA 18	20	3.0	♂:F > W, ♀:W > F	0.4	-----
	−18, −95, −17	L BA 18	12	3.2	♂:F > W, ♀:W > F	1.5	-----
	+10, −63, −08	R BA 19	10	2.6	♂:W > F, ♀:F > W	0.4	-----
	−38, −71, −01	L BA 19	10	3.2	♂:F > W, ♀:W > F	1.7, P < 0.10	♂:F > W, ♀:W > F
	−52, +01, +05	L BA 22	36	3.0	W > F : ♂ > ♀	1.1	-----
	+38, −46, −04	R BA 21	16	3.1	W > F, ♂ > ♀	0.8	-----
	+58, −06, −02	R BA 22	11	2.7	W > F: ♂ > ♀	1.7, P < 0.10	♂:F > W, ♀:W > F
	−16, −40, +38	L BA 31	13	2.5	♂:W > F, ♀:F > W	0.7	-----
	−45, −44, +49	L BA 40	110	3.8	♂:W > F, ♀:F > W	1.3	-----
	−54, −31, +25	L BA 40	86	3.6	♂:W > F, ♀:W = F	0.5	-----
	+50, −35, +32	R BA 40	24	3.3	♂:W > F, ♀:F > W	0.2	-----
	+19, −49, +58	R BA 7	49	3.4	♂:W > F, ♀:F > W	1.1	-----
	−16, −54, +54	L BA 7	53	3.0	♂:W > F, ♀:W = F	0.6	-----
	+06, −69, +50	R BA 7	11	2.9	♂:W > F. ♀:W = F	0.8	-----
	−19, −10, +43	L BA 24	36	3.2	♂:W > F, ♀:F > W	0.6	-----
	+07, +00, +41	R BA 24	17	3.0	♂:W > F, ♀:F > W	0.7	-----
	−15, +12, +42	L BA 32/24	29	2.9	♂:W > F, ♀:F > W	0.2	-----
	−25, −22, +65	L BA 4	9	3.1	♂:W > F, ♀:F > W	0.3	-----
	−03, −17, +58	L BA 6	12	2.6	♂:W > F, ♀:F > W	0.7	-----
Study 2	+28, −41, −34	R cerebellum	13	3.2	♂:W > F, ♀:F > W	1.2	------
	+26, −78, −25	R cerebellum	15	2.8	♂:F > W, ♀:W = F	0.1	------
	−29, −63, −14	L cerebellum	19	2.8	♂:F > W, ♀:W = F	1.0	------
	−04, −36, −11	Brainstem	53	3.5	♂:F > W, ♀:W > F	0.2	------
	+2, −20, +10	Thalamus	27	2.8	♂:F > W, ♀:W > F	1.2	------
	−19, +19, +16	Caudate nucleus	13	2.5	♂:F > W, ♀:W = F	0.9	------
	+19, −10, +22	Caudate nucleus	16	2.9	♂:F > W, ♀:W > F	1.9, P < 0.10	♂:W > F, ♀:F > W
	−32, −93, −20	L BA 18	18	2.9	♂:F > W, ♀:W > F	0.1	------
	−4, −102, −10	L BA 18	23	3.4	♂:F > W, ♀:W > F	1.8, P < 0.10	♂:F > W, ♀:W > F
	+38, −86, +11	R BA 18	17	2.6	♂:F > W, ♀:W > F	2.2, P < 0.05	♂:F > W, ♀:W > F
	+23, −85, +7	R BA 19	30	3.2	♂:F = W, ♀:W > F	1.0	------
	+39, −39, −10	R BA 37	9	3.5	♂:F > W, ♀:W > F	1.5	------
	−21, −65 +46	L BA 7	23	3.0	♂:F > W, ♀:W > F	1.3	------

Indicates the regions that show significant sex differences for working memory in Study 1 and Study 2, their Talairach coordinates, associated Brodmann areas, and the pattern of activation for words (W) and faces (F). The last two columns indicate if the region was significant in the other study and the pattern of activation for any significant regions. Note that few regions replicate and of those that do only two show the same patterns of sex differences in material specific effects across studies.

memory and recognition tasks with words tended to be more accurate and faster than tasks with face stimuli. However, there were no main effects of sex on any of these tasks and no sex by material type interactions.

Imaging data

Sex similarities in material type influences on working memory activation

We began our analysis of the working memory imaging data by examining the pattern of functional lateralization during working memory within each sex to obtain a global sense of whether men and women show qualitatively similar or different patterns. To do so, we identified regions within each sex that showed the following two effects: (1) significant task-related activity for either words or faces and (2) a significant material type by condition (task versus fixation) interaction. We conducted these analyses for each study separately. For ease of presentation and to save space, we present figures that show the regions that show significant material sensitivity effects in both studies. Further, presentation of the data in this manner helps to establish the degree of similarity in material sensitivity effects across the two studies. As shown in Fig. 1, men and women show qualitatively similar patterns of task-related brain activation as a function of material type. For example, both men and women show greater left inferior frontal, superior parietal, and middle temporal gyrus activation for words as compared to faces. Further, both men and women show greater right inferior frontal, superior parietal, middle temporal gyrus (including fusiform face

area) for faces as compared to words (see Fig. 1). Overall, the patterns shown by men and women appear to be qualitatively similar. However, we next conducted rigorous quantitative comparisons of the sexes to examine this question in more detail.

Sex differences in material type influences on working memory activation

As described in the Methods section, we used the conjunction of a series of specific tests to identify regions that showed sex differences in the influences of material types on functional brain activation in working memory and recognition tasks. We first conducted these analyses on the data from Study 1 and then applied any obtained ROIs to the data from Study 2 to determine if any of the effects replicated across studies. We then conducted the same analyses on the data from Study 2 and applied the ROIs to the data form Study 1. As shown in Table 3, there were 26 regions in Study 1 that met our criteria for regions showing sex differences in the influence of material type on functional brain activation: (1) significant task-related activation with at least one material type in at least one sex; (2) significant material type by condition (task versus fixation) in at least one sex; (3) significant sex by material type by condition interaction. The pattern demonstrated in a few of these regions could be taken as evidence for more bilateral activation in women as a function of material type. For example, in left BA 7 and left BA 40, men demonstrated greater working memory-related activation for words than faces, while women showed equal activation for words and faces. However, as also shown in Table 3, only 4 of these 26 regions showed significant (or
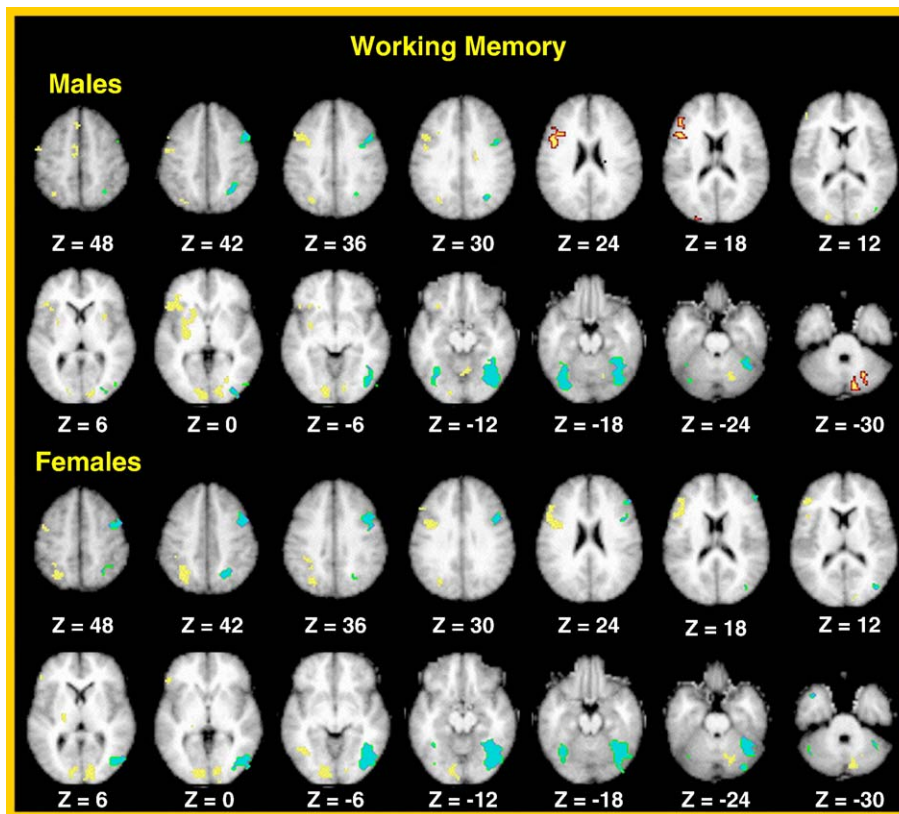

Fig. 2. Brain regions demonstrating significant material-specific activation during recognition in both Study 1 and Study 2, shown separately for males and females. The yellow regions represent regions where activity was greater to words than to faces. The blue regions represent regions where activity was greater to faces than to words. The right side of the image is the right side of the brain, and the left side of the image is the left side of the brain.

at least marginal) effects in Study 2. Further, of these 4 regions whose significance replicated, only 2 showed the same pattern in Study 2 as in Study 1. In right striate cortex (BA 17), women demonstrated greater working memory-related activation for words than faces, while males demonstrated the opposite pattern. In left extrastriate cortex (BA 18/19), we found the same pattern, with women showing greater task-related activation for words than faces and mean showing grater activation for faces than words. Thus, for both left and right occipital regions, women demonstrated greater activity for words than faces, with men showing the opposite pattern.

When we conducted the same conjunction analyses starting with the data from Study 2, we found 13 regions that meet our criteria for sex differences in the influence of material type on working memory-related activation (see Table 3). Of these 13 regions, 3 showed significant (or near significant) gender by material type interactions in Study 1. In one of these 3 regions (caudate), the pattern in Study 1 was opposite to the pattern seen in Study 2. The region in right BA 18 was very similar in location to the region identified in Study 1, and when we applied this ROI to the data from Study 1, we again found significant sex differences, with the same pattern in both studies. Again, in this right occipital region, women showed greater working memory-related activation for words than faces, while men showed greater activation for faces than words. One other region in left BA 17 showed a trend level replication across studies.

Sex similarities in material type influences on recognition-related activation

We began our analysis of the recognition imaging data by again examining the pattern of functional lateralization during recognition within each sex to obtain a global sense of whether men and women show qualitatively similar or different patterns. To do so,

we again identified regions within each sex that showed the following two effects: (1) significant task-related activity for either words or faces and (2) a significant material type by condition (task versus fixation) interaction. As with the working memory data, we show regions that demonstrate significant material sensitivity effects in both studies in Fig. 2. As shown in Fig. 2, men and women again demonstrated qualitatively similar patterns of recognition-related brain activation as a function of material type. For example, both men and women show greater left inferior frontal, left superior parietal, and right posterior cerebellum activation for words as compared to faces. Further, both men and women show greater right inferior frontal, right superior parietal, right fusiform, and left posterior lateral cerebellum activation for faces as compared to words. As with the working memory data, overall, the patterns shown by men and women appear to be qualitatively similar. However, we next conducted rigorous quantitatively comparisons for the sex to examine this question in more detail.

Sex differences in material type influences on recognition activation

We again used a series of conjunction tests to identify regions showing sex differences in material type influences on recognition related brain activation. As with the working memory data, we started by identifying such regions in the data from Study 1 and applying the obtained ROIs to the data from Study 2. As shown in Table 4, we found 11 regions that met our criteria. However, none of these regions replicated when applied to the data from Study 2. We then conducted the same analysis starting with the data from Study 2. We found 6 such regions that met our criteria. However, none of these regions from Study 2 replicated when applied to the data from Study 1. Although none of the exact ROIs replicated across

Table 4
Regions showing sex differences in material type effects in Recognition tasks

	Region coordinates (X, Y, Z)	Broadmann area	Volume (in voxels, each 3mm^3)	Mean Z value for ROI	Pattern	Replication mean Z value	Replication pattern (if significant)
Study 1	+26, −72, −39	R Cerebellum	104	4.2	W > F ;♂ > ♀	1.1	-----
	+44, −59, −29	R cerebellum	43	3.1	F > W, ♀ > ♂	0.2	-----
	+35, +89, +18	R BA 19	12	4.2	F > W, ♂ > ♀	0.9	-----
	+07, −31, −05	R BA 30	10	3.2	♂: W > F, ♀ : F > W	0.6	
	+37, −59, +00	R BA 37	28	2.7	♂: W > F, ♀ : F > W	0.8	-----
	−49, −65, +13	L BA 39	27	3.2	♂: W > F, ♀ : F > W	1.2	-----
	+20, −19, +31	R BA 24	21	3.4	♂: W > F, ♀ : F > W	0.2	-----
	−10,+18, +49	L BA 8	30	3.1	♂: W > F, ♀ : F > W	0.7	-----
	+17, −15, +52	R BA 6	18	3.2	♂: W > F, ♀ : F > W	0.7	-----
	+11, +08, +54	R BA 6	72	3.4	♂: W > F, ♀ :F > W	0.3	-----
	−23, −07, +50	L BA 4	49	3.6	♂:W > F, ♀ :F > W	0.6	-----
Study 2	+39, −76, −48	R cerebellum	9	2.8	♂:W > F, ♀ :F > W	1.3	-----
	+16, −84, −44	R cerebellum	16	2.6	♂:W > F, ♀ :F > W	1.2	-----
	−24, −14, −10	L Amygdala / Hippocampus	9	2.7	♂:W > F, ♀ :F > W	0.6	----- -----
	−23, +20, +5	Claustrum	13	2.5	♂:W > F, ♀ :F > W	0.3	
	−46, −80, −12	L BA 19	39	3.0	♂:W > F, ♀ :F > W	0.1	-----
	−50, −11, +43	L BA 3/4	13	3.0	♂:W > F, ♀ :F > W	1.0	-----

Indicates the regions that show significant sex differences for recognitions in Study 1 and Study 2, their Talairach coordinates, associated Broadmann areas, and the pattern of activation for words (W) and faces (F). The last two columns indicate if the region was significant in the other study. Note that none of the regions replicated across studies.

studies, we did find regions in right cerebellum in both studies that had somewhat similar, though not identical coordinates (e.g.,+26, −72, −39 versus +39, −76, −48). However, in the Study 1 right cerebellar region, both men and women demonstrated greater recognition related activation for words than faces, with a stronger effect in men than women. Such a pattern in right cerebellum is expected given data on material-related activation in the cerebellum. However, the right cerebellar regions identified in Study 2 showed greater recognition related activation for words than faces in men but the opposite pattern in women. Thus, although in somewhat similar locations, these two cerebellar regions did not show the same pattern of sex differences across the two studies.

Replicability of material-sensitive activation

A possible criticism of this study is that the methods we used to detect and verify sex differences were too stringent, and that they would fail to find any true activation patterns that would be similar between studies. To address this possibility, we employed similar conjunction analysis methods to identify regions showing material type specific influences on working memory and recognition related brain activation across studies. There is substantial evidence to indicate that language functions are left lateralized and face processing functions are right lateralized (Puce et al., 1996; Binder et al., 1997). As such, demonstrating that would identify regions showing such patterns that replicated across Study 1 and Study 2 would help to demonstrate the validity of this approach. We started by identifying regions demonstrating material specificity effects for working memory in the data from Study 1 and applying the obtained ROIs to the data from Study 2. We found 74 regions that met our criteria with activation for words greater than faces. Of these regions, 19 replicated in Study 2. Study 1 also showed 16 significant regions of interest where faces activated higher than words and 9 of these regions replicated in Study 2. We then followed the same procedure starting with Study 2. Of the 19 regions showing greater activation for words than faces, 14 replicated in Study 1. 25 regions were significant for faces greater than words in Study 2 and 11 of these replicated in Study 1. The regions that replicated across studies were in regions one would expect based on prior studies, including greater left hemisphere activation for words than faces and greater right hemisphere activation for faces than words in regions such as the fusiform gyrus. Thus, although not all regions replicated across studies, we did find consistent and reliable activation in regions expected to show material-sensitive activations across studies.

The same process was used to characterize the recognition data. When focusing on regions where face activation was greater than word activation, 21 regions met our criteria in Study 1 with 9 regions replicating in study two. In the reverse analysis, 23 ROIs were identified in Study 2 and 10 of those replicated to Study 1. Word task activation was higher than activation in face tasks in 44 regions in Study 1, 14 of which replicated to Study 2. In Study 2, 18 regions were found to be significant and 10 of those replicated to Study 1. As with the working memory tasks, the regions replicating across studies were ones expected to show material-sensitive activation based on prior research. These regions also included greater left lateralized activation for words than faces and greater right lateralized activation for faces than words. Thus, although this conjunction analysis and replication approach is stringent, it can detect consistent and reliable patterns of material-

sensitive activation across studies in regions one would expect to show such effects based on prior research.

Explicit assessment of lateralization

The analyses presented above focused on identification of regions showing material-sensitive effects, replicating previous findings of greater task-related activity with words than faces in left prefrontal and parietal regions (among others) and greater task-related activity with faces than words in right prefrontal and parietal regions (among others). However, we also quantitatively examined hemispheric differences in activation to words and faces in prefrontal and parietal regions. We conducted analyses identifying regions showing material-sensitive effects using the procedures described above but using the entire samples from both study1 and Study 2. We focused on prefrontal and parietal regions as they showed the clearest examples of homologous right and left regions that showed opposite patterns of material sensitivity. Specifically, we entered the left region of an area (i.e., either prefrontal or parietal) showing greater activity for words than faces and the right region showing greater activity for faces than words into an ANOVA with material type and hemisphere (left, right) as factors. For each task (working memory or recognition), we entered the regions (one analysis for prefrontal and one for parietal) in an ANOVA with material (word, face), hemisphere (right, left) as within-subject factors, and both study (1, 2) and gender (male, female) as between subject factors. For the prefrontal regions in recognition (Fig. 3), we found a significant material type × hemisphere interaction ($F(1,106) = 133.9$, $P < 0.0001$) that did not further interaction with either study or gender (Ps > 0.12). As shown in Fig. 3, the males and females demonstrated the same lateralization effects, with greater left than right hemisphere
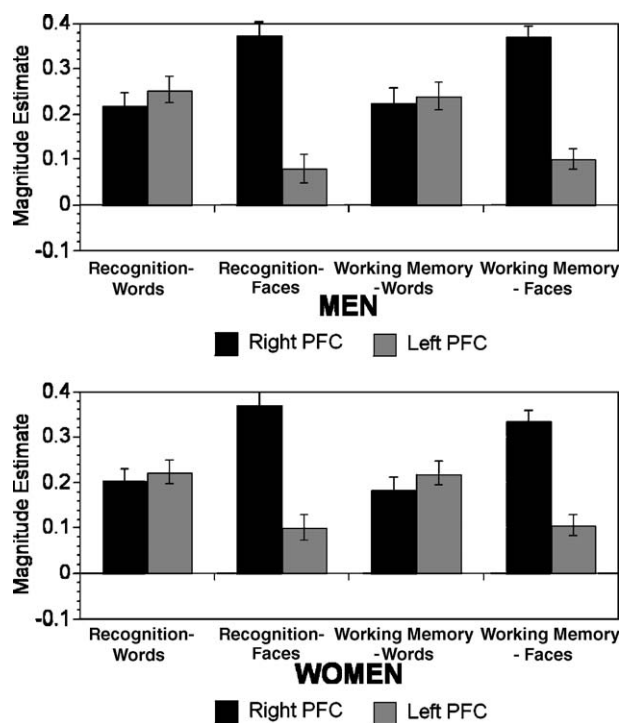

Fig. 3. Graphs demonstrating hemispheric lateralization effects for word and face materials in prefrontal cortex during both working memory and recognition. Data for males and females are plotted separately.
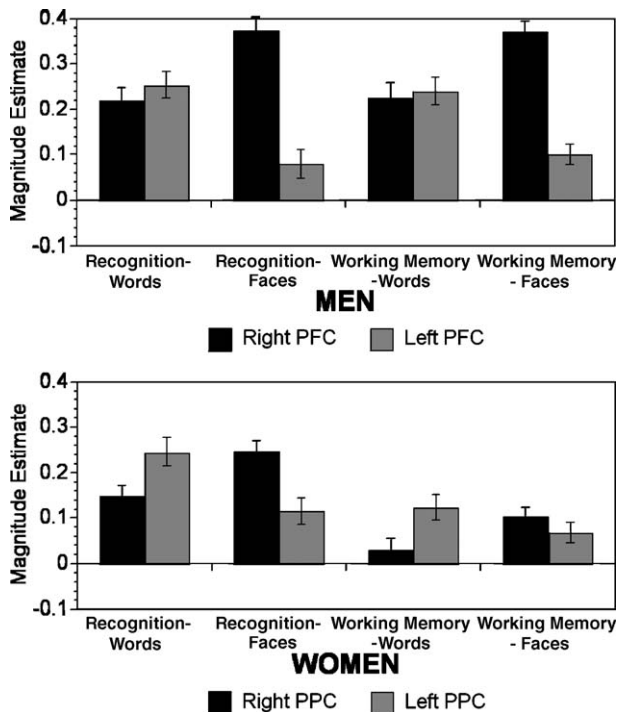
Fig. 4. Graphs demonstrating hemispheric lateralization effects for word and face materials in parietal cortex during both working memory and recognition. Data for males and females are plotted separately.

activity for words and greater right than left hemisphere activity for faces. We found the same result for the parietal cortex (see Fig. 4), with a significant material type × hemisphere interaction ($F(1,106) = 163.8$, $P < 0.0001$) that did not further interaction with either study or gender (all Ps > 0.09). As with the prefrontal cortex, both males and females showed greater left than right hemisphere activity for words and the opposite pattern for faces. We found the same results for the working memory task. For prefrontal cortex (Fig. 3), we found a significant material type × hemisphere interaction ($F(1,106) = 93.9$, $P < 0.0001$) that did not further interaction with either study or gender (all Ps > 0.60). For parietal cortex (Fig. 4), we also found a significant material type × hemisphere interaction ($F(1,106) = 72.95$, $P < 0.0001$) that did not further interaction with study. However, we did find a significant material type × hemisphere interactions for parietal cortex in working memory ($P < 0.05$). Post hoc analysis indicated that the material type by hemisphere interaction was significant for both males and females (both Ps < 0.001). However, there was a gender by hemisphere interaction for faces ($P < 0.05$) and not words ($P > 0.5$), the source of which was not clear. Nonetheless, as with recognition, males and females showed the same pattern of lateralization effects during working memory.

Discussion

The results of this study provide clear evidence that both males and females show the same patterns of lateralization of brain activation as a function of material type during both working memory and episodic recognition tasks. More specifically, both men and women show greater left inferior frontal, superior parietal, and middle temporal gyrus activation for verbal as compared to nonverbal working memory, and greater right inferior frontal,

superior parietal, and middle temporal gyrus activation for nonverbal as compared to verbal working memory. In addition, both men and women showed greater left inferior frontal, left superior parietal, and right posterior cerebellum activation for verbal as compared to nonverbal recognition, and both men and women showed greater right inferior frontal, right superior parietal, and left posterior cerebellum activation for nonverbal as compared to verbal recognition memory. Although we found a few regions that showed sex differences in material-specific lateralization in one study, these regional differences did not necessarily indicate more bilateral activation in females and did not replicate across studies. These results are not consistent with the result of prior studies, suggesting more bilateral activation in response to language processing among females as compared to men (Shaywitz et al., 1995). However, our results are consistent with several other studies showing clear left lateralized activation for a number of language processing functions in women (Buckner et al., 1995). Further, the results are consistent with a recent meta-analysis that there was no consistent evidence for more bilateral language representation in women than men (Sommer et al., 2004). The current study supports this finding, and, in particular, we note that both working memory and recognition show similar lateralization for material type across both sexes.

It should be noted, however, that this study does not rule out there being any sex differences in functional brain organization during working memory or episodic memory. For example, the current study found one region in right BA 18 that showed a consistent sex difference in material-sensitive effects during working memory, in which males activated more for faces than words and females activated more for words than faces. The functional implications of this sex difference are unclear, and it is possible that it is a spurious finding, despite our fairly stringent criteria. Nonetheless, this potential sex difference in working memory function should be examined further to determine if it is truly a robust phenomenon and, if so, to determine the implications of differential activation of this region across the sexes.

There were several potential limitations of the current study. First, the tasks included in this study were not ones reliably known to produce robust sex differences in performance. Further, we did not find any sex differences in behavioral performance for either working memory or recognition memory in either Study 1 or Study 2. One might argue that it is not surprising that we did not find clear evidence for sex differences in functional brain lateralization as a result of material type, given the absence of clear behavioral differences between the sexes. However, despite the lack of empirical evidence for sex differences in working memory or episodic memory performance, many researchers seem to implicitly assume that there may be sex differences in functional brain organization between men and women in such tasks. As such, the results of this study provide empirical evidence against the specific hypothesis that men and women show differential patterns of functional lateralization of brain activity during verbal as compared to nonverbal working memory and recognition memory tasks. It is still possible that there are true sex differences in brain activation in some language tasks that are specific to the particular aspect of language processing assessed in prior studies. However, the current results suggest that more bilateral activation during verbal processing is not characteristic of women across any task domain that may involve language processing. Second, the mean age of participants in Study 1 was higher than the mean age of participants in Study 2. Recent work suggests that functional

lateralization for language processing reaches maximal levels in the 20–25 year range and then begins to decrease (Szaflarski et al., in press). As such, one might predict somewhat less functional lateralization in response to material type in Study 1 (mean age 33) than in Study 2 (mean age 22), which might have influenced the ability to replicate gender differences in material sensitivity across studies. However, the analyses presented above suggested similar patterns of material sensitivity effects across studies, with both groups showing clear patterns of left lateralization for words in prefrontal and parietal regions and right hemisphere lateralization in prefrontal and parietal regions for faces. Thus, it seems unlikely that the 10-year mean difference in age across studies could have masked consistent gender differences in material sensitivity effects.

The results of the current study highlight the arguments made by Price et al. (1996) regarding the importance of replication and adequate sample size when examining functional neuroimaging data for sex differences. In particular, we found evidence that sex difference conclusions drawn from an exploratory analysis of one study rarely replicated to a second study, especially in the absence of any behavioral differences. One might argue that the lack of replication across Study 1 and Study 2 could have been attributed to the stringent replication requirements used. However, we did find reasonable replicable overall material-specific effects that generalized reasonable across the two studies, with patterns consistent with the prior literature. Although not all regions identified in each study showed significant effects in the other study, many more regions replicated across studies for material specificity effects than did for gender differences in material specificity. Specifically, for working memory, 40% of regions replicated across studies for material sensitivity effects, while only 10% replicated for gender differences in material sensitivity. For recognition, 41% of regions replicated across studies for material sensitivity effects, while no regions replicated for gender differences in material sensitivity. We would argue that such findings provide further evidence that sex differences in material-specific lateralization in working and episodic memory tasks are neither robust nor reliable. It is still possible that there are reliable sex differences as a function of material type that our study did not identify. However, if so, these are likely to be either small effects or highly sample dependent in some way.

The current study focused on sex differences in material-sensitive activation in working and episodic memory, examining only biological sex as the critical factor. We did not address the potentially important influence of hormones on functional activity. There is evidence that brain activation in women varies with the phase of their hormonal cycle (Hausmann et al., 2002; Fernandez et al., 2003). However, the implications of these hormonal influences are not entirely clear and the patterns have not necessarily been consistent across studies. For example, Fernandez et al. (2003) found effects of progesterone levels in the activation of superior temporal and medial superior frontal regions, yet Hausmann et al. (2002) did not show an effect of progesterone. Nonetheless, it is possible that there are hormonal effects on material-sensitive activation in females (or even in males) that the current study was not capable of examining as we did not gather data regarding where our female participants were in their cycle. For example, it is possible that females show an absence of material-sensitive lateralization of brain activity but only during certain phases of their cycle due to such hormonal influences. Future studies

might benefit from accounting for hormonal variants as well as biological sex when examining sex differences in cognitive functions.

In conclusion, this study provides further evidence that males and females show generally similar lateralization patterns in the higher functional aspects of verbal and nonverbal processing in working memory and recognition. We used a large sample size and a fairly stringent requirement of material-specific activation and replication across two studies with participants performing two different tasks. While this methodology does not negate the possibility of task specific sex differences, it provides strong evidence against any generalized lateralization differences between the sexes on cognitive tasks utilizing language functions.

References

Aboitiz, F., Scheibel, A.B., Zaidel, E., 1992. Morphometry of the Sylvian fissure and the corpus callosum, with emphasis on sex differences. Brain 115 (Pt. 5), 1521–1541.

Barch, D.M., Csernansky, J., Conturo, T., Snyder, A.Z., Ollinger, J., 2002. Working and long-term memory deficits in schizophrenia. Is there a common underlying prefrontal mechanism? J. Abnorm. Psychology, 478–494.

Baxter, L.C., Saykin, A.J., Flashman, L.A., Johnson, S.C., Guerin, S.J., Babcock, D.R., Wishart, H.A., 2003. Sex differences in semantic language processing: a functional MRI study. Brain Lang. 84, 264–272.

Binder, J.R., Frost, J.A., Hammeke, T.A., Cox, R.W., Rao, S.M., Prieto, T., 1997. Human brain language areas identified by functional magnetic resonance imaging. J. Neurosci. 17, 353–362.

Braver, T.S., Barch, D.M., Kelley, W.M., Buckner, R.L., Cohen, N.J., Meizin, F.M., Snyder, A.Z., Olinger, J.M., Conturo, T.E., Akbudak, E., Conturo, T.E., Peterson, S.E., 2001. Direct comparison of prefrontal cortex regions engaged by working and long-term memory tasks. NeuroImage, 48–59.

Buckner, R.L., Raichle, M.E., Petersen, S.E., 1995. Dissociation of human prefrontal cortical areas across different speech production tasks and gender groups. J. Neurophysiol. 74, 2163–2173.

Cohen, J.D., MacWhinney, B., Flatt, M.R., Provost, J., 1993. PsyScope: a new graphic interactive environment for designing psychology experiments. Behav. Res. Meth. Instrum. Comput., 257–271.

Conturo, T.E., McKinstry, R.C., Akbudak, E., Snyder, A.Z., Yang, T., Raichle, M.E., 1996. Sensitivity optimization and experimental design in functional magnetic resonance imaging. Society for Neuroscience Abstracts. Society for Neuroscience, Washington, DC, pp. 7.

De Renzi, E., Faglioni, P., Ferrari, P., 1980. The influence of sex and age on the incidence and type of aphasia. Cortex 16, 627–630.

Fernandez, G., Weis, S., Stoffel-Wagner, B., Tendolkar, I., Reuber, M., Beyenburg, S., Klaver, P., Fell, J., de Greiff, A., Ruhlmann, J., Reul, J., Elger, C.E., 2003. Menstrual cycle-dependent neural plasticity in the adult human brain is hormone, task, and region specific. J. Neurosci. 23, 3790–3795.

First, M.B., Spitzer, R.L., Miriam, G., Williams, J.B.W., 2002. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition (SCID-I/NP). Biometrics Research, New York State Psychiatric Institute, New York.

Frost, J.A., Binder, J.R., Springer, J.A., Hammeke, T.A., Bellgowan, P.S.,

Rao, S.M., Cox, R.W., 1999. Language processing is strongly left lateralized in both sexes. Evidence from functional MRI. Brain 122 (Pt. 2), 199–208.

Halpern, D.F., 1992. Sex Differences in Cognitive Abilities, 2nd ed. Erlbaum, Hillsdale, NJ.

Harasty, J., Double, K.L., Halliday, G.M., Kril, J.J., McRitchie, D.A., 1997. Language-associated cortical regions are proportionally larger in the female brain. Arch. Neurol. 54, 171–176.

Hausmann, M., Becker, C., Gather, U., Gunturkun, O., 2002. Functional cerebral asymmetries during the menstrual cycle: a cross-sectional and longitudinal analysis. Neuropsychologia 40, 808–816.

Iaccino, J.F., 1993. Left Brain–Right Brain Differences: Inquiries, Evidences, and New Approaches. Erlbaum, Hillsdale, NJ.

Jaeger, J.J., Lockwood, A.H., Van Valin Jr., R.D., Kemmerer, D.L., Murphy, B.W., Wack, D.S., 1998. Sex differences in brain regions activated by grammatical and reading tasks. NeuroReport 9, 2803–2807.

Kansaku, K., Yamaura, A., Kitazawa, S., 2000. Sex differences in lateralization revealed in the posterior language areas. Cereb. Cortex 10, 866–872.

Kelley, W.M., Miezin, F.M., McDermott, K.B., Buckner, R.L., Raichle, M.E., Cohen, N.J., Ollinger, J.M., Akbudak, E., Conturo, T.E., Snyder, A.Z., Petersen, S.E., 1998. Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and non-verbal memory encoding. Neuron, 927–936.

Kertesz, A., Benke, T., 1989. Sex equality in intrahemispheric language organization. Brain Lang. 37, 401–408.

Killgore, W.D., Yurgelun-Todd, D.A., 2001. Sex differences in amygdala activation during the perception of facial affect. NeuroReport 12, 2543–2547.

Kimura, D., 2000. Sex and Cognition. MIT Press, Cambridge, MA.

Kulynych, J.J., Vladar, K., Jones, D.W., Weinberger, D.R., 1994. Gender differences in the normal lateralization of the supratemporal cortex: MRI surface-rendering morphometry of Heschl's gyrus and the planum temporale. Cereb. Cortex 4, 107–118.

Logan, J.M., Sanders, A.L., Snyder, A.Z., Morris, J.C., Buckner, R.L., 2002. Under-recruitment and nonselective recruitment: dissociable neural mechanisms associated with aging. Neuron, 827–840.

McGlone, J., 1977. Sex differences in the cerebral organization of verbal functions in patients with unilateral brain lesions. Brain 100, 775–793.

Ojemann, J.G., Akbudak, E., Snyder, A.Z., McKinstry, R.C., Raichle, M.E., Conturo, T.E., 1997. Anatomic localization and quantitative analysis of gradient refocused echo-planar fMRI susceptibility artifacts. NeuroImage 6, 156–167.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia, 97–113.

Phillips, M.D., Lowe, M.J., Lurito, J.T., Dzemidzic, M., Mathews, V.P., 2001. Temporal lobe activation demonstrates sex-based differences during passive listening. Radiology 220, 202–207.

Price, J., Moore, C., Friston, K.J., 1996. Getting sex into perspective. NeuroImage, S586.

Puce, A., Allison, T., Asgari, M., Gore, J.C., McCarthy, G., 1996. Differential sensitivity of human visual cortex to faces, letterstrings, and textures: a functional magnetic resonance imaging study. J. Neurosci. 16, 5205–5215.

Pugh, K.R., Shaywitz, B.A., Shaywitz, S.E., Constable, R.T., Skudlarski, P., Fulbright, R.K., Bronen, R.A., Shankweiler, D.P., Katz, L., Fletcher, J.M., Gore, J.C., 1996. Cerebral organization of component processes in reading. Brain 119 (Pt. 4), 1221–1238.

Research Systems I IDL. In. Boulder, CO.

Rizzolatti, G., Buchtel, H.A., 1977. Hemispheric superiority in reaction time to faces: a sex difference. Cortex 13, 300–305.

Shaywitz, B.A., Shaywitz, S.E., Pugh, K.R., Constable, R.T., Skudlarski, P., Fulbright, R.K., Bronen, R.A., Fletcher, J.M., Shankweiler, D.P., Katz, L., et al., 1995. Sex differences in the functional organization of the brain for language. Nature 373, 607–609.

Sommer, I.E., Aleman, A., Bouma, A., Kahn, R.S., 2004. Do women really have more bilateral language representation than men? A meta-analysis of functional imaging studies. Brain 127, 1845–1852.

Speck, O., Ernst, T., Braun, J., Koch, C., Miller, E., Chang, L., 2000. Gender differences in the functional organization of the brain for working memory. NeuroReport 11, 2581–2585.

Szaflarski, J.P., Holland, S.K., Schmithorst, V.J., Byars, A.W., 2006. fMRI study of language lateralization in children and adults. Hum. Brain Mapp. 27, 202–212.

Talairach, J., Tournoux, P., 1988. Co-Planar Stereotaxic Atlas of the Human Brain 3-Dimensional Proportional System: An Approach to Cerebral Imaging. Thieme Medical Publishers, New York.

van der Kallen, B.F., Morris, G.L., Yetkin, F.Z., van Erning, L.J., Thijssen, H.O., Haughton, V.M., 1998. Hemispheric language dominance studied with functional MR: preliminary study in healthy volunteers and patients with epilepsy. AJNR Am. J. Neuroradiol. 19, 73–77.

Vikingstad, E.M., George, K.P., Johnson, A.F., Cao, Y., 2000. Cortical language lateralization in right handed normal subjects using functional magnetic resonance imaging. J. Neurol. Sci. 175, 17–27.

Voyer, D., 1998. On the reliability and validity of noninvasive laterality measures. Brain Cogn. 36, 209–236.

Witelson, S.F., Kigar, D.L., 1992. Sylvian fissure morphology and asymmetry in men and women: bilateral differences in relation to handedness in men. J. Comp. Neurol. 323, 326–340.