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Developmental changes in the neural correlates of semantic processing

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Functional magnetic resonance imaging (fMRI) was used to explore the neural correlates of semantic judgments in the auditory modality in a group of 9- to 15-year-old children. Subjects were required to indicate if word pairs were related in meaning. Consistent with previous findings in adults, children showed activation in bilateral superior temporal gyri (BA 22) for recognizing spoken words as well as activations in bilateral inferior frontal gyri (BAs 47, 45) and left middle temporal gyrus (BA 21) for semantic processing. The neural substrates of semantic association and age differences were also investigated. Words with strong semantic association elicited significantly greater activation in the left inferior parietal lobule (BA 40), whereas words with weak semantic association elicited activation in left inferior frontal gyrus (BAs 47/45). Correlations with age were observed in the left middle temporal gyrus (BA 21) and the right inferior frontal gyrus (BA 47). The pattern of results for semantic association implies that the left inferior parietal lobule effectively integrates highly related semantic features and the left inferior frontal gyrus becomes more active for words that require a greater search for semantic associations. The developmental results suggest that older children recruit the right inferior frontal gyrus as they conduct a broader semantic search and the left middle temporal gyrus to provide more efficient access to semantic representations.

Introduction

Previous studies on spoken word comprehension in adults have shed light on the functional architecture of word recognition systems for speech. These studies have consistently found bilateral superior temporal activation (BA 22) (Petersen et al., 1989; Price et al., 1992, 1996), consistent with a role for converting sensory inputs into word forms for recognition (Booth et al., 2002, 2003a; Mesulam, 1998). Researchers also have identified brain regions for spoken words in bilateral inferior frontal gyri (BAs 47, 45) and left middle temporal gyrus (BA 21) (Booth et al., 2002; Chee et al., 1999; Howard et al., 1992; Shaywitz et al., 2001; Simos et al., 1999). These two regions are thought to be associated with higher-level language processing of meaning. While these studies have explored the functional architecture of word recognition systems in adults, we do not know whether these findings can be generalized to children.

The roles of these brain areas in semantic association have been further explored in adults by comparing activation to semantic judgments involving closely related pairs (e.g., king–queen) vs. 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 the left inferior frontal gyrus was interpreted as evidence for the difficulty of selecting appropriate semantic features since the distantly related pairs shared very 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. These studies include high vs. low requirement for selection among alternatives (Thompson-Schill et al., 1997; Thompson-Schill et al., 1999), weak vs. strong association strength (Wagner et al., 2001), naming low vs. high familiarity objects (Whatmough et al., 2002), generating novel vs. repeated base nouns (Seger et al., 2000), naming low vs. high agreement pictures (Kan and Thompson-Schill, 2004), deep vs. shallow processing of words (Fujii et al., 2002), and producing words for pre-specified semantic categories vs. over-learned letter sequences (Gurd et al., 2002). In the current study, we manipulated the difficulty of the semantic task by varying the 'free association strength' between the words in a pair (Nelson et al., 1998), expecting from the adult literature that there would be greater activation in inferior frontal gyrus for low (compared to high) association pairs due to increased retrieval or selection demands.

Although we expected children to show brain activation patterns similar to those reported for adults during semantic processing tasks, we also expected that there could be some age and skill differences because previous studies have reported skill

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and learning differences using semantic tasks. In terms of skill differences, increases in accuracy have been associated with greater activation in the occipito-temporal and temporo-parietal regions during category judgments to visually presented words (Shaywitz et al., 2002) and in the middle and inferior temporal gyri during association judgments to visual or auditory words (Blumenfeld et al., in press). Improvement in accuracy from semantic training has similarly resulted in greater activation in the left middle temporal gyrus, especially for high skill participants (Sandak et al., 2004), perhaps due both to a larger number of lexical entries and to greater connections between these entries (McGregor and Appel, 2002; McGregor et al., 2002). Based on these findings, we expected that there may be skill-related increases in the amount of activation in the lateral temporal region.

Studies have also shown developmental increases in activation in the inferior frontal gyrus during silent verb generation to auditorily presented concrete nouns (Holland et al., 2001), for verbal semantic fluency to auditorily presented categories (Gaillard et al., 2003), and for category judgments to visually presented words (Shaywitz et al., 2002). In an apparent contradiction, increased activation in the middle and inferior frontal gyri was found in children with lower skill during a semantic association judgment task (Blumenfeld et al., in press). This apparent contradiction may be resolved with the interpretation that the increase in activation in frontal regions for lower skill children may result from the increased demands on the feature search process, due to their underdeveloped posterior semantic representations in the middle temporal gyrus. Hence, skill and development may have different effects on the pattern and amplitude of neural activation (Schlaggar et al., 2002; Sowell et al., 2002; Turkeltaub et al., 2003). Lower skill children may show more activation in the inferior frontal gyrus because they have to work harder at the lexical tasks given limited neural processing resources, while older children may show more activation in the inferior frontal gyrus because their cortex has matured to a greater extent.

The first goal of this study was to identify lexical brain areas activated in 9- to 15-year-old children during a semantic judgment task in the auditory modality. The second goal was to examine how the strength of semantic association between two words in this task would influence brain activation (particularly in the inferior frontal gyrus). The third and final goal was to determine whether age or skill was correlated with activation in prefrontal and middle temporal regions.

Materials and methods

Participants

Twenty-six healthy children (mean age = 12.1, SD = 2.0 years; age range 9–15 years) participated in the fMRI study. Children 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, (6) no history of intelligence, reading, or oral-language deficits, and (7) no learning disability or Attention Deficit Hyperactivity Disorder (ADHD). 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. Standardized intelligence testing was then administered, using the Wechsler Abbreviated Scale of Intelligence (WASI) (The Psychological Corporation, 1999) with two verbal subtests (vocabulary, similarity) and two performance subtests (block design, matrix reasoning). Participants' mean standard scores (mean ± SD) were 118 ± 12 on WASI verbal scale and 107 ± 17 on WASI performance scale. The correlation between age and WASI verbal scale was not significant, $r(26) = -0.37$, $P > 0.05$.

Functional activation tasks

In the word judgment task, a black fixation cross appeared throughout the trial. At the same time, two auditory 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. The participant had to determine whether the word pair was related in meaning. 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. Forty-eight word pairs were semantically related according to their free association values (mean = 0.45, SD = 0.21, ranging from 0.85 to 0.12) (Nelson et al., 1998). These word pairs included both closely related pairs (e.g., *web-spider*) with higher association values and distantly related pairs (e.g., *guide-tour*) with lower association values. Twenty-four word pairs were semantically unrelated with zero association values (e.g., *bone-mountain*). The participants were instructed to quickly and accurately press the yes button to the related pairs and the no button to the unrelated pairs.

There were three kinds of control tasks. The simple perceptual control had 24 pairs of single pure tones, ranging from 325 to 875 Hz. The tones were 600 ms in duration and contained a 50 ms linear fade in and a 50 ms linear fade out. The complex perceptual control had 24 pairs of three-tone stimuli, where all the component tones were within the aforementioned frequency range. Each tone was 200 ms with a 50 ms fade in and out. For both the simple and complex perceptual controls, participants determined whether the stimuli were identical or not by pressing a yes or no button. The tones were equal in maximum amplitude to the words and the procedures for presenting stimuli were the same as the word judgment task. The third control task involved 30 baseline events. The participant was instructed to press a button when a black fixation-cross at the center of the visual field turned red. We chose to compare the word pairs to this baseline event, because this event showed little developmental difference with very high accuracy and the least variability (accuracy [mean ± SD] for the baseline event, simple perceptual, and complex perceptual was 97 ± 4%, 91 ± 12%, and 73 ± 14%, respectively). In addition, the baseline event had exactly the same visual stimuli and response characteristics as the lexical task and the perceptual controls. For all conditions, subjects were asked to look at the black fixation cross and to make a button press when the black cross turned red. The contrast of the simple perceptual and the baseline was used as an exclusive mask to exclude nonlexical auditory processing.

Stimulus characteristics

Several lexical variables were controlled across the related and unrelated conditions and for the high and low association pairs. First, no homophones were included in the experimental lists. Second, the conditions contained about the same number of nouns (55–65%), verbs (25–35%), and adjectives (10–20%) based on their most frequent usage in the Oxford English Dictionary. Third, none of the words were more than two syllables in length. Fourth, words were matched for written word frequency for adults and children (The Educator's Word Frequency Guide, 1996) and for adult word frequency for written and spoken language (Baayen et al., 1995) (see Table 1). A 2 word (first, second) by 2 condition (related, unrelated) ANOVA showed no main effects or interactions with the different frequency measures. The correlations of word frequency measures with association strength were not significant indicating that any association effects could not be due to frequency differences. Fifth, words were matched for imageability. Although not every word had an imageability rating according to the MRC psycholinguistic database (University of Western Australia), a 2 word (first, second) by 2 condition (related, unrelated) ANOVA showed no main effects or interactions with the imageability rating. The correlations of word imageability rating with association strength were not significant for the first or second word.

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, 1997). Different stimuli were used in the practice and fMRI sessions. Within a week of the practice session, participants were administered the fMRI session.

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; TR = 2000 ms. The first functional run had 203 image 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 ms, 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.

Image analysis

Data analysis was performed using SPM2 (Statistical Parametric Mapping). 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 3.0 mm of movement in any plane and the mean amount of movement in the maximum plane (z translation) was 1.0 mm. Co-registered images were normalized to the MNI average template (12 linear affine parameters for brain size and position, 8 nonlinear iterations and 2 × 2 × 2 nonlinear 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 were entered into a general linear model using an event-related analysis procedure (Josephs and Henson, 1999). 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). Four general types of analyses were done with the use of the exclusive mask of the simple perceptual vs. the baseline. For all analyses, the dependent variable was peak signal strength across all event-related responses for a particular stimulus type. This is appropriate for event-related studies to examine developmental effects (Richter and Richter, 2003). First, we compared the related and unrelated pairs separately to the baseline condition as well as the related to the unrelated pairs. Second, we examined the correlation of the continuous variable of association strength (Nelson et al., 1998) for the related pairs with inclusive masks of

Table 1

Stimulus characteristics for first (1st) words and second (2nd) words in the related and unrelated conditions for written word frequency for adults and children (Educator's Word Frequency Guide, 1996) and for adult word frequency for written and spoken language (Baayen et al., 1995)

	Written adults		Written children		Written adults		Spoken adults	
	Related	Unrelated	Related	Unrelated	Related	Unrelated	Related	Unrelated
1st word frequency	14 (39)	9 (14)	17 (33)	8 (9)	58 (126)	43 (56)	53 (112)	28 (49)
2nd word frequency	17 (37)	9 (13)	17 (32)	7 (10)	57 (99)	39 (42)	37 (73)	41 (62)
1st word correlation	−0.11		−0.01		−0.04		−0.03	
2nd word correlation	−0.01		0.11		0.09		0.04	

The correlations of word frequency with association strength in the related condition are also presented.

Note. Standard deviations are in parentheses.

related–null and related–unrelated. This allowed us to examine association-related increases or decreases in activation. Third, we used multiple regression to compute partial correlations for the continuous variable of age in months with signal intensity in the related and unrelated pairs. We used inclusive masks of related–null and related–unrelated for the related pairs and an inclusive mask of unrelated–null for the unrelated pairs. After either accuracy or reaction time was entered into the equation, we examined whether remaining variance was explained by age. This allowed us to examine age-related increases or decreases in activation that were independent of skill differences. Fourth, we used multiple regression to compute partial correlations for the continuous variable of accuracy or reaction time on the semantic judgment task with signal intensity in the related and unrelated pairs. We used inclusive masks of related–null and related–unrelated for the related pairs and an inclusive mask of unrelated–null for the unrelated pairs. After age was entered into the equation, we examined whether the remaining variance was explained by accuracy or reaction time. This allowed us to examine skill-related increases or decreases in activation that were independent of age. All reported areas of activation were significant using $P < 0.05$ corrected for false discovery rates (Genovese et al., 2002).

Results

Behavioral performance

Statistical analyses revealed no main effects or interactions involving accuracy or reaction times on the practice vs. fMRI sessions, indicating that the environment of the scanner did not adversely affect the behavioral performance of the children. Furthermore, the children could effectively perform the task in the fMRI scanner, as all mean accuracy levels were above 90% and no individual participant scored below 70% in any condition. The accuracies (mean ± SD) for the related, unrelated, and baseline events were 94 ± 5%, 91 ± 8%, and 97 ± 4%, respectively. A one-way ANOVA on accuracy was significant, $F(2,50) = 7.36$, $P < 0.01$, due to the fact that the baseline event was more accurate than either the related event, $t(25) = 2.85$, $P < 0.01$, or the unrelated event, $t(25) = 3.42$, $P < 0.01$. The related and the unrelated pairs were not significantly different. The correlations of age to accuracy were not significant for the related, unrelated, and baseline events [$r(26) = 0.31$, $P > 0.05$; $r(26) = 0.33$, $P > 0.05$; and $r(26) = 0.21$, $P > 0.05$, respectively]. The reaction times (mean ± SD) for the related, unrelated, and baseline events were 1264 ± 280 ms, 1445 ± 303 ms, and 1388 ± 320 ms, respectively. A one-way ANOVA on reaction times was significant, $F(2,50) = 8.53$, $P < 0.001$, due to the fact that the related events were faster than either the unrelated events, $t(25) = 6.11$, $P < 0.001$ or the baseline events, $t(25) = 2.75$, $P < 0.05$. The reaction times for the unrelated and baseline events were not significantly different. The correlations of age to reaction times were not significant for the related, unrelated, and baseline events [$r(26) = -0.17$, $P > 0.05$; $r(26) = -0.12$, $P > 0.05$; and $r(26) = -0.33$, $P > 0.05$, respectively]. The correlation between accuracy and association strength was positive and significant, $r(48) = 0.32$, $P < 0.05$; and the correlation between reaction times and association strength was negative and significant, $r(48) = -0.36$, $P < 0.05$.

Brain activation patterns

Table 2 and Fig. 1a show greater activation for the related and unrelated pairs compared to the baseline condition. Both related and unrelated pairs produced greater activation in bilateral anterior

Table 2

Greater activation for the related or unrelated conditions compared to the baseline condition and greater activation for the related compared to the unrelated condition

Condition	Regions	H	BA	z test	Voxels	x	y	z
Related–null	Superior temporal/middle temporal gyri/temporal operculum	L	22/21	6.73	480	−54	−38	7
	Anterior superior temporal/anterior middle temporal gyri/temporal operculum	R	22/21	5.33	149	54	−12	−7
	Inferior frontal gyrus	L	47/45	5.47	824	−36	26	−1
		R	47	4.43	60	36	29	−4
	Medial frontal gyrus	L	8	4.40	50	−6	20	46
	Posterior cingulate gyrus	R	30	3.71	81	22	−64	9
		L	30	3.48	16	−22	−68	6
Unrelated–null	Superior temporal/middle temporal/inferior frontal gyri/temporal operculum	L	22/21/47/45	6.59	1415	−53	−37	6
	Anterior superior temporal/anterior middle temporal gyri/temporal operculum	R	22/21	5.12	193	56	−12	−7
	Inferior frontal gyrus	R	47	5.00	188	33	20	−1
	Posterior cingulate gyrus	R	30	4.92	774	22	−64	11
	Anterior cingulate/medial frontal gyrus	L	32/24/8	5.03	249	−5	20	40
	Parahippocampal gyrus	L	36	3.80	17	−28	−34	−13
Related–unrelated	Superior parietal/Inferior parietal lobule	L	7/40	6.23	568	−36	−62	50
	Superior parietal/inferior parietal lobule	R	7/40	5.03	303	36	−62	45
	Precuneus	L	7	4.52	613	−6	−59	39
	Superior frontal gyrus	L	8	4.45	303	−30	17	49
	Superior frontal gyrus	R	8	3.95	48	30	23	49

Note. Coordinates of activation peaks are given in the Talairach stereotactic space. H: left (L), right (R). BA: Brodmann's area of activation. The superior temporal and middle temporal gyrus in the left hemisphere include both anterior and posterior portions for the related and the unrelated condition. All effects were significant at $P < 0.05$ corrected for false discovery rate (FDR).

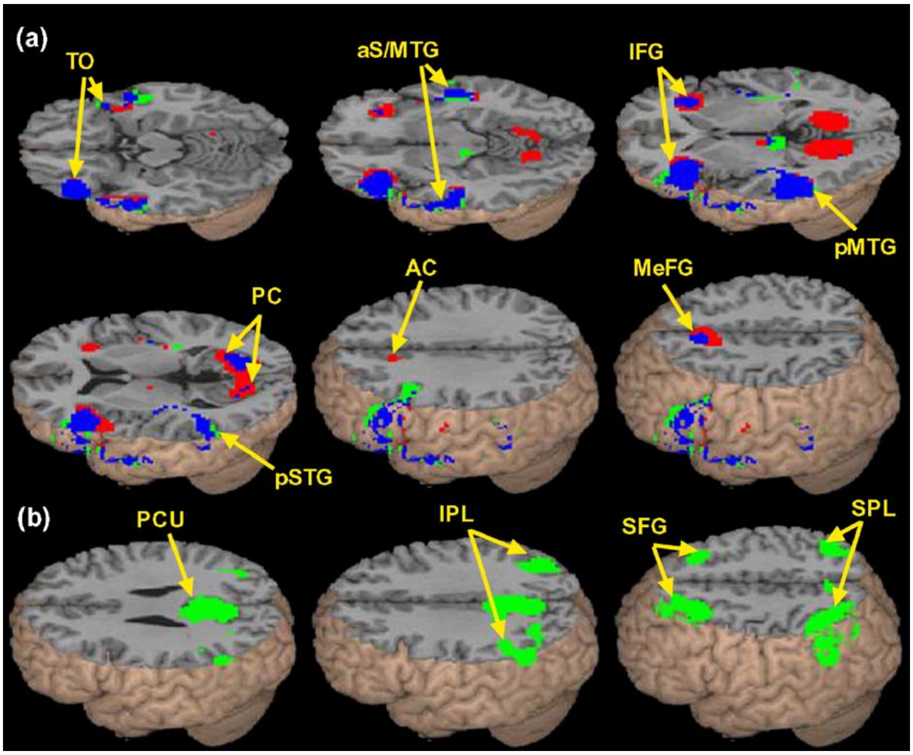

Fig. 1. (a) Brain activations for the related vs. baseline (green) and for the unrelated vs. baseline (red). The overlap between the two contrasts is represented in blue. Both related and unrelated pairs activated bilateral anterior superior temporal gyri (aSTG), left posterior superior temporal gyrus (pSTG), bilateral anterior middle temporal gyri (aMTG), left posterior middle temporal gyrus (pMTG), bilateral temporal opercula (TO), bilateral inferior frontal gyri (IFG), left medial frontal gyrus (MeFG), and bilateral posterior cingulate gyri (PC). Unrelated pairs produced additional activation in left anterior cingulate gyrus (AC). (b) Brain activations for the related vs. unrelated pairs in bilateral superior parietal lobules (SPL), bilateral inferior parietal lobules (IPL), left precuneus (PCU), and bilateral superior frontal gyri (SFG).

and left posterior superior temporal gyri (BA 22), bilateral anterior and left posterior middle temporal gyri (BA 21), bilateral inferior frontal gyri (BA 47, 45), bilateral temporal opercula (BA 21), left medial frontal gyrus (BA 8), and bilateral posterior cingulate gyri (BA 30). The unrelated pairs produced additional activation in left anterior cingulate (BA 32, 24) and left parahippocampal gyri (BA 36). Table 2 and Fig. 1b show greater activation for the contrast of the related vs. unrelated pairs in bilateral superior parietal lobules (BA 7), bilateral inferior parietal lobules (BA 40), left precuneus (BA 7), and bilateral superior frontal gyri (BA 8).

The correlations between signal intensity and the strength of semantic association for related word pairs with a mask of related–null and related–unrelated are presented in Table 3. Greater activation was correlated with higher association values in left inferior parietal lobule (BA 40) for the related–unrelated mask (Fig. 2a) but not for the related–null mask. Greater activation was correlated with lower association values in the left inferior frontal gyrus (BA 47, 45) for the related–null mask (Fig. 2b) but not for the related–unrelated mask.

Table 3
Correlation of activation with semantic association for the related word pairs using a related–null or related–unrelated mask

	Regions	H	BA	z test	Voxels	x	y	z
Higher association								
Related–unrelated	Inferior parietal lobule	L	40	3.37	15	−51	−50	47
Lower association								
Related–null	Inferior frontal gyrus	L	47/45	3.42	17	−30	21	−3

Note. See Table 2 note.

The correlations between signal intensity and age in months, partialled for accuracy on the semantic task, are shown in Table 4 and Fig. 2c. Using the related–null mask, increasing age was correlated with greater activation for the related pairs in left superior/middle temporal gyri (BA 22, 21), right inferior frontal gyrus (BA 47), and left medial frontal gyrus (BA 8). The correlation of increasing age and signal intensity did not exceed our threshold for the related pairs using the related–unrelated mask or for the unrelated pairs using the unrelated–null mask. No significant correlations were found between signal intensity and decreasing age for any comparison. The same clusters with slightly lower significance levels and smaller sizes were obtained when partialling age for reaction time.

The correlations between signal intensity and accuracy or reaction time on the semantic task, partialled for age in months, did not reach significance. The lack of robust correlations with accuracy could have resulted from near-ceiling level performance that limited behavioral variability. The lack of correlations with reaction time could have resulted from the computer-paced format of the semantic task. In order to further explore whether skill is related to activation patterns, we examined the correlation of signal intensity with verbal raw scores of the WASI (The Psychological

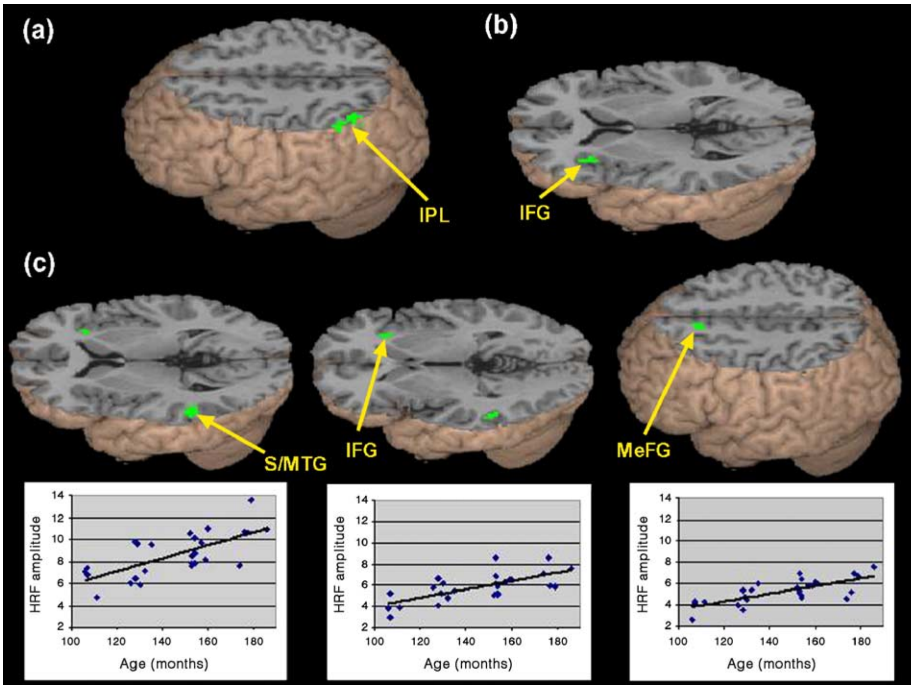

Fig. 2. (a) Increasing activation with stronger semantic association in left inferior parietal lobule (IPL) for the related pairs using a related–unrelated mask; (b) increasing activation with weaker semantic association in left inferior frontal gyrus (IFG) for the related pairs using a related–null mask; (c) increasing activation with age in left superior/middle temporal gyrus (S/MTG), right inferior frontal gyrus (IFG), and left medial frontal gyrus (MeFG) for the related pairs using a related–null mask. The scatterplots of these correlations of age with the HRF amplitude are presented at the bottom of the brain maps.

Corporation, 1999). No significant correlation was found for any comparison when partialling out the effect of age.

Discussion

The neural correlates of spoken word comprehension were examined with a task requiring semantic judgments as to whether word pairs were related in meaning. The children showed activations in bilateral superior temporal gyri, bilateral inferior frontal gyri, and left posterior middle temporal gyrus. Our finding that both related and unrelated word pairs activated bilateral superior temporal gyrus (BA 22) in children is consistent with previous adult studies suggesting that spoken word forms are phonologically processed in the auditory association cortex (Booth et al., 2002, 2003a; Mesulam, 1998). Moreover, previous studies implicate the inferior frontal gyri and middle temporal gyrus with semantic processes (Booth et al., 2002; Chee et al., 1999; Howard et al., 1992; Shaywitz et al., 2001; Simos et al., 1999). Our finding that both the related and the unrelated word pairs activated left middle temporal gyrus (BA 21) and bilateral inferior frontal gyri (BA 47, 45) during auditory semantic judgments in children is consistent with these findings in adults. Some studies have suggested that the middle temporal gyrus is involved in the representation of verbal semantic information (Blumenfeld et al., in press; Booth et al., 2002; Martin, 2001), whereas the inferior frontal gyrus may be involved in on-line semantic monitoring such as a search for overlapping semantic features (Fletcher et al., 2000; Kapur et al., 1996).

Table 4
Correlation of activation with age for the related word pairs using a related–null mask

Increase with age	Regions	H	BA	*z* test	Voxels	*x*	*y*	*z*
Related–null	Superior/middle temporal gyrus	L	22/21	3.69	15	−53	−41	3
	Inferior frontal gyrus	R	47	3.61	10	35	20	−1
	Medial frontal gyrus	L	8	4.04	10	−9	23	43

Note. See Table 2 note.

Although the related and unrelated pairs mainly showed overlap in patterns of activation, the unrelated word pairs additionally activated anterior cingulate cortex (BA 32). This region has been associated with attention, response selection, executive control, and online monitoring (Botvinick et al., 1999; Carter et al., 1998, 1999). In addition, this region has been implicated in attentional modulation of semantic processing (Chan et al., 2004; Mummery et al., 1999; Peelle et al., 2004). The unrelated pairs may have produced greater activation in the anterior cingulate because the search for overlapping semantic features was extensive but unsuccessful within the assigned time. This increased processing load may place greater demands on available resources during semantic judgments. This interpretation is supported by the significantly longer reaction times for the unrelated compared to the related pairs.

Stronger semantic association was correlated with greater activation in left inferior parietal lobule (BA 40). This region is located more anterior and inferior than the parietal cortex regions implicated in phonological or orthographic processing as reported by previous studies (Bitan et al., 2005; Booth et al., 2004). Left inferior parietal lobule activation has 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 vs. abstract word judgments (Chee et al., 1999). Some studies have interpreted the 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; Smith, 1995). 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 allow for more integration because either 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 inferior parietal lobule activation with increasing association strength.

Weaker semantic association was correlated with greater activation in left inferior frontal gyrus (BA 47, 45). Previous studies suggest that the left inferior frontal gyrus is involved in effortful semantic processing, particularly when there is increased demands on the process of selecting relevant semantic knowledge or when comparing words along semantic features (Blumenfeld et al., in press; Fletcher et al., 1998; Thompson-Schill et al., 1997; Thompson-Schill et al., 1999; Whatmough et al., 2002). The inferior frontal gyrus has also been implicated in conditions with increased retrieval demands (Kikyo et al., 2002; Kirchhoff et al., 2000; Seger et al., 2000; Wagner et al., 2001). Of particular relevance to the current study, semantic judgments in adults to lower association pairs produce more activation in the inferior frontal gyrus as compared to higher association pairs (Fletcher et al., 2000). Greater activation for lower association pairs could result from increased demands on the retrieval or selection of appropriate semantic features. Our finding that decreasing association strength was correlated with increasing activation in left inferior frontal gyrus is consistent with the adult literature.

Increasing age was correlated with greater activation in left superior/middle temporal gyrus (BA 22, 21). The middle temporal gyrus has been implicated in semantic processing (Booth et al., 2002) and studies have also shown that increasing skill and learning on semantic tasks are associated with greater activation in the temporal region (Blumenfeld et al., in press; Sandak et al., 2004; Shaywitz et al., 2002). Greater activation may be associated with increasing elaboration of semantic representations, i.e., a greater number of semantic representations with more interconnections between these representations. Behavioral research shows that as vocabulary knowledge increases, the child's semantic system is gradually elaborated due to the greater number of conceptual links (McGregor and Appel, 2002; McGregor et al., 2002). Although we did not find a correlation of activation in the middle temporal gyrus with behavioral performance, we did find that increasing age was associated with greater activation in this region. Older children may show greater activation because their semantic representations are more elaborated. The lack of a correlation with behavioral performance may have resulted from the fact that the semantic task was quite easy, as evidenced by the high accuracy levels.

In addition to the left middle temporal gyrus, increasing age was correlated with greater activation in right inferior frontal gyrus (BA 47). Several studies have shown developmental increases in activation in the inferior frontal gyrus during semantic tasks (Gaillard et al., 2003; Holland et al., 2001; Shaywitz et al., 2002), but in the left hemisphere. Our findings of greater right hemisphere activation with age is consistent with the findings of another developmental study that showed developmental increases in the right inferior frontal gyrus during association judgments (Booth et al., 2003b). The discrepant results for the inferior frontal gyrus may be accounted for by task differences between studies. The studies that found greater activation in the left inferior frontal gyrus used verbal fluency or categorization judgments, whereas studies that have used association judgments found greater activation in the right inferior frontal gyrus. It may be that association judgments require a greater degree of feature search and selection, and that older children engage in this process more thoroughly because they have a greater number of conceptual links (McGregor and Appel, 2002; McGregor et al., 2002). Alternatively, some studies argue that the right hemisphere has larger semantic fields that allow for the more effective generation of distant semantic associations (Beeman et al., 2000; Bowen and Beeman, 1998). Thus, the greater recruitment of the right hemisphere in older children during the association judgment tasks may reflect this hemispheric specialization.

Finally, greater activation for semantically related pairs was associated with increasing age in medial frontal gyrus (BA 8). This same region also showed reliable activation in the related pairs but not the unrelated pairs when compared to baseline. Previous adult studies (Demonet et al., 1992) have shown greater activation in the medial frontal gyrus during category judgments to auditory words in which subjects had to keep two semantic criteria in working memory to perform category judgments, a list of animals categorized by size (e.g., smaller than a chicken) and adjectives categorized by "positive" affect (e.g., happy vs. horrible). This region was also activated during semantic plausibility judgments to auditory (Caplan et al., 1999) and visually presented sentences (Stromswold et al., 1996), in a task requiring subjects to maintain words from sentences in working memory. In our study, the sequential presentation of two words required at least the first word to be kept in working memory. The increasing activation with age in the medial frontal gyrus may correspond to greater engagement of working memory for older children during association judgments.

In conclusion, the children in our study showed activation in similar brain regions to those reported in previous studies of adults, including the middle temporal and inferior frontal gyri. We suggest that the middle temporal gyrus is involved in representing verbal semantic information and the inferior frontal gyrus is involved in the selection of these representations. We also showed that greater activation in the left inferior frontal gyrus was associated with decreasing association strength between words, suggesting that distantly related pairs required more semantic feature selection. In contrast, greater activation in the left inferior parietal lobule was correlated with increasing association strength between words, suggesting that closely related pairs allow for a more complete semantic integration. Although children showed generally similar patterns of activation to previous reports on adults, there were some interesting developmental differences. Increasing age was associated with greater activation in the left middle temporal gyrus and the right inferior frontal gyrus, findings that respectively suggest that older children have a more elaborated semantic representational system and a more thorough search of distant associations.

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