

## Sex differences in neural processing of language among children

Douglas D. Burman<sup>a,b,\*</sup>, Tali Bitan<sup>c</sup>, James R. Booth<sup>a,b</sup>

<sup>a</sup> Department of Communication Sciences and Disorders, Northwestern University, Evanston, IL, USA

<sup>b</sup> Department of Radiology, Evanston Northwestern Healthcare, Evanston, IL, USA

<sup>c</sup> Department of Communication Disorders, Haifa University, Mt. Carmel, Haifa, Israel

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### Abstract

Why females generally perform better on language tasks than males is unknown. Sex differences were here identified in children (ages 9–15) across two linguistic tasks for words presented in two modalities. Bilateral activation in the inferior frontal and superior temporal gyri and activation in the left fusiform gyrus of girls was greater than in boys. Activation in the left inferior frontal and fusiform regions of girls was also correlated with linguistic accuracy irregardless of stimulus modality, whereas correlation with performance accuracy in boys depended on the modality of word presentation (either in visual or auditory association cortex). This pattern suggests that girls rely on a supramodal language network, whereas boys process visual and auditory words differently. Activation in the left fusiform region was additionally correlated with performance on standardized language tests in which girls performed better, additional evidence of its role in early sex differences for language.

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Language performance is generally better among females than among males, even in children as young as 2–3 years (Bornstein, Haynes, Painter, & Genevro, 2000; Dionne, Dale, Boivin, & Plomin, 2003). Girls begin talking earlier (Murray, Johnson, & Peters, 1990), acquire vocabulary faster (Roulstone, Loader, & Northstone, 2002), and show more spontaneous language (Bauer, Goldfield, & Reznick, 2002; Lutchmaya, Baron-Cohen, & Raggatt, 2002; Morisset, 1995). Although small, female advantages for verbal and written language persist through the school years (Lynn, 1992; Mann, Sasanuma, Sakuma, & Masaki, 1990; Martin & Hoover, 1987; Undheim & Nordvik, 1992) and into adulthood (Parsons, Rizzo, van der Zaag, McGee, & Buckwalter, 2005).

Among adults, a biological basis for sex differences has been suggested from differences in laterality of activation during language tasks (Jaeger et al., 1998; Shaywitz et al., 1995). More bilateral brain activation among women is reported in the inferior frontal gyrus (Baxter et al., 2003; Clements et al., 2006; Pugh et al., 1996; Pugh et al., 1997; Rossell, Bullmore,

Williams, & David, 2002) and posterior regions of the middle/superior temporal gyrus (Kansaku, Yamaura, & Kitazawa, 2000; Phillips, Lowe, Lurito, Dzemidzic, & Mathews, 2001; Rossell et al., 2002; Vikingstad, George, Johnson, & Cao, 2000). These differences are not always evident (Brickman et al., 2005; Buckner, Raichle, & Petersen, 1995; Frost et al., 1999; Gur et al., 2000; Haut & Barch, 2006; Hund-Georgiadis, Lex, Friederici, & von Cramon, 2002; Knecht et al., 2000; Roberts & Bell, 2002; Sommer, Aleman, Bouma, & Kahn, 2004; Xu et al., 2001), however, especially when controlling for performance accuracy (Frost et al., 1999; Weiss et al., 2003). Without controlling for performance accuracy, any observed differences in brain activation might result from overall group differences in skill performing the task rather than the sex of the subjects.

Direct comparisons between sexes generally fail to demonstrate differences in intensity of activation. Apparent laterality differences could potentially arise from threshold effects, differences in response variability (Vikingstad et al., 2000), or differences in developmental rate between hemispheres (Thatcher, Walker, & Giudice, 1987). Sex effects can also depend on the task (Pugh et al., 1996) or modality of word presentation (Frost et al., 1999), suggesting a possible role of sensory or other nonlinguistic factors. Sex differences in some reports may arise from group differences in age (Brickman et al.,

\* Corresponding author at: Roxelyn and Richard Pepper Department of Communication Sciences and Disorders, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, USA. Tel.: +1 847 467 1549; fax: +1 847 491 4975.  
E-mail address: d-burman@northwestern.edu (D.D. Burman).

2005; Clements et al., 2006; Thatcher et al., 1987), as sex-related differences in volume of the inferior frontal gyrus interact with age (Blanton et al., 2004).

Although initial attempts failed to demonstrate sex effects among children (Gaillard, Balsamo, Ibrahim, Sachs, & Xu, 2003; Gaillard, Sachs et al., 2003), a recent study demonstrated small sex-by-age interactions in frontal and temporal regions on three of four language tasks (Plante, Schmithorst, Holland, & Byars, 2006). Neither laterality differences nor main effects of sex were observed, suggesting that the differences are small, task-specific, and acquired during development.

We sought to identify sex differences in brain activation during language tasks that could account for observed behavioral differences already apparent in young children. To demonstrate generalized differences, we tested for sex differences across language tasks after accounting for differences in task, stimulus modality, age, and performance accuracy. Correlation with standardized test scores demonstrated the relevance of identified sex differences in brain activation to differences in linguistic skill. The nature of sex differences was further explored by examining the relationship between brain activation and performance accuracy.

## 1. Materials and methods

### 1.1. Subjects

Sixty-two children (including 31 girls) participated in this functional magnetic resonance imaging (fMRI) study, ranging in age from 9 years to 15 years. Subjects met the following inclusionary criteria: (1) native English speakers; (2) right-handed; (3) normal or corrected-to-normal hearing and vision; (4) no neurological disease or psychiatric disorders; (5) no medication affecting the central nervous system; (6) no history of intelligence, reading, or oral-language deficits; and (7) no learning disability or Attention Deficit Hyperactivity Disorder (ADHD). Informed consent was obtained, using procedures approved by the Institutional Review Board at Northwestern University and Evanston Northwestern Healthcare Research Institute.

Children were given standardized intelligence tests (Wechsler Abbreviated Scale of Intelligence (WASI), which showed an average full-scale IQ = 112 (range = 85–141, S.D. = 15.3); verbal IQ = 113 (range = 79–142, S.D. = 14.1); and performance IQ = 108 (range = 78–144, S.D. = 15.3). Other standardized tests were also administered to evaluate language skills that might impact performance on the lexical tasks, including the Peabody Picture Vocabulary Test-III (Dunn & Dunn, 1997), the Wide Ranging Achievement Test-III (Wilkinson, 1993), Woodcock-Johnson III Tests of Cognitive Abilities (Woodcock, Mather, McGrew, & Schrank, 2001), Comprehensive Test of Phonological Processing (Wagner, Torgesen, & Rashotte, 1999), and Test of Word Reading Efficiency (Torgesen, Wagner, & Rashotte, 1999). Sex differences were observed on some of these tests, as described in the results.

### 1.2. Behavioral tasks

Two language judgment tasks were used. *Orthographic judgment* (“spelling”) tasks required a subject to judge whether two words presented sequentially shared all letters after the first consonant or consonant cluster. Ninety-six word pairs were presented whose orthographic and phonological similarity was manipulated independently. This resulted in 24 word pairs in each of four categories—consistent orthography and phonology (O+P+, *gate–hate*), consistent orthography but inconsistent phonology (O+P–, *pint–mint*), inconsistent orthography but consistent phonology (O–P+, *has–jazz*), and inconsistent orthography and phonology (O–P–, *press–list*). Orthographic matches and non-matches occurred equally often, so accurate performance required attention to the orthography of both presented words. All words were single syllable

words, and were matched for frequency across tasks and conditions (Baayen, Piepenbrock, & Gulikers, 1995; Zeno, Ivens, Millart, & Duwuri, 1995).

The duration of each word was 500–800 ms for auditory stimuli (800 ms for visual words), with the second word presented 1000 ms after the onset of the first. A response was required during the 2600 ms interval following the second word presentation, prompted by the appearance of a red fixation-cross. Subjects indicated their judgments via keypress.

In the *phonology judgment* (“rhyming”) tasks, the subject had to determine whether two sequential words rhymed. Phonological matches and non-matches occurred equally often; although different word pairs were used, word characteristics and task parameters were otherwise the same as in the orthography judgment tasks.

A visual and an auditory version of each task were presented. The visual spelling and auditory rhyming tasks require intramodal word segmentation based upon linguistic processes, whereas the auditory spelling and visual rhyming tasks require cross-modal conversion of word forms; both intra- and cross-modal tasks have been shown to activate linguistic as well as sensory regions of the brain (Bitan et al., 2005; Booth et al., 2001, 2002a, 2003, 2004). The auditory versions of the tasks were presented four or more weeks later in order to reduce rehearsal effects.

A fixation control task was used as a baseline for all comparisons. In this task, a black fixation-cross appeared in the center and subjects pressed a button once it turned red; as a baseline, this task removed nonlinguistic effects of target fixation and motor response present in both auditory and visual versions of our language tasks. In addition, a perceptual control task (24 trials) was used for examining the effect of nonlinguistic sensory processing in each modality. In the visual modality, two visual stimuli were presented sequentially, each consisting of three rearranged letters that bore no resemblance to alphabetic stimuli; in the auditory modality, two triplets of pure tones were presented. The subject indicated whether the second triplet matched the first. A simpler version of this perceptual control task was also presented (24 trials), but was not included in the results presented here. The timing parameters for all control tasks were the same as for the lexical tasks.

Detailed descriptions of these tasks have been reported elsewhere (Bitan et al., 2007; Cao, Booth, Bitan, Burman, & Chou, 2006).

### 1.3. Data exclusion due to subject performance

Prior to fMRI data collection, subjects were given a practice session in a MRI simulator for acclimation to the scanner environment and to ensure that the behavioral requirements of each task were understood. A practice session was given 1 week or less prior to each of two fMRI sessions (one for visual word presentation and one for auditory). During fMRI sessions, a task was halted in those rare cases when a subject’s performance was inconsistent with task requirements (e.g., failure to respond on several consecutive trials or consistently making the wrong type of language judgment). Data from such cases were not used; when possible, subjects were scheduled for a makeup fMRI session following review of the tasks in another practice session. Data from an individual was also excluded if performance between scanning and practice sessions exceeded 20%.

Some subjects did not continue in the study for both fMRI sessions; the data from other subjects on one or more modality/task combination was excluded due to excessive movement (>4 mm within a run), poor signal-noise-ratio in primary visual cortex or primary auditory cortex in the complex perceptual condition (more than 2 standard deviations below the mean), or near-chance accuracy on a task (<60%). Functional MRI data from 43 subjects in the auditory rhyming task (19 boys and 24 girls), 42 subjects in the auditory spelling task (17 boys and 25 girls), 54 subjects in the visual rhyming task (26 boys and 28 girls), and 48 subjects in the visual spelling task (25 boys and 23 girls) were used in our analyses.

### 1.4. Data acquisition

Brain images were acquired from a 1.5 Tesla GE scanner. The BOLD (Blood Oxygen Level Dependent) functional images were acquired using the EPI (Echo Planar Imaging) method. The following parameters were used for scanning: TE = 35 ms, flip angle = 90°, matrix size = 64 × 64, field of view = 24 cm, slice thickness = 5 mm, number of slices = 24; TR = 2000 ms. For each task, a subject

performed two functional runs of 8.0 min for a total of eight runs, with 240 repetitions each. In addition, structural T1 weighted 3D image were acquired (SPGR, TR = 21 ms, TE = 8 ms, flip angle = 20°, matrix size = 256 × 256, field of view = 22 cm, slice thickness = 1 mm, number of slices = 124), using the same orientation as the functional images.

### 1.5. Pre-processing

SPM2 software (Statistical Parametric Mapping) was used for processing fMRI data. Differences in slice-acquisition time and motion were corrected; movement during a run did not exceed 4.0 mm in any plane. Co-registered images were normalized to the MNI (Montreal Neurological Institute) average template, statistical analyses were calculated on smoothed data (10 mm isotropic Gaussian kernel), and a high pass filter removed signal drift and other low frequency artifacts. Global normalization scaled the mean of each scan to a common value in order to correct for whole brain differences over time.

Data from a participant in each modality-specific task was entered into a general linear model using an event-related analysis procedure. Word pairs were treated as individual events for first-level (individual) analyses and modeled using a canonical hemodynamic response function. Lexical trials were contrasted with fixation trials to reduce the effects of fixation and motor responses. Because a parameter estimate of the differential response to the word pairs versus fixation was created for each task in each modality, a total of four parameter estimates were created for those subjects tested on both language judgments tasks in both modalities (one each for auditory spelling, visual spelling, auditory rhyming, and visual rhyming tasks).

Different trial types (O+P+, O+P-, O-P+, or O-P-) were not modeled as separate events because we were looking for language effects that were non-specific for task requirements or trial type. Behavioral analyses indicated that this was justified; with sex (male, female), age (9, 11, 13, 15), and modality/task (auditory rhyming, auditory spelling, visual rhyming, visual spelling) as fixed factors in an ANCOVA model and the mean accuracy across all trial types as a covariate, variance in accuracy unique to each of the four task conditions did not produce a main effect of sex or an interaction between sex and age or sex and modality/task. An ANCOVA model with the mean reaction time as a covariate similarly indicated that variability in reaction time associated with each trial type did not produce a main effect of sex or an interaction between sex and age or sex and modality/task. We therefore did not exclude error trials, thus avoiding differences in statistical power for age groups that differed in accuracy.

### 1.6. Behavioral analyses

Each of several behavioral measures was analyzed with an age (9, 11, 13, 15) × sex (male, female) × task (auditory rhyming, auditory spelling, visual rhyming, visual spelling) ANOVA. This statistical model was applied for each of the standardized test measures; this model was also applied to performance accuracy and to reaction time for tasks performed in the scanner.

### 1.7. fMRI analyses: main effects

An ANCOVA model was used for group (random effects) analyses of fMRI data. In this model, parameter estimates from each of the four modality/task combinations were entered (auditory rhyming, auditory spelling, visual rhyming, visual spelling), grouped as discrete factors by subject sex (male, female), age (9, 11, 13, 15 years), task (rhyming, spelling), and stimulus modality (auditory, visual). Task accuracy from each task was entered as a continuous covariate; reaction time was not covaried because differences related to age or sex were not specific to language tasks. This provided a model with 32 discrete cells (4 age × 2 sex × 4 modality/task combinations) to estimate variance from 187 parameter estimates (approximately 6 subjects per cell). This model allowed us to examine sex effects that are not specific to a particular language task, stimulus modality, or age group after accounting for differences in performance accuracy.

Using a family-wise error correction for multiple comparisons, a threshold of  $p = 0.05$  was applied to the main effects to create a mask for subsequent analyses. This mask ensured that identified group differences and correlations with accuracy were limited to areas active during language tasks. Sex differences in activation were identified using an extent threshold of 15 voxels and a voxel-wise

intensity threshold of  $p = 0.05$ , applying a false discovery rate (FDR) correction for multiple comparisons. The same approach was used for identifying sex differences for activation by the complex perceptual control.

An additional region-of-interest (ROI) analysis was performed to characterize sex differences in linguistic areas activated during orthographic and phonological tasks presented in either modality. Using a family-wise error correction and a threshold of  $p = 0.05$ , activation maxima demonstrating sex differences from the ANCOVA model were identified within a mask consisting of the inferior frontal gyrus, superior+middle temporal gyrus, and the fusiform+inferior temporal gyrus. ROIs were created as a 5 mm-radius sphere surrounding each maxima, thereby increasing the volume to better approximate the cluster size demonstrated using the more sensitive FDR method of correction (Genovese, Lazar, & Nichols, 2002; Heller, Stanley, Yekutieli, Rubin, & Benjamini, 2006; Hsueh, Chen, & Kodell, 2003; Marchini & Presanis, 2004). The MarsBar toolbox was used to find the mean activation within each ROI, and a Bonferroni correction applied for multiple comparisons across ROIs. An ANCOVA model was applied to identify each subject's mean ROI activation on each task (after accounting for individual differences in performance accuracy). The resulting contrast values were exported to SPSS statistical software, where an ANOVA allowed the mean BOLD signal associated with sex on each task to be estimated and plotted.

### 1.8. fMRI analyses: parametric analyses

Parametric effects of accuracy on activation were tested separately for males and females. Parametric analyses were carried out to identify correlation of brain activation to accuracy in either the language judgment (rhyming, spelling) or the stimulus modality (auditory, visual). Each analysis combined two task conditions in an ANCOVA model in order to better characterize the brain/behavior relationship. For example, correlations with a language judgment (such as rhyming) used the two stimulus modalities as fixed factors in order to eliminate effects specific to sensory processing; analysis was masked by the main effects of activation for this task across both stimulus modalities. Similarly, correlations within a stimulus modality (such as auditory) used the two language judgments as fixed factors in order to eliminate effects specific to language judgments; analysis was masked by the main effects of activation for this modality across both rhyming and spelling judgments. Similar ANCOVA models were used to look for a correlation of activation with skill estimates derived from standardized test scores.

## 2. Results

### 2.1. Subject performance on standardized tests

A series of age × sex ANOVAs were conducted to characterize the potential influence of these factors on the standardized test scores of our subject pool. For IQ measures, there were no significant age differences on verbal IQ ( $F[3,54] = 1.814$ ,  $p = 0.156$ ), although there were significant effects of age on both performance IQ ( $F[3,54] = 4.210$ ,  $p = 0.010$ ) and full-scale IQ ( $F[3,54] = 3.440$ ,  $p = 0.023$ ). Examination of IQ by age group showed that this resulted from a progressive decline with age; the highest scores were for the youngest subjects (age 9, mean performance IQ = 118 and full-scale IQ = 120) and the lowest scores were for the oldest subjects (age 15, mean performance IQ = 98 and full-scale IQ = 105). There were no significant effects of sex on verbal IQ ( $F[1,54] = 0.037$ ,  $p = 0.849$ ), performance IQ ( $F[1,54] = 0.285$ ,  $p = 0.596$ ), or full-scale IQ ( $F[1,54] = 0.067$ ,  $p = 0.797$ ), nor were there any sex × age interactions ( $F[1,54]$  values ranging from 0.421 to 0.556,  $p \geq 0.647$ ).

A marginal significance of sex was observed for spelling (WRAT-III,  $F[1,50] = 3.264$ ,  $p = 0.077$ ) and reading fluency (WJ-III,  $F[1,50] = 3.459$ ,  $p = 0.069$ ), as well as significant effects

Table 1  
Standardized scores of subjects by age and sex

| Age                       | PPVT         | WRAT spelling*                  | WJ-III wordID | WJ-III read** | CTOP PA      | CTOPPPM      | CTOPPRN**    | TOWRE PDE**                     |
|---------------------------|--------------|---------------------------------|---------------|---------------|--------------|--------------|--------------|---------------------------------|
| Girls standardized scores |              |                                 |               |               |              |              |              |                                 |
| 9 ( <i>n</i> = 6)         | 117.2 (21.9) | 112.0 (14.0)                    | 112.5 (14.4)  | 110.3 (16.0)  | 107.0 (9.0)  | 100.0 (3.8)  | 97.0 (7.6)   | 108.2 (13.9)                    |
| 11 ( <i>n</i> = 8)        | 117.3 (13.2) | 117.8 (11.0)                    | 112.5 (8.4)   | 117.1 (22.3)  | 99.6 (10.6)  | 101.1 (9.5)  | 100.4 (14.2) | <b>108.3</b> <sup>†</sup> (6.2) |
| 13 ( <i>n</i> = 11)       | 115.5 (9.0)  | 111.7 (10.2)                    | 110.3 (7.8)   | 115.3 (15.8)  | 99.7 (8.1)   | 97.3 (7.9)   | 103.3 (11.4) | 98.7 (7.4)                      |
| 15 ( <i>n</i> = 6)        | 108.2 (7.4)  | <b>112.8</b> <sup>†</sup> (6.8) | 101.8 (4.6)   | 116.3 (8.4)   | 107.5 (7.5)  | 97.5 (13.3)  | 105.5 (10.1) | <b>97.7</b> <sup>†</sup> (4.6)  |
| Boys standardized scores  |              |                                 |               |               |              |              |              |                                 |
| 9 ( <i>n</i> = 8)         | 115.1 (21.5) | 111.6 (12.8)                    | 114.9 (12.2)  | 110.1 (13.1)  | 105.6 (15.7) | 95.9 (8.9)   | 100.0 (8.9)  | 107.5 (8.7)                     |
| 11 ( <i>n</i> = 10)       | 118.9 (16.1) | 107.3 (13.9)                    | 111.8 (11.2)  | 100.8 (13.5)  | 103.3 (10.2) | 96.4 (11.4)  | 94.3 (9.2)   | <b>98.5</b> <sup>†</sup> (11.0) |
| 13 ( <i>n</i> = 8)        | 111.5 (12.1) | 109.3 (14.6)                    | 108.9 (10.5)  | 100.6 (10.7)  | 92.1 (16.9)  | 100.4 (13.6) | 97.0 (14.6)  | 94.9 (8.3)                      |
| 15 ( <i>n</i> = 5)        | 112.2 (7.9)  | <b>102.6</b> <sup>†</sup> (5.8) | 101.4 (7.4)   | 113.2 (15.0)  | 97.6 (9.1)   | 94.0 (10.2)  | 88.0 (10.6)  | <b>93.6</b> <sup>†</sup> (3.8)  |

Mean standardized scores and standard deviation (in parentheses) are provided for each sex and age group. Bold headings identify tests that had sex differences across age groups using an ANOVA with sex and age as factors; bold scores in a cell identify sex differences significant within an age group. PPVT = Peabody Picture Vocabulary Test-III; WRAT = Wide Ranging Achievement Test-III (spelling subtest); WJ-III = Woodcock-Johnson III Tests of Cognitive Abilities (wordID = word identification, read = reading fluency); CTOPP = Comprehensive Test of Phonological Processing (PA = phonological awareness; PM = phonological memory; RN = rapid naming); TOWRE = Test of Word Reading Efficiency (PDE = pseudoword decoding efficiency).

\* ANOVA, main effect of sex,  $p < 0.10$ .

\*\* ANOVA, main effect of sex,  $p < 0.05$ .

† Student *t*-test (girls vs. boys of same age),  $p < 0.05$ .

on rapid naming (CTOPP,  $F[1,50] = 5.154$ ,  $p = 0.028$ ) and phonetic decoding efficiency (TOWRE,  $F[1,50] = 4.839$ ,  $p = 0.032$ ). Consistent with previous studies, girls showed an overall advantage in each comparison. Examination of mean scores by age group, however, suggests that the reading advantages for girls on these measures may have been driven by the older children (see Table 1).

## 2.2. Subject performance in scanner

Performance on the language tasks performed in the scanner was analyzed with an ANOVA using factors of sex (male, female), age (9, 11, 13, 15 years), and task/modality combinations (auditory rhyming, auditory spelling, visual rhyming, visual spelling). The ANOVA for performance accuracy showed a main effect of age ( $F[3,155] = 11.264$ ,  $p < 0.001$ ) and task ( $F[3,155] = 28.726$ ,  $p < 0.001$ ). No significant effects on accuracy were observed for sex or its interaction with age or task. The analysis was repeated to analyze accuracy on the perceptual control trials, except that the ANOVA model specified two modalities rather than four task/modality combinations. (The perceptual control task was the same for both auditory tasks and for both visual tasks). Main effects were observed for modality ( $F[1,92] = 34.074$ ,  $p < 0.001$ ), but not for sex or its interaction with age or modality. Performance accuracy on each task is summarized in Table 2.

The ANOVA for reaction time on the language tasks showed a main effect for age ( $F[3,155] = 10.327$ ,  $p < 0.001$ ), task ( $F[3,155] = 11.415$ ,  $p < 0.001$ ), and sex ( $F[1,155] = 18.336$ ,  $p < 0.001$ ), but not a sex  $\times$  age interaction ( $F[3,155] = 2.002$ ,  $p = 0.116$ ), a sex  $\times$  task interaction ( $F[3,155] = 1.231$ ,  $p = 0.300$ ), or a sex  $\times$  age  $\times$  task interaction ( $F[9,155] = 0.151$ ,  $p = 0.998$ ). Overall, girls were faster than boys ( $1317 \pm 31.8$  ms for girls,  $1520 \pm 35.0$  ms for boys), with reaction time inversely correlated with accuracy after accounting for age, task, and sex ( $r = -0.469$ ,  $p < 0.001$ , d.f. = 182.) Differences in reaction time

were not specific to the language tasks, however, as an ANOVA model showed a main effect of age for the perceptual control ( $F[3,155] = 5.835$ ,  $p = 0.001$ ) and for the fixation control ( $F[3,155] = 5.419$ ,  $p = 0.001$ ), as well as a main effect of sex for the perceptual control ( $F[1,155] = 9.583$ ,  $p = 0.002$ , mean reaction time of  $1159 \pm 29.7$  for girls and  $1296 \pm 32.7$  for boys).

## 2.3. Main effects of language tasks on brain activation

Fig. 1 shows sex differences and the area of brain activation common to boys and girls during performance of two language tasks across two modalities. The area of brain activation common to boys and girls (Fig. 1, yellow and Table 3) included areas previously implicated in language function, including the inferior frontal gyrus, posterior superior/middle temporal gyrus, inferior parietal lobule, and fusiform gyrus. Within the area of language activation common to both sexes, planned follow-up *t*-tests within the ANCOVA model demonstrated significantly greater activation by girls bilaterally in the inferior frontal gyrus

Table 2  
Accuracy performance on perceptual and lexical tasks

| Age            | Perceptual |      | Spelling |      | Rhyming |      |
|----------------|------------|------|----------|------|---------|------|
|                | Boy        | Girl | Boy      | Girl | Boy     | Girl |
| Auditory tasks |            |      |          |      |         |      |
| 9              | 71.3       | 69.0 | 72.9     | 70.5 | 87.6    | 89.6 |
| 11             | 81.5       | 73.1 | 78.3     | 76.1 | 85.9    | 95.2 |
| 13             | 81.4       | 75.5 | 77.6     | 76.9 | 89.7    | 93.3 |
| 15             | 81.0       | 75.0 | 82.8     | 86.4 | 90.7    | 97.0 |
| Visual tasks   |            |      |          |      |         |      |
| 9              | 84.3       | 90.5 | 83.3     | 89.2 | 79.7    | 81.3 |
| 11             | 88.7       | 92.4 | 91.3     | 90.0 | 81.2    | 86.7 |
| 13             | 90.6       | 90.7 | 94.7     | 93.4 | 88.6    | 88.7 |
| 15             | 94.0       | 93.1 | 97.6     | 95.9 | 90.3    | 89.7 |

For each task and modality, accuracy is listed by age and sex. Numbers represent mean percent accuracy.

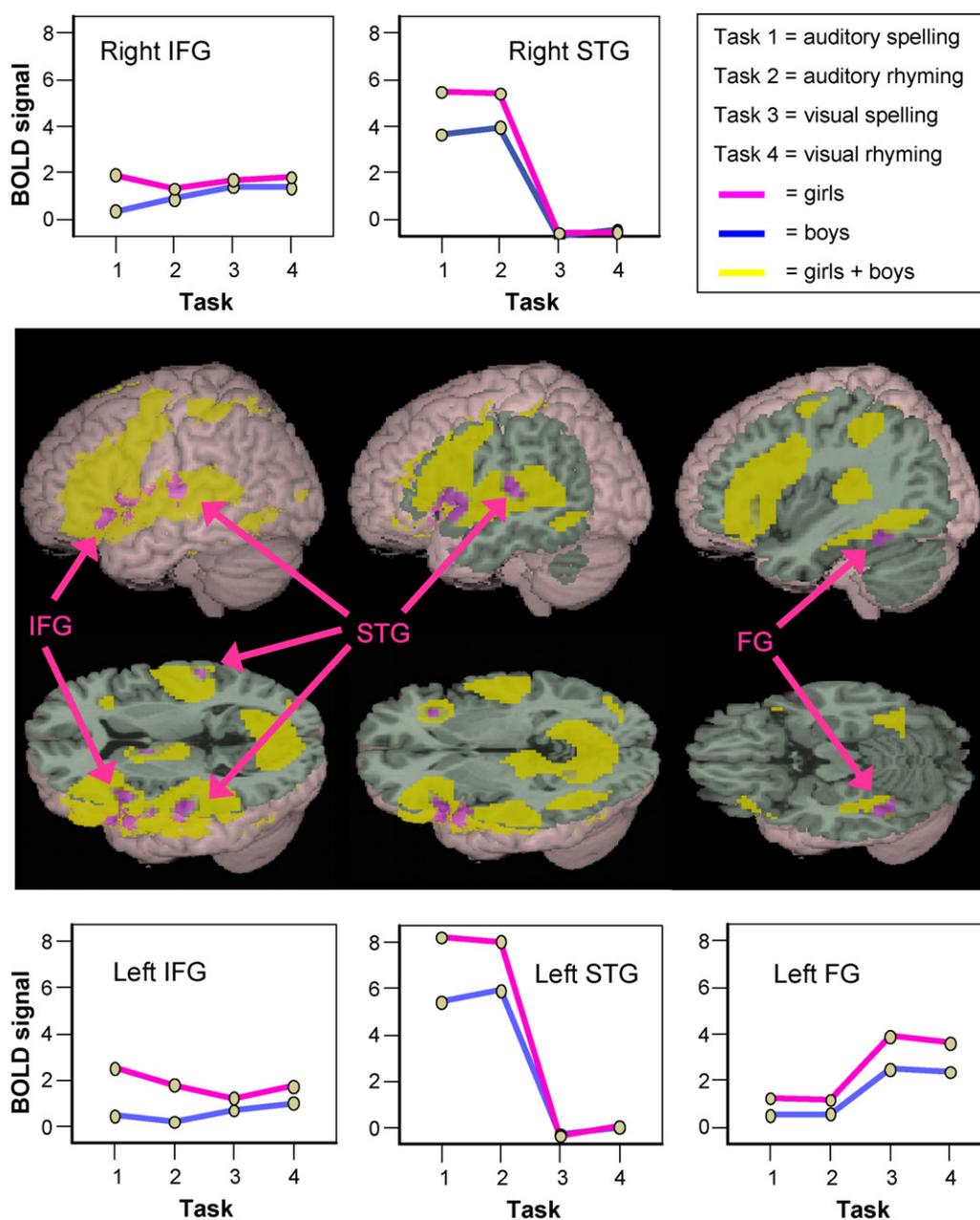


Fig. 1. Activation and sex differences during language tasks. Activation across both language judgment tasks and sensory modalities was elicited across all age groups irrespective of sex (yellow in brain images), but girls (pink) showed significantly greater activation than boys (blue) in bilateral regions of IFG and STG as well as left FG. Task, modality, age, and sex were entered into an ANCOVA model with accuracy as a covariate. Graph data were derived from ROI analysis of five regions showing significant sex effects ( $p < 0.005$  with a Bonferroni correction); the BOLD signal represents the estimated partial means derived from the mean activity of each region-of-interest after removing variance attributable to age and accuracy.

and superior temporal gyrus, and in the left fusiform gyrus (Fig. 1, pink and Table 4). Greater activation was evident among girls across all four task/modality combinations in the inferior frontal gyrus and the left fusiform gyrus; greater activation by girls in the superior temporal gyrus was limited to the auditory tasks.

Fig. 2 and Table 5 show the effect of increasing the threshold on the activation maps by girls (pink) and boys (dark blue), with regions of overlap shown in cyan. These results demonstrate an effect of threshold on perceived laterality differences between the sexes. With this stringent threshold ( $p = 1.0 \times 10^{-7}$ ), boys

show unilateral left activation in the inferior frontal gyrus (Broca's area), posterior part of the superior temporal gyrus (Wernicke's area), and the fusiform/inferior temporal gyrus. Girls also show left fusiform/inferior temporal activation, but bilateral activation in the inferior frontal gyrus, superior temporal gyrus, and occipital cortex.

Sex differences were also evident from activation in the perceptual control tasks (Fig. 3 and Table 6). Girls showed greater activation than boys in the left occipital and fusiform gyri for visual stimuli (Fig. 3A), whereas they showed greater activation than boys bilaterally in the superior temporal gyrus for auditory

Table 3  
Main effects of language tasks after partialing out effects of accuracy

| Region(s)   | Brodmann area(s)                                | Side       | Voxels | Z-value  | Coordinates |     |    |
|---|---|------------|--------|----------|-------------|-----|----|
|   |   |            |        |          | x           | y   | z  |
| IFG, MFG, insula, precentral gyrus, STG/Heschl's gyrus, MTG, IT/fusiform                              | 44, 45, 46, 47, 13, 6, 8, 9, 41, 42, 21, 22, 37 | L          | 3492   | Infinite | -33         | 24  | 0  |
|   |   |            |        | Infinite | -45         | 9   | 24 |
|   |   |            |        | Infinite | -42         | 27  | 12 |
| MeFG, cingulate, cuneus/calcarine sulcus, lingual gyrus, AC, caudate, thalamus, parahippocampal gyrus | 6, 8, 17, 18, 19, 24, 32, 30, 36, 37            | L (mostly) | 2945   | Infinite | -6          | 15  | 48 |
|   |   |            |        | Infinite | -3          | -78 | 9  |
|   |   |            |        | Infinite | 6           | -75 | 12 |
| IFG, insula, STG, Heschl's gyrus  | 45, 47, 13, 22, 42, 41                          | R          | 1056   | Infinite | 36          | 24  | 0  |
|   |   |            |        | Infinite | 66          | -18 | 6  |
|   |   |            |        | Infinite | 51          | -24 | 6  |
| IPL, precuneus  | 40, 19  | L          | 370    | Infinite | -45         | -39 | 48 |
|   |   |            |        | 7.12     | -27         | -63 | 42 |
| Precentral gyrus  | 4   | R          | 21     | 6.68     | 57          | -6  | 45 |

The statistical threshold was  $p=0.05$  with a family-wise error correction for multiple comparisons. Brain activation maxima are listed in MNI coordinates, with Brodmann areas estimated from the PickAtlas and aal toolboxes for SPM2. IFG = inferior frontal gyrus; MFG = middle frontal gyrus; STG = superior temporal gyrus; MTG = middle temporal gyrus; IT = inferior temporal gyrus; fusiform = fusiform gyrus; MeFG = medial frontal gyrus; AC = anterior cingulate gyrus; IPL = inferior parietal lobule.

stimuli (Fig. 3B). Boys did not show greater activation than girls for perceptual stimuli in either modality.

#### 2.4. Brain/behavior correlations

In order to identify brain areas most directly related to language judgments, ANCOVA models were created for each sex that identified a correlation between performance accuracy and the required language judgment (rhyming or spelling), irrespective of the stimulus modality of the words or the age of the participants. Correlations of accuracy with rhyming or spelling judgments are shown in Fig. 4A and Table 7 for boys (blue) and girls (pink). Fig. 4B and Table 8 show the results of similar ANCOVA models in which performance accuracy was cor-

related with the modality of the words (auditory or visual), irrespective of the language judgment or the age of the participants.

Among girls, brain activation in the left inferior frontal gyrus and the left middle temporal/fusiform gyrus was correlated with performance accuracy during both rhyming and spelling language judgments (Fig. 4A, pink); the same areas were correlated with accuracy in both tasks. No correlations were observed for either judgment among boys. A correlation with accuracy among boys was observed according to the modality of word presentation (Fig. 4B, blue). A left inferior frontal area was correlated with accuracy in auditory word tasks among boys, partially overlapping the inferior region correlated with accuracy among girls (cyan). A left superior temporal region was also correlated with

Table 4  
Location of sex effects (female > male) during language tasks after partialing out effects of age and accuracy

| Region(s)        | BA         | Side | Voxels | Z-value | Coordinates |     |     |
|------------------|------------|------|--------|---------|-------------|-----|-----|
|                  |            |      |        |         | x           | y   | z   |
| IFG              | 44, 45, 47 | L    | 274    | 5.85    | -51         | 12  | 3   |
|                  |            |      |        | 4.89    | -51         | 21  | -9  |
|                  |            |      |        | 3.74    | -63         | -3  | 6   |
| STG              | 41, 42, 22 | L    | 130    | 5.15    | -60         | -24 | 6   |
|                  |            |      |        | 4.54    | -39         | -48 | -21 |
| Fusiform         | 37         | L    | 44     | 4.54    | -39         | -48 | -21 |
|                  |            |      |        | 3.59    | -9          | 3   | 9   |
| Caudate/thalamus | -          | L    | 56     | 3.30    | -3          | -9  | 6   |
|                  |            |      |        | 3.54    | 36          | 24  | -3  |
| IFG              | 47         | R    | 57     | 3.54    | 36          | 24  | -3  |
|                  |            |      |        | 3.53    | 60          | -33 | 9   |
| STG              | 42         | R    | 44     | 3.53    | 60          | -33 | 9   |
|                  |            |      |        | 3.38    | -24         | -57 | 3   |
| Precuneus        | 30         | L    | 40     | 3.38    | -24         | -57 | 3   |
|                  |            |      |        | 3.26    | 6           | 27  | 45  |
| MeFG, cingulate  | 8, 32      | R    | 70     | 3.26    | 6           | 27  | 45  |
|                  |            |      |        | 3.20    | 9           | 18  | 42  |

Sex differences in the magnitude of activation were identified in an ANCOVA model that partialled out effects of age and accuracy, using the main effects map of activation by language tasks as a mask. The threshold was  $p < 0.05$ , using a FDR correction for multiple comparisons and an extent threshold of 25 voxels. Regional abbreviations as in Table 3.

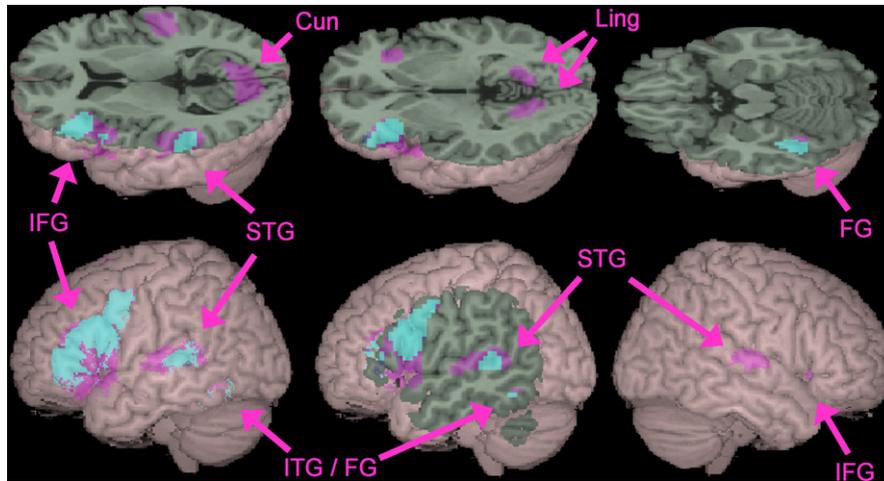


Fig. 2. Sex differences in laterality reflect a threshold effect. Using a more stringent statistical threshold ( $p = 1.0 \times 10^{-7}$  with a FDR correction), the left hemisphere showed similar patterns of activation by boys (blue) and girls (pink), including substantial overlap (cyan), but only girls showed bilateral activation in IFG and STG. IFG = inferior frontal gyrus; STG = superior temporal gyrus; FG = fusiform gyrus; ITG = inferior temporal gyrus; Cun = cuneus; Ling = lingual gyrus.

accuracy in the auditory tasks among boys, and was located almost entirely anterior to the middle temporal/fusiform region correlated with accuracy among girls. For visual word tasks, accuracy among boys was correlated with activation in the left superior parietal cortex and precuneus; accuracy on visual word tasks was not correlated with brain activation anywhere among girls.

In the perceptual control tasks, activation was not correlated with performance accuracy for either girls or boys (not shown).

To determine whether observed sex differences in brain activation are related to the observed differences in standardized

scores for reading skills (shown in Table 1), we performed ANCOVA analyses to correlate activation to visually presented words with standardized test scores (see Table 9). The CTOPP rapid naming scores were not correlated with brain activation to visually presented words at any location showing sex differences; however, the WRAT-III spelling scores, WJ-III reading fluency scores, and TOWRE phonetic decoding efficiency scores were all correlated with activation at the left fusiform site that showed sex effects (MNI coordinates  $[-39, -48, -21]$ , encompassed by each left fusiform cluster in Table 4 and Table 9).

Table 5  
Activation maps with a stringent threshold show laterality differences between sexes

| Sex  | Region(s)            | Brodmann area(s)  | Side | Voxels | Z-value      | Coordinates |     |     |          |
|------|----------------------|-------------------|------|--------|--------------|-------------|-----|-----|----------|
|      |                      |                   |      |        |              | x           | y   | z   |          |
| M    | IFG                  | 9, 44, 45, 46, 47 | L    | 848    | Infinite     | -48         | 9   | 24  |          |
|      |                      |                   |      |        | Infinite     | -33         | 27  | 0   |          |
|      |                      |                   |      |        | Infinite     | -48         | 33  | 9   |          |
|      | MeFG, cingulate      | 6, 8, 32          | L    | 227    | Infinite     | -6          | 15  | 48  |          |
|      |                      |                   |      |        | IT, fusiform | 37          | L   | 95  | Infinite |
|      | STG                  | 22                | L    | 98     | Infinite     | -57         | -39 | 6   |          |
| F    | IFG                  | 9, 44, 45, 46, 47 | L    | 1180   | Infinite     | -36         | 24  | -3  |          |
|      |                      |                   |      |        | Infinite     | -45         | 27  | 12  |          |
|      |                      |                   |      |        | Infinite     | -45         | 9   | 21  |          |
|      | MeFG, cingulate      | 6, 8, 32          | L    | 340    | Infinite     | -3          | 18  | 48  |          |
|      |                      |                   |      |        | IT, fusiform | 37          | L   | 137 | Infinite |
|      |                      |                   |      |        |              | Infinite    | -45 | -51 | -18      |
|      | STG, Heschl's        | 22, 41, 42        | L    | 269    | Infinite     | -54         | -45 | 9   |          |
|      | IFG, insula          | 47, 13            | R    | 90     | Infinite     | 33          | 24  | 0   |          |
|      | Cuneus/lingual gyrus | 17, 18, 19, 30    | R, L | 521    | Infinite     | 12          | -66 | 6   |          |
|      |                      |                   |      |        | Infinite     | -9          | -78 | 9   |          |
|      |                      |                   |      |        | Infinite     | 6           | -75 | 9   |          |
|      | STG, Heschl's gyrus  | 41, 42            | R    | 115    | 7.07         | 57          | -21 | 6   |          |
| 7.04 |                      |                   |      |        | 51           | -30         | 9   |     |          |
| 7.03 |                      |                   |      |        | 66           | -18         | 6   |     |          |

Sex differences in laterality were seen after increasing the threshold for activation ( $p = 1.0 \times 10^{-7}$  using a FWE correction and extent threshold of 25 voxels for the ANCOVA model described for Table 4). The sites of activation for girls and for boys are listed. Regional abbreviations as in Table 3.

Table 6  
Location of sex effects during perceptual tasks

| Sex | Modality | Region(s)                  | Brodmann area(s) | Side | Voxels | Z-value | Coordinates |     |     |
|-----|----------|----------------------------|------------------|------|--------|---------|-------------|-----|-----|
|     |          |                            |                  |      |        |         | x           | y   | z   |
| F   | Auditory | STG/Heschl's gyrus, insula | 42, 40           | L    | 43     | 4.42    | −60         | −21 | 9   |
|     |          |                            |                  |      |        | 3.09    | −48         | −24 | 15  |
|     |          | STG                        | 22               | R    | 76     | 5.23    | 60          | −36 | 9   |
|     |          | STG                        | 22               | R    | 59     | 4.44    | 57          | −6  | −3  |
| F   | Visual   | Middle occipital gyrus, FG | 18, 19, 37       | L    | 53     | 5.70    | −33         | −54 | −28 |
|     |          |                            |                  |      |        | 4.81    | −36         | −78 | −3  |
|     |          |                            |                  |      |        | 4.15    | −33         | −63 | −12 |

Sex differences in activation magnitude during nonlinguistic perceptual tasks identified in an ANCOVA model with age and accuracy as covariates; the area of activation during language tasks was used as a mask. The threshold for these sex effects was  $p < 0.05$ , using a FDR correction for multiple comparisons and an extent threshold of 25 voxels. Regional abbreviations as in Table 3.

Table 7  
Sex correlations of activation with accuracy on rhyming and spelling tasks after partialing out effects of sensory modality and age

| Sex | Task     | Region(s)             | BA    | Voxels | Z-value | Coordinates |     |      |     |    |    |
|-----|----------|-----------------------|-------|--------|---------|-------------|-----|------|-----|----|----|
|     |          |                       |       |        |         | x           | y   | z    |     |    |    |
| F   | Rhyme    | Cuneus, lingual gyrus | 18    | 61     | 5.28    | −6          | −69 | 12   |     |    |    |
|     |          |                       |       |        | 4.4     | −15         | −60 | 6    |     |    |    |
|     |          |                       |       |        | 4.41    | −54         | −54 | 0    |     |    |    |
|     |          |                       |       |        | 4.17    | −45         | 12  | 21   |     |    |    |
| F   | Spelling | MTG/FG                | 21/37 | 34     | 3.68    | −51         | −51 | −3   |     |    |    |
|     |          |                       |       |        | IFG     | 10          | 15  | 3.59 | −51 | 42 | 0  |
|     |          |                       |       |        | IFG     | 44/45       | 58  | 3.54 | −45 | 9  | 21 |

Brain activation was correlated with performance accuracy separately for each sex within an ANCOVA model that partialled out effects of sensory modality and age; the conjunction map of activation by both rhyming tasks at  $p < 0.05$  (uncorrected) was used as a mask for accuracy on rhyming judgments, whereas the conjunction map of activation by both spelling tasks at  $p < 0.05$  (uncorrected) was used as a mask for accuracy on spelling judgments. The activation threshold was  $p = 0.05$ , using a FDR correction for multiple comparisons and an extent threshold of 15 voxels. Regional abbreviations as in Table 3.

Table 8  
Sex correlations of activation with accuracy on auditory and visual tasks after partialing out effects of language judgment task and age

| Sex | Task     | Region(s)                | BA           | Voxels    | Z-value  | Coordinates |      |      |
|-----|----------|--------------------------|--------------|-----------|----------|-------------|------|------|
|     |          |                          |              |           |          | x           | y    | z    |
| F   | Auditory | MTG/FG                   | 21/37        | 114       | 5.74     | −51         | −54  | 0    |
|     |          |                          |              |           | IFG, MFG | 45, 46      | 222  | 5.03 |
|     |          | Insula                   | 13           | 28        | 3.51     | −48         | 30   | 24   |
|     |          |                          |              |           | 3.34     | −36         | −27  | 21   |
| M   | Auditory | IFG/MFG                  | 45, 46, 44/6 | 399       | 4.40     | −48         | 18   | 6    |
|     |          |                          |              |           | 4.23     | −45         | 27   | 21   |
|     |          |                          |              |           | 4.22     | −39         | 6    | 27   |
|     |          |                          |              |           | 4.11     | −51         | −33  | 3    |
|     |          |                          |              |           | 3.73     | −33         | −33  | 12   |
|     |          |                          |              |           | 3.66     | −54         | −12  | −3   |
|     |          | Heschl's gyrus, STG, MTG | 41, 22, 21   | 307       | 3.77     | 42          | −30  | 12   |
|     |          |                          |              |           | 3.72     | 33          | −33  | 12   |
|     |          |                          |              |           | 3.53     | 57          | −18  | 0    |
|     |          | Thalamus                 | MD           | 43        | 3.57     | −6          | −15  | 6    |
|     |          | MeFG                     | 6            | 65        | 3.41     | −9          | 30   | 39   |
|     |          | MFG                      | 47           | 20        | 3.22     | −45         | 45   | −6   |
|     |          | M                        | Visual       | Precuneus | 7, 19    | 47          | 4.76 | −24  |
| SPL | 7        |                          |              |           |          |             | 30   | 4.03 |

Brain activation was correlated with performance accuracy separately for each sex and sensory modality within an ANCOVA model that partialled out effects of language judgment task and age. The conjunction map of activation by both auditory language tasks at  $p < 0.05$  (uncorrected) was used as a mask for auditory accuracy judgments, whereas activation by both visual language tasks at  $p < 0.05$  (uncorrected) was used as a mask for visual accuracy judgments. The activation threshold was  $p = 0.05$ , using a FDR correction for multiple comparisons and an extent threshold of 15 voxels. Regional abbreviations as in Table 3.

Table 9  
Brain areas where activation on visual tasks was correlated with standardized test scores

| Test (subtest)                       | Region(s)                   | BA     | Side | Voxels | Z-value | Coordinates |     |     |
|--------------------------------------|-----------------------------|--------|------|--------|---------|-------------|-----|-----|
|                                      |                             |        |      |        |         | x           | y   | z   |
| WJ-III (reading fluency)             | Fusiform                    | 37     | L    | 28     | 4.34    | −42         | −42 | −18 |
| TOWRE (phonetic decoding efficiency) | Fusiform                    | 37     | L    | 84     | 4.73    | −30         | −48 | −18 |
|                                      | Fusiform                    | 37, 19 | R    | 33     | 4.28    | 36          | −48 | −18 |
|                                      | Lingual gyrus               |        |      |        |         |             |     |     |
|                                      | Lingual gyrus               | 19     | L    | 34     | 3.80    | −12         | −51 | 0   |
|                                      | Lingual gyrus               | 18, 19 | R    | 72     | 3.70    | 18          | −45 | −6  |
|                                      | Parahippocampal gyrus       | 30     |      |        | 3.15    | 21          | −60 | 6   |
| WRAT (spelling)                      | Cuneus                      | 17     | L    | 117    | 4.94    | −18         | −84 | 6   |
|                                      | Fusiform                    | 37     | R    | 204    | 4.68    | 12          | −51 | −6  |
|                                      |                             |        |      |        | 3.76    | 18          | −90 | 3   |
|                                      |                             |        |      |        | 3.66    | 15          | −78 | 9   |
|                                      |                             |        |      |        | 4.49    | 42          | −60 | −18 |
|                                      | Fusiform, inferior temporal | 37     | L    | 84     | 4.21    | −39         | −48 | −21 |
|                                      |                             |        |      |        | 3.48    | −48         | −66 | −9  |
|                                      |                             |        |      |        | 3.07    | −45         | −39 | −15 |
|                                      | Lingual                     | 19     | L    | 48     | 3.81    | −15         | −51 | −6  |
|                                      | Precuneus                   | 7      | L    | 35     | 3.81    | −24         | −72 | 39  |
| IFG, insula                          | 45, 46, 13                  | L      | 67   | 3.28   | −51     | 30          | 21  |     |
|                                      |                             |        |      | 3.05   | −45     | 12          | 12  |     |

The activation threshold was  $p < 0.05$ , using a FDR correction for multiple comparisons and an extent threshold of 15 voxels. Test abbreviations as in Table 1.

### 3. Discussion

This study demonstrated greater activation of language areas in girls, using a statistical model that generalized across task, stimulus modality, and age while accounting for variability in performance accuracy. Activation in frontal and temporal regions was bilaterally stronger among girls, yet because right-hemisphere activation was weaker among boys, reducing sensitivity with a higher threshold created the appearance of

a laterality difference similar to that reported by others. The left fusiform and superior temporal gyri showed similar sex differences during nonlinguistic sensory tasks, yet activation of the fusiform (as well as the left inferior frontal gyrus) was correlated with performance accuracy only during linguistic judgments. Correlation of the left fusiform activation with standardized reading scores further demonstrated its relevance to sex differences in language function. Finally, differences in brain-behavior correlations collapsed across language judgments or stimulus modality demonstrated that girls and boys rely on different brain areas for accurate language performance.

#### 3.1. Main effects of sex

Our study is the first to demonstrate a main effect of sex on the magnitude of activation. Neuroimaging studies on language have often failed to show sex differences (Buckner et al., 1995; Frost et al., 1999; Gur et al., 2000; Hund-Georgiadis et al., 2002; Roberts & Bell, 2002; Xu et al., 2001), even when using sample sizes larger than here (Brickman et al., 2005; Knecht et al., 2000; Sommer et al., 2004). In studies of adults that did find sex differences, effects have been weak, usually only demonstrable as differences in laterality (see introduction). A weak interaction of sex with age has also been demonstrated in children, evident as sex differences in the rate of developmental change in intensity (Plante et al., 2006). No previous study has looked for statistical differences between sexes across tasks (although some did look for sex differences on each of several tasks), and none controlled for all the other variables that potentially affect performance (age, accuracy, modality of word presentation and task). Our approach of examining effects across tasks and stimulus modalities is similar to that used by prior studies of amodal language processing (Booth et al., 2002b, 2003;

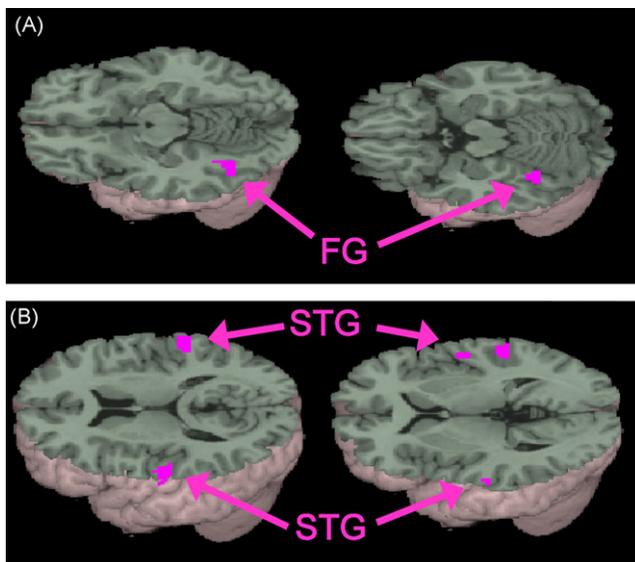


Fig. 3. Activation during nonlinguistic sensory tasks and sex effects. (A) Activation by nonlinguistic visual stimuli showed greater activation by girls (pink) in fusiform gyrus (FG); boys did not show greater activation anywhere. (B) Activation by nonlinguistic auditory stimuli showed greater activation by girls in superior temporal gyrus. STG = superior temporal gyrus; FG = fusiform gyrus.

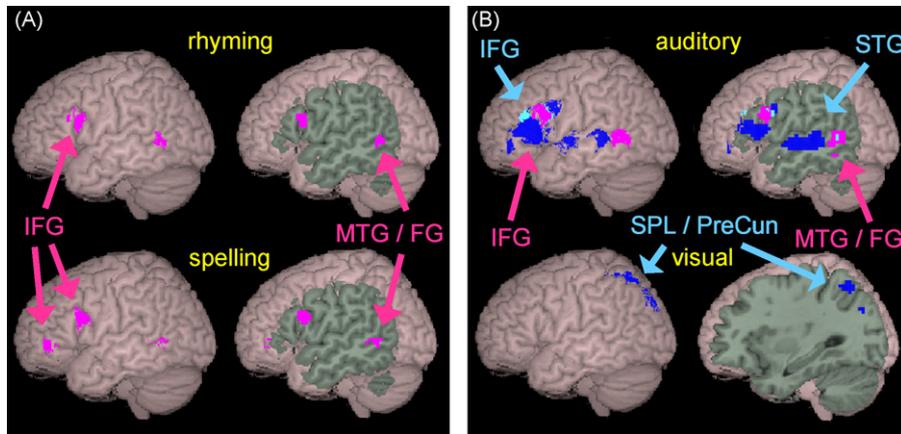


Fig. 4. Sex differences in correlation of activation with performance accuracy grouped by judgment task and by modality. (A) After accounting for modality effects, activation in MTG/FG and IFG was correlated with performance accuracy on both rhyming and spelling tasks among girls (pink) but not boys. (B) After accounting for task effects (rhyming vs. spelling), activation by auditory word stimuli among boys (blue) was correlated with performance accuracy in STG and IFG, whereas activation by visual word stimuli was correlated with performance accuracy in SPL/PreCun. Among girls (pink), correlation of accuracy with activation for auditory word stimuli was generally distinct from regions correlated with accuracy among boys, although overlap (cyan) was evident in IFG and (slightly) in posterior MTG. Activation by visual word stimuli was not correlated with performance accuracy irrespective of language judgment among girls. IFG = inferior frontal gyrus; MTG/FG = middle temporal gyrus extending into fusiform gyrus; SPL/PreCun = superior parietal lobule extending into precuneus.

Buchel, Price, & Friston, 1998; Demonet, Thierry, & Cardebat, 2005; Gabrieli, Poldrack, & Desmond, 1998; MacSweeney et al., 2002), which demonstrate higher-level linguistic functions by eliminating modality of word presentation as a confound.

Accounting for all these factors in our fMRI model apparently increased sensitivity to sex differences, as this study is one of the first to detect sex differences in activation magnitude using direct statistical comparisons. Although both boys and girls showed bilateral activation, increasing our statistical threshold (thereby lowering sensitivity) resulted in marked sex differences in laterality, with frontal and temporal lobe activation appearing in the right-hemisphere of girls where their activation was stronger than boys. This laterality pattern is similar to what is sometimes reported by others—particularly among smaller studies with limited statistical power (Sommer et al., 2004). However, right-hemisphere regions showing greater activation by girls were embedded within an area of activation jointly activated by both sexes, suggesting differences in laterality exist only when there is insufficient power to detect weak right-hemisphere activation among boys.

Our results are generally consistent with the sex effects reported in children by Plante et al. (2006). Both studies found sex effects bilaterally across multiple tasks in inferior frontal gyrus and posterior temporal areas. Whereas we demonstrated main effects, most sex differences in Plante et al. (2006) were evident as an interaction with age, but task differences and differences in baseline makes detailed comparisons between studies difficult. Plante et al. (2006) used a block design with pure tones as the baseline. We found sex differences in activation for pure tones in the same regions of superior temporal gyrus as the sex differences found for words, so sex differences in activation to linguistic stimuli relative to tones (i.e., “word – tones”) will depend on the regional specialization for language. The interaction of sex  $\times$  age for “words – tones” reported by Plante et al. (2006) may thus reflect increasing specialization for language with age among girls.

Increased brain activation may reflect either greater task difficulty (Desai, Conant, Waldron, & Binder, 2006; Gould, Brown, Owen, ffytche, & Howard, 2003; Speck et al., 2000) or improved processing and performance (Booth et al., 2003; Tagamets, Novick, Chalmers, & Friedman, 2000). Evidence suggests that increased fusiform and inferior frontal activation by girls is beneficial for performance. In the fusiform region activated more by girls, activation is positively correlated both with performance accuracy on our language tasks and with word identification skills on standardized tests. Benefits from greater bilateral activation in the inferior frontal gyrus is consistent with greater language retention among females (compared to males) following strokes in the left inferior frontal gyrus (McGlone, 1977). Apparently the increased hemodynamic response observed among girls reflects processes relevant to skilled language performance beyond what was required to accurately perform the tasks used here.

### 3.2. Brain/behavior correlations

Accuracy correlations reported here indicate that girls and boys preferentially use different brain areas for performing cognitive functions required by our language tasks. These brain/behavior correlations were limited to the language tasks (and not the sensory control tasks), and are thus unlikely to be due to generalized differences in sensory processing.

Among boys, brain areas required for accurate performance of a language task depended on the modality of the presented words; accurate responses to visually presented words utilized visual association cortex and posterior parietal regions, whereas accurate response to auditory word forms utilized areas involved in auditory and phonological processing. In boys, correlations with accurate spelling and rhyming judgments were not seen. By contrast, accuracy for rhyming and spelling judgments among girls were each correlated with activation in the left inferior frontal gyrus and the left middle temporal/fusiform

gyrus, regardless of stimulus modality. These same areas were also correlated with accuracy during auditory word tasks, perhaps reflecting automatic access of spoken words to the linguistic system (Cobianchi & Giaquinto, 1997; Pulvermuller & Shtyrov, 2006). Among girls, no correlation with accuracy was observed across visual tasks, indicating that accurate performance on visual word tasks involving different linguistic judgments was not limited by visual processes.

Activation by language tasks across stimulus modalities provides strong evidence that high-level linguistic processes are engaged in these areas (Booth et al., 2002a). Correlation of activity with multimodal linguistic accuracy among girls is consistent with the known roles of the left inferior frontal gyrus in linguistic functions such as semantics and phonology (Vigneau et al., 2005), the left middle temporal gyrus in semantics (Booth et al., 2002b; Booth et al., 2006; Chou et al., 2006; Devlin et al., 2002; Muller, Kleinhans, & Courchesne, 2003), and the left fusiform gyrus in orthographic processing (Cohen et al., 2000; Dehaene, Le Clec, Poline, Le Bihan, & Cohen, 2002). The pattern of accuracy correlations suggests that girls' linguistic judgments depended on information available to the language network regardless of the modality of word presentation, whereas accurate performance for boys depended on the modality of word presentation rather than the linguistic judgment required. These dramatic sex differences in the pattern of brain-behavior correlations reflect fundamental differences in the nature of processing required for accurate performance.

The sensory association areas correlated with accuracy in boys have been implicated in auditory and visuospatial processing, respectively (LaBar, Gitelman, Parrish, & Mesulam, 1999; Poeppel et al., 2004; Simos et al., 2000). Correlation of performance accuracy with activation in these sensory association areas may reflect the quality of sensory processing before the word is accessed by the language network. If boys do not convert sensory information to language as well as girls, the quality of sensory processing in sensory association areas may act as a bottleneck that limits the accurate representations of words, thereby limiting performance accuracy. Sex differences for the perceptual controls (as well as words) suggests that boys are indeed less effective in sensory processing. If improvement in sensory processing during maturation eliminates the bottleneck in boys, then accurate performance should no longer be limited by (and correlated with) activity in the sensory association cortex, allowing accurate performance to reflect activity in the language network. This may indeed be the case. In a mixed-sex group of adults, accuracy of spelling and rhyming judgments are correlated with activation in linguistic regions of the fusiform and superior temporal gyri, respectively (Booth et al., 2003), suggesting that adult males and females depend on the same specialized language areas. If so, sex differences in linguistic activation during childhood may reflect developmental differences in maturation rate (Blanton et al., 2004; Cohn, 1991).

The correlation of brain activation in unimodal cortex with performance accuracy among boys may additionally reflect word associations or familiarity with the words used in this task. Practice-related increases in activation have been reported

in medial extrastriate cortex when rehearsing word associations (Raichle et al., 1994); this region has also been implicated in domain-general learning that supports novice performance (Chein & Schneider, 2005). These various possibilities need not be mutually exclusive. Regardless of whether the behavioral correlations in unimodal association cortices represent a sensory bottleneck, word associations, or word familiarity, the findings indicate that boys rely on different brain areas for accurate performance on language tasks than girls. Language in girls carries the advantage of utilizing supramodal processes, perhaps representing a more abstract, conceptual knowledge of words and their representations.

### 3.3. *Developmental inferences*

The pattern of behavioral correlations seen for a mixed-sex group of adults (Booth et al., 2003) does differ from the pattern reported here for girls as well as for boys. In girls, the middle temporal/fusiform activation is correlated with accuracy for both spelling and rhyming judgments activation, whereas fusiform activation in adults is correlated with accuracy for spelling but not rhyming judgments. This difference may reflect a developmental trend for more focal activation and greater regional specialization with increased age (Durston et al., 2006).

Sex differences in response magnitude and in brain-behavior correlations can both help explain sex differences in language performance. The region of left fusiform gyrus preferentially activated by girls during language tasks was also correlated with standardized scores of spelling and reading on which girls showed an advantage. Similarly, the region of left inferior frontal gyrus preferentially activated by girls was correlated with performance accuracy on our language tasks. Thus, observed sex differences in activation were relevant to language performance, with increased activation reflecting better skill and performance.

## 4. **Conclusions**

After accounting for differences associated with age, linguistic judgment, modality of word presentation, and performance accuracy, girls were still found to have significantly greater activation in linguistic areas of the brain. The pattern of activation differences and the relationship of activation with performance accuracy and reading skill suggest that these differences underlie childhood sex differences in language performance. Furthermore, the results indicate that accurate performance among boys and girls depends on different brain regions, perhaps reflecting different approaches to linguistic processing despite extensive overlap in activated regions. Girls make language judgments based on linguistic content by accessing a common language network regardless of the sensory input, whereas boys rely on a modality-specific network.

Although such differences reflect early differences in processing language, evidence does not currently suggest that differences in brain-behavior correlations persist into adulthood. Instead, such differences may disappear as the development of

sensory processing in boys catches up to girls, so that by adulthood language processing in both sexes relies on the efficiency of the brain's linguistic network. This possibility warrants further study. Nonetheless, by characterizing the nature of sex differences in processing language during a period in which reading acquisition occurs, our findings represent an important step toward identifying the developmental basis for sex differences in language performance.

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