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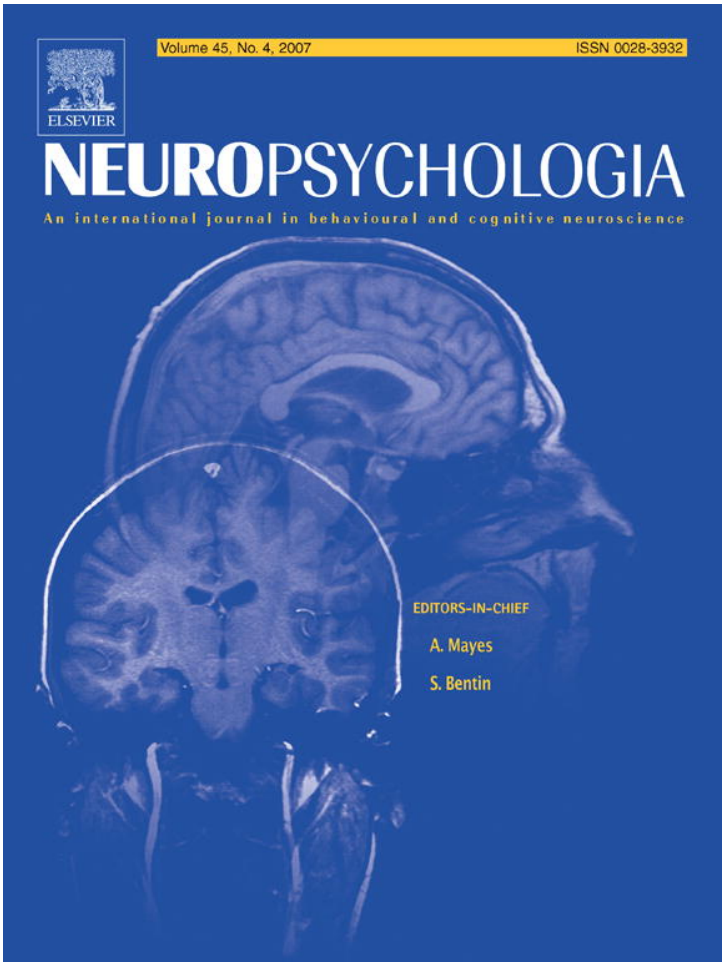

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Children with reading disorder show modality independent brain abnormalities during semantic tasks

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Abstract

Neuroimaging studies have suggested that left inferior frontal gyrus, left inferior parietal lobule and left middle temporal gyrus are critical for semantic processing in normal children. The goal of the present functional magnetic resonance imaging (fMRI) study was to determine whether these regions are systematically related to semantic processing in children (9- to 15-year-old) diagnosed with reading disorders (RD). Semantic judgments required participants to indicate whether two words were related in meaning. The strength of semantic association varied continuously from higher association pairs (e.g., king–queen) to lower association pairs (e.g. net–ship). We found that the correlation between association strength and activation was significantly weaker for RD children compared to controls in left middle temporal gyrus and left inferior parietal lobule for both the auditory and the visual modalities and in left inferior frontal gyrus for the visual modality. These results suggest that the RD children have abnormalities in semantic search/retrieval in the inferior frontal gyrus, integration of semantic information in the inferior parietal lobule and semantic lexical representations in the middle temporal gyrus. These deficits appear to be general to the semantic system and independent of modality.
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1. Introduction

Examining how the difficulty of a semantic task systematically relates to brain activation allows one to be more confident that particular brain region is involved in a specific cognitive process. For example, one study with adults compared brain activation patterns to semantic judgments involving closely related pairs (e.g., king–queen) versus distantly related pairs (e.g., net–ship). Distantly related pairs with weaker semantic association produced more activation in left inferior frontal gyrus as compared to closely related pairs with stronger semantic association. The greater activation in left inferior frontal gyrus was interpreted as evidence for the difficulty of searching/retrieving appropriate semantic features because distantly related pairs shared few semantic features (Fletcher et al., 2000). Indeed, there are many studies showing greater inferior frontal gyrus activation in more difficult semantic tasks and in other cases of increasing retrieval or selection demands (Gurd et al., 2002; Seger et al., 2000; Thompson-Schill et al., 1999; Whatmough et al., 2002). Consistent with previous findings in adults, Chou et al. (2006a, b) demonstrated that weaker semantic association in children was correlated with greater activation in left inferior frontal gyrus (BA 45, 47) (Chou et al., 2006a, b). Chou et al. (2006a, b) also showed that weaker semantic association in children was correlated with greater activation in left middle temporal gyrus (BA 21). Activation in this region has been implicated in the representation of verbal semantic information when words are presented auditorily or visually (Chee et al., 1999) and semantic priming studies have shown modulation of activation in this region (Devlin et al., 2004; Gold et al., 2006; Rissman et al., 2003). Greater activation in this region for low association pairs may result from more extensive access to semantic representations in order to identify overlapping features.

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Chou et al. (2006a, b) also showed that stronger semantic association was correlated with greater activation in left inferior parietal lobule (BA 40). Activation in this region has previously been identified in semantic tasks, including associative judgments (Binder et al., 1997), similarity judgments (Price et al., 1999), category judgments (Pugh et al., 1996) and concrete versus abstract word judgments (Chee et al., 1999). Some studies have interpreted the left inferior parietal lobule activation as related to feature integration and semantic categorization to form a coherent concept so that semantic relationships between words can be determined (Grossman et al., 2003). Neuro-anatomical connectivity patterns also suggest that semantic lexical integrative processes involve heteromodal association cortices in the inferior parietal lobule (Mesulam, 1998). High association pairs may involve greater integration because there are more overlapping features between the words or because the shared features are more characteristic of each of the words (Fletcher et al., 2000). Greater integration for high association word pairs may account for the increase in left inferior parietal lobule activation with increasing association strength.

Few studies have used semantic tasks to examine neural activity differences between those with and without reading disorders. Several studies measured brain activation differences between controls and patients with dyslexia during a semantic category judgment task in which single words were presented in the visual modality. Shaywitz et al. (1998) reported that dyslexic adults show less activation in bilateral angular gyrus and more activation in bilateral inferior frontal gyrus (Shaywitz et al., 1998). Shaywitz et al. (2002) later reported that dyslexic children showed less activation than control children in left angular gyrus and bilateral middle temporal gyrus (Shaywitz et al., 2002). Furthermore, higher accuracy across both groups of children was associated with greater activation in bilateral angular gyrus and bilateral middle temporal gyrus. Shaywitz et al. (2003) later investigated differences between persistently poor adult readers and accuracy-improved adult readers (compensated) (Shaywitz et al., 2003). They reported that persistently poor readers showed less activation than accuracy-improved readers in left middle temporal gyrus and control readers showed greater activation than accuracy-improved readers in left middle temporal gyrus. Another study by Pugh et al. (2000) examined functional connectivity in adults with and without reading disorders. They found that left angular gyrus activation was correlated with activation posterior left superior temporal gyrus for the control subjects, but not for patients with dyslexia (Pugh et al., 2000). Altogether, research using the semantic category judgment task shows disruption of the left inferior parietal cortex, left inferior frontal gyrus and left superior/middle temporal cortex in patients with dyslexia.

Other studies have examined the neural correlates of semantic processing in patients with dyslexia using different tasks. Using magnetoencephalography (MEG), Helenius et al. (1999) presented sentences in the visual modality that either ended in a semantically anomalous word or not (Helenius et al., 1999). They found no differences between patients with dyslexia and controls in the location of activation in left superior/middle temporal gyrus, but activation was weaker and delayed by about 100 ms in patients with dyslexia. Using positron emission tomography (PET), Rumsey et al. (1994) presented sentences in the auditory modality and asked control adults and patients with dyslexia to make judgments as to whether two sentences with different syntactic structure had the same meaning (Rumsey et al., 1994). During rest, patients with dyslexia showed less activation in inferior parietal cortex around the angular/supramarginal gyrus. Patients with dyslexia showed greater activation in a right lateral frontal region and were less left lateralized in the same inferior parietal region that produced a group difference during rest. These studies are consistent with the fMRI studies implicating abnormalities in the frontal and temporo-parietal cortices in patients with dyslexia.

Many have argued that the central deficit in reading disorder is phonological processing (Paulesu et al., 2001; Pugh et al., 2000; Shaywitz et al., 1998; Temple et al., 2001) and less attention has been given to whether children with reading disorders have deficits in semantic processing. The goal of the current study was to examine the neural correlates of semantic processing in reading disorder (RD) children by using a parametric manipulation of semantic association to determine if RD children (9- to 15-year-old) exhibit the same correlation between association strength and activation as do age-match control children. If RD children show weaker correlations between association and activation, it would suggest abnormal semantic search/retrieval in the inferior frontal gyrus, integration of semantic information in the inferior parietal lobule and semantic lexical representations in middle temporal gyrus. The advantage of using a parametric manipulation of semantic association is to more precisely determine regions critical for processing meaning-based representations. Furthermore, the examination of semantic processing in RD and normal children in both visual and auditory modalities enables the determination of whether abnormal activation is domain general or modality-dependent.

2. Materials and methods

2.1. Participants

Children (9- to 15-year-old) were recruited from the Chicago metropolitan area. Parents of children were given an informal interview to insure that they met the following inclusionary criteria: (1) native English speakers, (2) right-handedness, (3) normal hearing and normal or corrected-to-normal vision, (4) free of neurological disease or psychiatric disorders, (5) not taking medication affecting the central nervous system, and (6) no Attention Deficit Hyperactivity Disorder (ADHD). The control children had no history of intelligence, reading, or oral-language deficits, and the RD children had a diagnosis of learning disability by a clinical psychologist. Furthermore, all RD children had less than a 95 scaled-score on the average of the four standardized reading measures. After the administration of the informal interview, informed consent was obtained. The informed consent procedures were approved by the Institutional Review Board at Northwestern University and Evanston Northwestern Healthcare Research Institute.

Fifteen RD children participated in the auditory task (mean age = 10.7, S.D. = 2.24 years, three females) and 13 RD children participated the visual task (mean age = 10.5, S.D. = 2.31 years, two females). Thirteen RD children participated in both the auditory and visual tasks. Fifteen control children (mean age = 10.6, S.D. = 2.14 years, five females) were age matched to the RD children in the auditory task and 13 control children (mean age = 10.5, S.D. = 2.19 years, four females) were age matched to the RD children in the visual task. Eleven control children participated in both the auditory and visual tasks. Each control

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Table 1
Means (and standard deviations) for test performance for the control and RD groups in the auditory and visual experiment

Test	Auditory		Visual	
	Control	RD	Control	RD
WASI				
Verbal (VIQ)[#]	108 (13)	97 (15)	112 (15)	99 (16)
Performance (PIQ)[*]	111 (17)	98 (16)	111 (18)	101 (14)
WRAT				
Spelling[△]	115 (11)	82 (14)	115 (9)	86 (12)
WJ-III				
Word reading accuracy (Word ID)[△]	113 (10)	85 (18)	113 (8)	90 (10)
Nonword reading accuracy (Word Att)[△]	108 (10)	83 (14)	110 (10)	86 (11)
TOWRE				
Word reading speed (SWE)[△]	106 (6)	84 (16)	107 (7)	89 (12)
Nonword reading speed (PDE)[△]	103 (7)	80 (17)	104 (8)	84 (16)

Note. WASI, wechsler abbreviated intelligence scale; VIQ, verbal intelligence quotient; PIQ, performance intelligence quotient; WRAT, wide range achievement test; WJ-III, Woodcock Johnson III tests of achievement; Word ID, word identification; WordAtt, word attack; TOWRE, test of word reading efficiency; SWE, word reading efficiency. PDE, pseudo-word reading efficiency. Standard scores are presented (mean = 100, S.D. = 15). [*]$p < 0.05$ for auditory experiment; [#]$p < 0.01$ for visual experiment; [△]$p < 0.001$ for both experiments.

child was matched within 4 months to each RD child, so there was no need to partial out age when statistically comparing the two groups. This age-match design did not allow us to determine whether abnormal patterns of activation were due to deviance or delay, as we would have also needed to include a reading-match group.

2.2. Standardized testing

Mental ability was measured with the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) with two verbal subtests (Vocabulary, Similarities) and two performance subtests (Block Design, Matrix Reasoning). Spelling was measured by the Wide Range Achievement Test (WRAT) (Wilkinson, 1993). Word and nonword reading accuracy was measured with the Woodcock Johnson III Tests of Achievement (WJ-III) (Woodcock et al., 2001). Word and nonword reading speed was measured by the Tests of Word Reading efficiency (TOWRE) (Torgeson et al., 1999). See Table 1 for a summary of performance on these tasks by the control and RD groups, and the significant differences between the groups. Although some RD children had relatively high scores on some reading/spelling tests suggesting compensation, there were significant differences between groups on all of these measures.

2.3. Functional activation tasks

In the auditory word judgment task, a fixation-cross appeared throughout the trial while two words were presented sequentially. The duration of each word was between 500 and 800 ms followed by a brief period of silence, with the second word beginning 1000 ms after the onset of the first. Variable length was unavoidable because lengthening the words too much resulted in artificial sounding phonology. In the visual word judgment task, two visual words were presented sequentially. The duration of each word was 800 ms followed by a 200 ms blank interval. For both modalities, a red fixation-cross appeared on the screen after the second word, indicating the need to make a response during the subsequent 2600 ms interval. For the visual modality, the words were lower case, and were offset 1/2 a letter from each other in the pair (50% to the right and 50% to the left) so that judgment could not be based on visual persistence.

Forty-eight word pairs were semantically related according to their free association values for the auditory (mean = 0.45, S.D. = 0.21, range = 0.85–0.12) and visual modalities (mean = 0.45, S.D. = 0.19, range = 0.77–0.14) (Nelson et al., 1998). These word pairs included both closely related pairs (e.g., king–queen) with higher association values and distantly related pairs (e.g., net–ship) with lower association values. Twenty-four word pairs were semantically unrelated with zero association values (e.g., tree–car). The participants were instructed to quickly and accurately press the yes button with their right hand to the related pairs and the no button to the unrelated pairs. Several lexical variables were controlled for the wordpairs (see Chou et al., 2006a, b).

There were also three control tasks for both modalities. The auditory control tasks involved simple (24 trials) and complex (24 trials) tone matching judgments and the visual control tasks involved simple (24 trials) and complex (24 trials) false font matching judgments. For both modalities, participants determined whether the pair of stimuli were identical or not by pressing a yes or no button. Both modalities also had a null condition with 60 trials that required a button press when a black fixation-cross turned red. The order of lexical and control trials and was optimized for event-related design using OptSeq (http://www.surfer.nmr.mgh.harvard.edu/optseq) (Burock et al., 1998). The order of stimuli within task was fixed for all subjects. Because the focus of this paper is on the correlation of association strength to activation, we did not use the control or unrelated conditions in our analyses. See Chou et al. (2006a, b) for details of the control tasks.

2.4. Experimental procedure

Before the fMRI session, participants were trained to keep their head still using an infrared tracking device, and then practiced one run of the semantic judgment task in a simulator in order to acclimate themselves to the scanner environment (Rosenberg et al., 1997). Different stimuli were used in the practice and fMRI sessions. Within a week of the practice session, participants were administered the fMRI session.

2.5. MRI data acquisition

Participants lay in the scanner with their head position secured with a specially designed vacuum pillow (Bionix, Toledo, OH). An optical response box (Current Designs, Philadelphia, PA) was placed in the participants' right hand. The head coil was positioned over the participants' head. Participants viewed visual stimuli that were projected onto a screen via a mirror attached to the inside of the head coil. Participants wore headphones to hear auditory stimuli (Resonance Technology, Northridge, CA). Each participant performed two functional runs. The first run took 6.7 min and the second 6.6 min.

All images were acquired using a 1.5 T GE scanner. Gradient-echo localizer images were acquired to determine the placement of the functional slices. For the functional imaging studies, a susceptibility weighted single-shot EPI (echo planar imaging) method with BOLD (blood oxygenation level-dependent) was used. Functional images were interleaved from bottom to top in a whole brain EPI acquisition. The following scan parameters were used: TE = 35 ms, flip angle = 90°, matrix size = 64 × 64, field of view = 24 cm, slice thickness = 5 mm, number of slices = 24 and TR = 2000 ms. The first functional run had 203 image

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volumes and the second had 198 image volumes. In addition, a high resolution, T1 weighted 3D image was acquired (SPGR, TR = 21 ms, TE = 8 m, flip angle = 20°, matrix size = 256 × 256, field of view = 22 cm, slice thickness = 1 mm, number of slices = 124). The orientation of the 3D image was identical to the functional slices.

2.6. Image analysis

Data analysis was performed using SPM2 (Statistical Parametric Mapping) (http://www.fil.ion.ucl.ac.uk/spm). The functional images were corrected for differences in slice-acquisition time to the middle volume and were realigned to the first volume in the scanning session using affine transformations. No participant had more than 4.0 mm of movement within run in any plane. Co-registered images were normalized to the MNI average template (12 linear affine parameters for brain size and position, 8 non-linear iterations and 2 × 2 × 2 non-linear basis functions). Statistical analyses were calculated on the smoothed data (10 mm isotropic Gaussian kernel), with a high pass filter (128 s cutoff period) in order to remove signal drift, cardiac and respiratory effects, and other low frequency artifacts. We used global normalization to scale the mean of each scan to a common value in order to correct for whole brain differences over time.

Data from each participant was entered into a general linear model using an event-related analysis procedure. Word pairs were treated as individual events for analysis and modeled using a canonical HRF. Parameter estimates from contrasts of the canonical HRF in single subject models were entered into random-effects analysis using one-sample *t*-tests across all participants to determine whether activation during a contrast was significant (i.e., parameter estimates were reliably greater than 0).

In order to determine the general language network, we calculated *t*-tests comparing the related word pairs to the null conditions separately for the RD and control groups and separately for the auditory and visual modalities in a whole brain analysis using a significance criterion of $p < 0.001$ uncorrected with a cluster size of 15 voxels or greater. However, our primary analytic approach was to concentrate on regions of interest that showed a correlation between association strength and activation in our larger sample of control children (Chou et al., 2006a, b). Using anatomical masks of left inferior frontal gyrus, left inferior parietal lobule and left middle temporal gyrus, we created activation maps for the control children in the current study for the correlation of lower association with greater activation in left inferior frontal gyrus and left middle temporal gyrus, and of higher association with greater activation in left inferior parietal lobule. This was done separately for both modalities by entering the continuous variable of association strength as a covariate of interest using a relatively liberal threshold ($p < 0.05$ uncorrected with a cluster size of 10 voxels or greater) to maximize the size of the cluster to be used as the region of interest in subsequent analyses. We then calculated two kinds of analyses. First, we determined whether RD children showed a correlation between association strength and activation in any of these regions of interest as defined by our control group ($p < 0.05$ uncorrected with a cluster size of 10 voxels or greater). Second, we determined whether the correlation between association strength and activation in these regions of interest was significantly stronger for the control than the RD children by directly comparing the contrasts of the correlation between association strength and activation. We used a threshold of $p < 0.001$ uncorrected with a cluster size of 15 voxels or greater, but also indicate when these contrasts reached a false discovery rate (FDR) corrected level of significance because these were the critical contrasts of interest in this study.

3. Results

3.1. Behavioral performance

For the control group, all mean accuracy levels were above 93% and no individual participant scored below 70% in any condition. For the RD group, all mean accuracy levels were above 75% and no individual participant scored below 55% in any condition (see Table 2). An ANCOVA, with group as a dichotomous variable (control, RD) and association strength as a continuous variable, was calculated separately for accuracy and reaction time and separately for the auditory and visual modality. The RD group was less accurate than the control group for both the auditory, $F(1, 91) = 18.81$, $p < 0.001$, and visual, $F(1, 91) = 61.93$, $p < 0.001$, modalities. The RD group was also slower than the control group for both the auditory, $F(1, 91) = 25.67$, $p < 0.001$, and visual, $F(1, 91) = 35.38$, $p < 0.001$, modalities. Lower association pairs did not produce significantly lower accuracy than higher association pairs for either the auditory, $F(1, 91) = 2.93$, $p = 0.090$, or visual, $F(1, 91) = 0.71$, $p = 0.403$, modalities. Lower association pairs did produce slower reaction times than higher association pairs for the auditory, $F(1, 91) = 7.27$, $p = 0.008$, but not the visual, $F(1, 91) = 0.32$, $p = 0.576$, modalities. There was no interaction between group and association for either modality indicating that association was correlated with accuracy and reaction time similarly in the RD and control groups. Even though association showed a similar correlation to behavioral performance in the two groups, group differences in the correlation between brain activation and association strength cannot be ruled out. A comparison between modalities revealed that controls were less accurate and slower for the auditory as compared to the visual modality ($t = 2.26$, 2.46, respectively, $p < 0.05$), but that there were no significant differences between modalities for children with dyslexia.

Table 2
Mean accuracy and reaction time (and standard deviations) on the related pairs for the control and RD groups

Group	Modality	Accuracy	Reaction time
Control	Auditory	92 (7)	1353 (350)
	Visual	96 (4)	1276 (374)
RD	Auditory	81 (10)	1562 (266)
	Visual	76 (14)	1455 (304)

Note. Accuracy is given as a percentage, and reaction time is given in milliseconds.

3.2. Brain activation patterns

Table 3 and Fig. 1 show greater neural activation for related word pairs compared to the null condition (fixation-cross) for the control and RD groups. For the auditory modality, both groups showed activation in left inferior frontal gyrus and bilateral superior/middle temporal gyrus. The RD group additionally showed activation in bilateral visual association areas including the lingual gyrus and cuneus. For the visual modality, both groups showed activation in left inferior frontal gyrus, left middle temporal gyrus, and bilateral fusiform gyrus and other visual association regions (e.g., inferior or middle occipital gyrus). The control group additionally showed a large cluster of activation in left superior frontal gyrus, and the RD group showed activation in left supplementary motor area. A direct statistical comparison between the two groups revealed few significant differences. In the visual modality, the control group showed greater activation in left inferior frontal gyrus and the RD group showing greater activation in right supramarginal gyrus (see Table 3). No differ-

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Table 3
Greater activation for related word pairs compared to the null condition for the control and RD groups in the auditory and visual modalities

Group	Modality	Region	H	BA	Z-score	Voxels	X	Y	Z
Control	Auditory	Inferior/middle frontal gyrus	L	45, 47, 11	3.88	157	−42	33	−15
		Superior + middle temporal gyrus	L	42, 41, 22, 21	5.65	1203	−60	−15	9
		Superior + middle temporal gyrus	R	42, 41, 22, 21	5.91	1039	57	−15	6
RD	Auditory	Inferior frontal gyrus	L	45, 47	4.24	68	−39	30	−3
		Inferior frontal gyrus	L	45	3.92	43	−51	18	15
		Superior + middle temporal gyrus, Heschl's gyrus, insula	L	22, 21, 41,42	5.67	1179	−60	−21	12
		Superior + middle temporal gyrus, Heschl's gyrus, insula	R	22, 21, 41, 42	5.68	1072	60	−18	9
		Cuneus, lingual gyrus	L	18	4.05	46	−9	−66	6
		Cuneus, lingual gyrus	R	18	3.69	41	12	−66	6
		Cerebellum	B		3.78	51	−6, 6	−36, −33	−9, −9
Control	Visual	Inferior frontal gyrus	L	45, 47	6.15	1002	−54	30	12
		Fusiform gyrus, middle temporal gyrus, inferior + middle occipital gyrus, cuneus, posterior cingulate	B	37, 17, 18, 19, 23, 30	5.87	2002	−42, 36	−63, −60	−18, −18
		Superior frontal gyrus	L	6, 8	4.68	166	−3	12	60
		Middle frontal gyrus	R	9	4.01	31	30	33	−12
		Thalamus	L		3.72	24	−12	−12	12
RD	Visual	Inferior frontal gyrus	L	45	3.96	112	−57	21	15
		Inferior frontal gyrus	L	45, 47	3.50	79	−36	27	−3
		Middle temporal gyrus	L	22	4.67	80	−57	−45	6
		Fusiform gyrus	L	18, 19, 37	4.31	285	−39	−69	−12
		Fusiform gyrus	R	37	4.26	68	42	−60	−15
		Inferior + middle occipital gyrus	R	18, 19	4.02	65	18	−87	−9
		Inferior occipital gyrus	L	19	3.65	21	−12	−51	−6
		Supplementary motor area	L	8	4.41	146	0	24	48
Control–RD	Visual	Inferior frontal gyrus	L	45	4.83	26	−54	30	15
RD–control	Visual	Supramarginal gyrus	R	40	3.54	19	57	−51	30

Note. H, hemisphere; L, left; R, right; B, bilateral; BA, Brodmann's area. Coordinates of activation peaks are given in MNI stereotaxic space. All effects were significant at $p < 0.001$ uncorrected with at least 15 voxels.

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ences were found in the direct comparison between groups in the auditory modality.

To test our main hypothesis, we compared between groups the correlation of association strength and activation in three critical regions of interest—left inferior frontal gyrus, left middle temporal gyrus, and left inferior parietal lobule. This approach can determine whether group differences in activation are related to a variable relevant to semantic processing. Table 4 shows increasing activation for lower and higher association word pairs for the control and RD groups in the auditory and visual modalities. For the control group and for both modalities, lower association was correlated with greater activation in left middle temporal gyrus and left inferior frontal gyrus, whereas higher association was correlated with greater activation in left inferior parietal lobule. However, for the RD group, lower association was correlated with greater activation in left inferior frontal gyrus for the auditory modality and left middle temporal gyrus for the visual modality. Fig. 2 shows these correlations for the RD group and how they overlap with the correlations for the control group.

A direct statistical comparison was calculated in order to determine whether there were significant differences in correlation between groups. Table 5 shows that controls had significantly stronger correlations between association strength and activation than RD. For both modalities, the control group showed a greater negative correlation between activation and association in left middle temporal gyrus and a greater positive correlation in left inferior parietal lobule. For the auditory modality, the control group showed a greater negative correlation of association and activation in left inferior frontal gyrus. Fig. 3 shows these significant group differences and how they overlap with the main effect of the correlation between activation and association in the control group.

4. Discussion

In this study reading disorder (RD) and control children made association judgments to word pairs that were related in meaning in the visual and auditory modalities. Both groups showed activation in left inferior frontal gyrus and left middle temporal gyrus, regions previously implicated in semantic processing (Booth et al., 2002). The main finding of our study is that RD children showed a weaker correlation between association strength and activation in left middle temporal gyrus, left inferior parietal lobule and left inferior frontal gyrus. This is broadly consistent with previous semantic studies that have shown abnormal activation by patients with dyslexia in these regions using the visual modality (Helenius et al., 1999; Shaywitz et al., 1998, 2002, 2003) and by patients with dyslexia in left inferior pari-

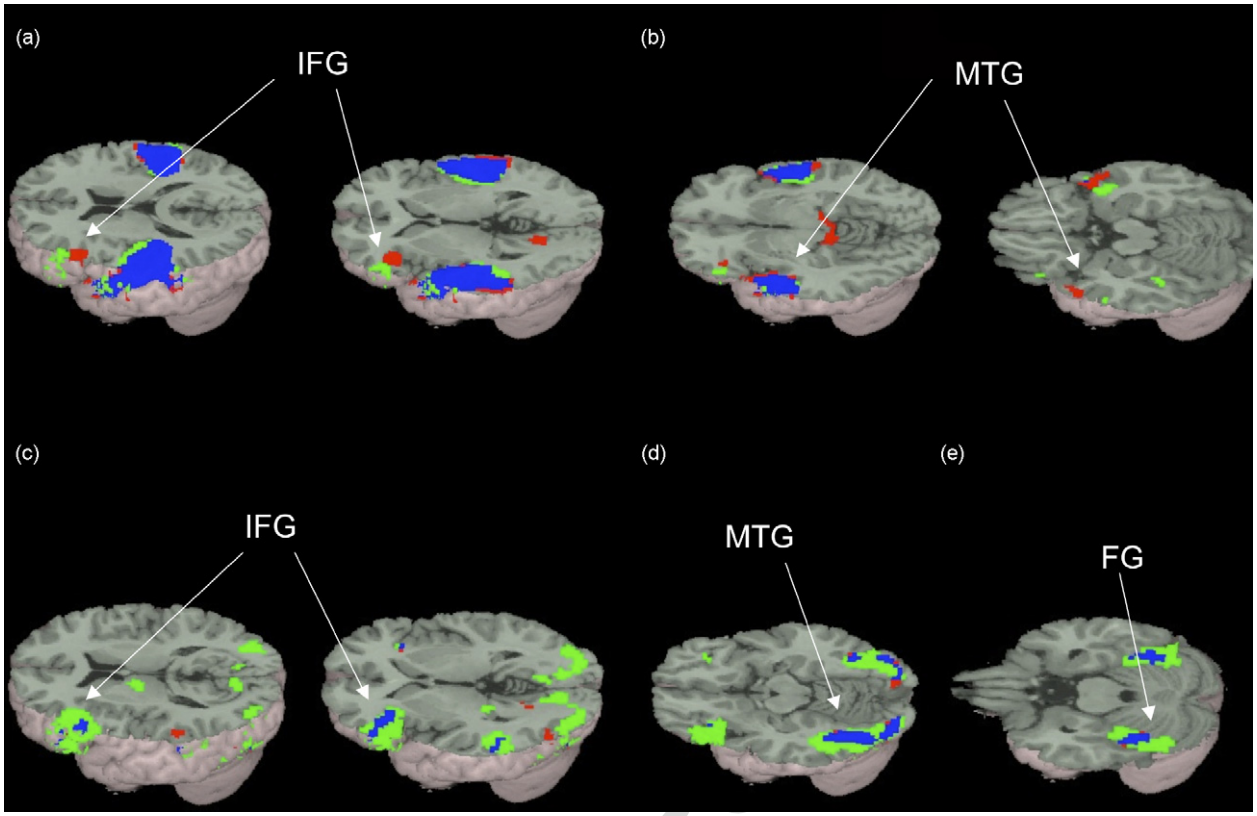

Fig. 1. Greater neural activation for the related word pairs compared to the null condition for the auditory modality (top row) and for the visual modality (bottom row). Control group is represented in green, RD group is represented in red, and the overlap between the control and RD group is represented in blue. For the auditory modality, both groups showed activation in left inferior frontal gyrus (a) and left middle temporal gyrus (b). For the visual modality, both groups showed activation in left inferior frontal gyrus (c), left middle temporal gyrus (d), and left fusiform gyrus. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

etal cortex using the auditory modality (Rumsey et al., 1994). Abnormal functional connectivity of left inferior parietal cortex with other brain regions has also been demonstrated in patients with dyslexia during semantic processing (Pugh et al., 2000).

Studies examining children with specific language impairment (SLI) using spoken language tasks have demonstrated abnormalities in brain regions similar to patients with dyslexia. Although no direct contrast between SLI and control groups was performed, one study reported less activation by SLI in left middle temporal gyrus and left inferior frontal gyrus when listening to pseudo-words and words (Hugdahl et al., 2004). Another study showed less activation by SLI in left inferior frontal gyrus and left parietal cortex during a verbal working memory task (Weismer et al., 2005). Evidence suggests that some reading disorders stem specifically from language disorders (Aram et al., 1984; Silva et al., 1987), and as many as 70% of children with language disorders develop reading disorders (Catts et al., 1999; Snowling et al., 2000). Although mean verbal IQ was in

Table 4
Increasing neural activation for lower and higher association word pairs for the control and RD groups in the auditory and visual modalities

Group modality	Associate	Regions	H	BA	*Z*-score	Voxels	*X*	*Y*	*Z*
Controls									
Auditory	Lower	Middle temporal gyrus	L	21	2.67	170	−42	−57	9
	Lower	Inferior frontal gyrus	L	45, 47	2.99	334	−36	27	12
	Higher	Inferior parietal lobule	L	40	3.46	155	−51	−54	51
Visual	Lower	Middle temporal gyrus	L	21	2.47	56	−48	3	−18
	Lower	Inferior frontal gyrus	L	45, 47	2.48	149	−48	12	15
	Higher	Inferior parietal lobule	L	40	2.95	103	−39	−27	42
RD									
Auditory	Lower	Inferior frontal gyrus	L	47	2.43	10	−27	27	−15
Visual	Lower	Middle temporal gyrus	L	21	2.38	14	−51	3	−15

Note. H, hemisphere; L, left; BA, Brodmann's area. Coordinates of activation peaks are given in MNI stereotaxic space. All effects were significant at $p < 0.05$ uncorrected.

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Table 5
Comparison between control and RD children on the correlation between association strength and neural activation in the visual and auditory modalities

Modality	Associate	Regions	H	BA	Z-score	Voxels	X	Y	Z
Auditory	Lower	Middle temporal gyrus	L	21	3.34*	175	−60	−52	8
	Lower	Inferior frontal gyrus	L	46	3.05#	29	−45	30	10
	Higher	Inferior parietal lobule	L	40	2.20△	58	−45	−50	42
Visual	Lower	Middle temporal gyrus	L	21	1.91†	10	−45	−12	−12
	Higher	Inferior parietal lobule	L	2.40	3.18*	84	−45	−24	45

Control children show a stronger correlation than RD children for all brain regions. *Note*. H, hemisphere; L, left; BA, Brodmann's area. Coordinates of activation peaks are given in MNI stereotaxic space. Symbols and their associated p values: #$p < 0.01$ FDR (false discovery rate) corrected; *$p < 0.05$ FDR corrected; △$p < 0.001$ uncorrected; †$p < 0.05$ uncorrected.

the normal range for the RD children in our study, their verbal ability was nearly one standard deviation below the control children, so it is likely that some of them had a history of language impairment. Our results for RD children are therefore consistent with studies of SLI children showing abnormalities in left inferior frontal gyrus, left middle temporal gyrus and left parietal cortex.

Our study showed that the correlation of lower association strength with greater activation in left middle temporal gyrus was significantly stronger in control than RD children for both the auditory and visual modalities. The finding of a strong correlation for the control children is consistent with our previous studies using larger samples of which the current sample is a subset (Chou et al., 2006a, b). Greater activation for weakly associated pairs may result from more extensive activation of the semantic system to identify distant relationships. Skill and learning related differences have also been reported in the middle temporal gyrus for semantic tasks. Higher accuracy among children on this same task is correlated with greater activation in the middle temporal gyrus for both the visual and auditory modalities (Blumenfeld et al., 2006). Learning studies with adults also show that semantic training on nonwords presented visually results in more activation in the middle temporal gyrus (Sandak et al., 2004). Altogether, these studies suggest that acquisition of semantic representations is associated with greater activation in middle temporal gyrus. Because behavioral studies have shown both a larger number of lexical entries and greater semantic connections between these entries in older, more-skilled compared to younger, less-skilled children (McGregor et al., 2002), the finding of a weaker correlation between association strength and activation for our RD children suggests that they have less structured and elaborated semantic representations.

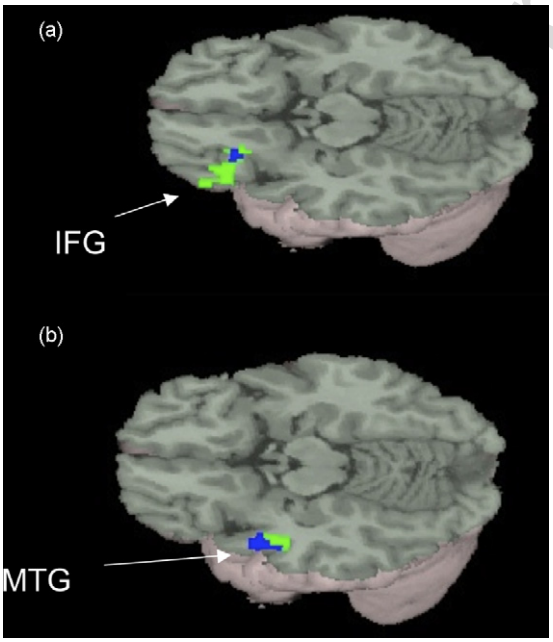

Fig. 2. Greater neural activation correlated with lower association in left inferior frontal gyrus for the auditory modality (a) and in left middle temporal gyrus for the visual modality (b). Control group is represented in green, and the overlap between the control and RD group is represented in blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

Our study showed that the correlation of higher association strength with greater activation in left inferior parietal lobule was significantly stronger in control than RD children for both the auditory and visual modalities. The finding of a strong correlation for the control children in this area is consistent with our previous studies using larger samples (Chou et al., 2006a, b). The inferior parietal cortex has been argued to be involved in feature integration and semantic categorization to form a coherent concept so that semantic relationships between words can be determined (Grossman et al., 2003), so the weaker correlation between association strength and activation in our RD children may reflect a deficit in this semantic integration process. The locus of activation in the inferior parietal cortex for our control children is more inferior to the locus of activation found for rhyming tasks that showed developmental increases (Bitan et al., 2006), suggesting that the inferior parietal lobule may have distinct areas for processing semantic versus phonological information. This specialization within the inferior parietal cortex may be similar to that shown for the anterior ventral inferior frontal gyrus in semantic processing and for the posterior dorsal inferior frontal gyrus in phonological processing (Poldrack et al., 1998).

Our study showed that the correlation of lower association strength with activation in left inferior frontal cortex was significantly stronger in control than RD children only for the auditory modality. However, when examining this correlation in the visual modality within each group, we found that the control children but not the RD children showed a significant correlation, suggesting that there is a difference between groups that did not

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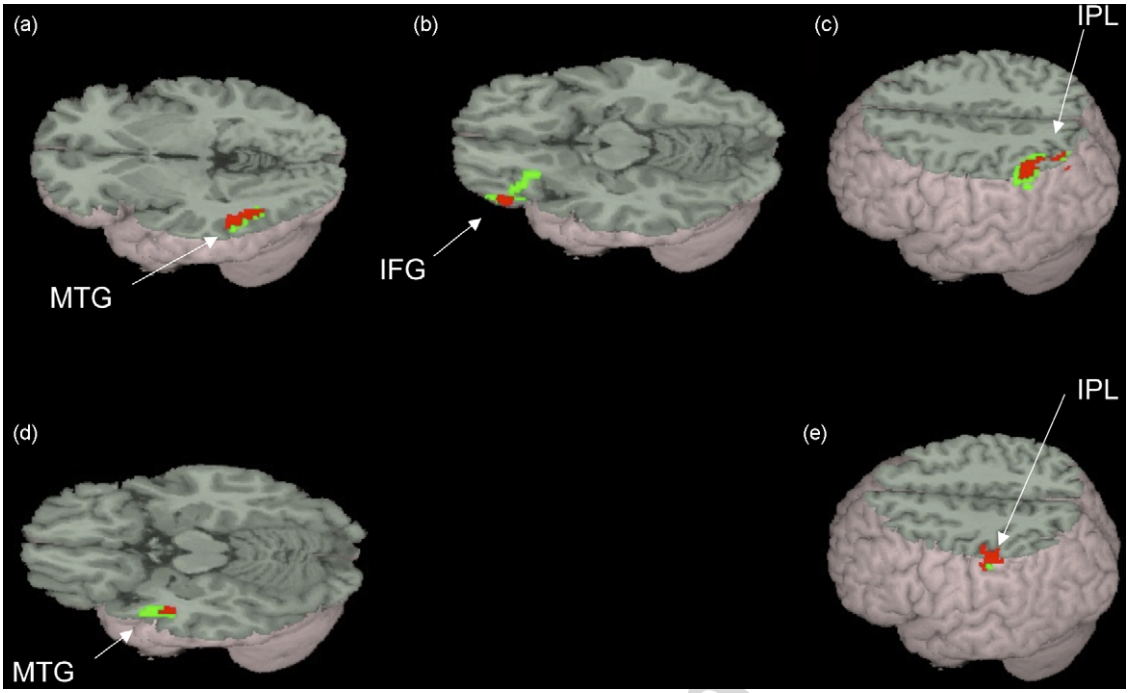

Fig. 3. Controls show a stronger correlation between association strength and neural activation than RD children. Green represents correlation for the control group and red represents that this correlation is stronger for the control compared to the RD group. For the auditory modality, greater activation correlated with lower association in left middle temporal gyrus (a) and left inferior frontal gyrus (b), and with higher association in left inferior parietal lobule (c). For the visual modality, greater activation correlated with lower association in left middle temporal gyrus (d) and with higher association in left inferior parietal lobule (e). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

reach a significant threshold. A large body of research in adults suggests that more activation in the inferior frontal cortex is associated with more effortful retrieval or greater selection demands (Gurd et al., 2002; Seger et al., 2000; Thompson-Schill et al., 1999; Whatmough et al., 2002). Overall, the weaker correlation for the RD children could result from their deficit in posterior semantic representations in left middle temporal gyrus. If these representations are poorly structured and less elaborated, the retrieval or selection demands imposed on the inferior frontal gyrus will not be systematically related to association strength. In a previous study with normal reading children, we showed that lower skill was correlated with greater activation in the inferior frontal gyrus during semantic tasks in the auditory and visual modalities (Blumenfeld et al., 2006). It was argued that because lower accuracy children have under-developed semantic representations in middle temporal gyrus, they may rely more on retrieval and search mechanisms. Although the current study did not find greater activation for the RD compared to the control children in left inferior frontal gyrus, we did find that association strength was not systematically associated with activation in this region, suggesting that it is not functioning normally.

In conclusion, this study demonstrated that children with reading disorders showed a weaker correlation between association strength and activation in three regions of a language processing network. This study goes beyond previous work by using a parametric manipulation of semantic difficulty to more directly target critical regions involved in semantic computation and by showing the semantic deficit is domain general cutting across the auditory and visual modalities. Altogether, these results suggest that RD children have deficits in the quality of their semantic representations, the integration of semantic features, and the access and manipulation of these processes.

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