

Differential prefrontal–temporal neural correlates of semantic processing in children

Henrike K. Blumenfeld, James R. Booth^{*}, Douglas D. Burman

Department of Communication Sciences and Disorders, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, USA

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Abstract

This study used functional magnetic resonance imaging (fMRI) to examine brain–behavior correlations in a group of 16 children (9- to 12-year-olds). Activation was measured during a semantic judgment task presented in either the visual or auditory modality that required the individual to determine whether a final word was related in meaning to one of two previous words (e.g., *found–tank–lost*). The main finding was that higher performers (i.e., accuracy) were associated with more activation in posterior representational systems including the inferior and middle temporal gyri, whereas lower performers were associated with more activation in anterior regions including the inferior and middle frontal gyri. This pattern of results was interpreted as reflecting an elaborated semantic representational system in temporal areas for the high accuracy performers that allowed them to efficiently and accurately make meaning based judgments. The low accuracy performers may have an inaccurate or weakly interconnected semantic system that results in greater use of frontal areas in a feature selection process.

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1. Introduction

Left inferior frontal gyrus (IFG) and middle (MTG) and inferior (ITG) temporal gyri have repeatedly been implicated in semantic processing (Binder et al., 1997; Demonet et al., 1992; Poldrack et al., 1999; Price, Moore, Humphreys, & Wise, 1997; Wagner, Desmond, Demb, Glover, & Gabrieli, 1997). Further, functional connectivity between IFG (BA 47/11) and MTG (BAs 37, 20, 21) has been established for semantic processing (Bokde, Tagamets, Friedman, & Horwitz, 2001), suggesting that these areas act as a semantic network (for review, see Bookheimer, 2002; Price, 2000). Within this network, temporal cortex has often been associated with the storage of semantic representations (for review, see Martin, 2001), and frontal cortex has been implicated

in on-line manipulation of these representations (Kapur et al., 1994, 1996). The goal of the current study is to establish correlations between behavioral performance and activation within this semantic network. Specifically, we hypothesize that better performance on an on-line semantic association judgment task correlates with more activation of elaborated semantic representations in temporal cortex, and with less activation (i.e., more efficient semantic manipulation processes) in prefrontal cortex. Inferior frontal gyrus, specifically BAs 47, 44, and 45, has been implicated in various tasks involving on-line manipulation of semantic representations. In general, these are tasks where the participant must focus on features of the stimulus to make a decision. These tasks include verb-generation (Petersen, Fox, Posner, Mintum, & Raichle, 1988; Petersen, Fox, Posner, Mintum, & Raichle, 1989; Seger, Desmond, Glover, & Gabrieli, 2000), category-decision (Petersen et al., 1988, 1989), various semantic judgment tasks (Binder

^{*} Corresponding author. Fax: +1 847 491 4975.
E-mail address: j-booth@northwestern.edu (J.R. Booth).

et al., 1997; Devlin, Matthews, & Rusworth, 2003; Poldrack et al., 1999; Price et al., 1997), semantic comparison tasks (Chee et al., 2000; Pugh et al., 1996; Ricci et al., 1999), semantic encoding (Kapur et al., 1994, 1996; Petersen & Fiez, 1993; Shallice et al., 1994; Wagner et al., 1997, 1998), and semantic priming (Demb et al., 1995; Seger et al., 2000; Wagner et al., 1997). Thus, there is extensive evidence that inferior frontal gyrus is implicated in semantic manipulations, as well as playing a role during semantic encoding and retrieval.

Similar to tasks that triggered activation in inferior frontal gyrus, middle and inferior temporal gyri have been implicated in studies of both semantic decision and word generation. Middle and inferior temporal gyri have been implicated in semantic judgment tasks (Binder et al., 1997; Pugh et al., 1996; Wise et al., 1991), semantic category monitoring (Demonet et al., 1992), semantic matching (Chee et al., 2000), and word-generation given a category (Gourovitch et al., 2000). Further, MTG by itself has been implicated on an animacy-decision task (Price et al., 1997), and ITG by itself has been implicated on semantic matching tasks (Ricci et al., 1999) and successful semantic access (Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996; Wagner et al., 1998). Moreover, semantic categories distinguished by specific attributes (e.g., animals [+ animate], tools [– animate]) have been localized to specific regions within temporal cortex (e.g., see Farah & McClelland, 1991; Perani, Schnur, Tettamanti, Gorno-Tempini, & Cappa, 1999), suggesting that semantic content is represented here.

1.1. Parametric designs

Parametric studies have significantly contributed to our understanding of brain–behavior relationships, and especially frontal lobe involvement in semantic tasks. Various studies have correlated behavioral variables with neural activation to find reliable changes in the activity within the semantic network. These studies suggest that activation in left IFG is associated with increased task difficulty, selection/retrieval demands, and lower performance, while activation in temporal cortex is correlated with higher performance.

1.1.1. Within-subjects brain–behavior correlations

A sizable amount of research has varied parameters within-subject in order to draw brain–behavior correlations. Here, manipulations of task difficulty are of particular interest. Although task difficulty has been operationalized in various ways, increased activation in IFG has been associated with increased difficulty across these definitions. In a PET study in which high- and low-familiarity objects were overtly named, increased activation across inferior (BA 45/47) and middle (BA 10) frontal gyri was identified in the low-familiarity

(i.e., high difficulty) condition (Whatmough, Chertkow, Murtha, & Hanratty, 2002). Thompson-Schill, D'Esposito, Aguirre, and Farah (1997) and Thompson-Schill, D'Esposito, and Kan (1999) used word-generation paradigms given a base word, where the amount of inhibitory effort (selection demands) needed to generate an appropriate item was varied. High selection demands were associated with increased activation in BAs 44, 45. In a similar study where participants were asked to generate 'usual' and 'unusual' verbs given novel and repeated base nouns, Seger et al. (2000) found increased activation in BAs 44, 45 associated with increased retrieval demands (novel vs. repeated base nouns), and activation in bilateral middle frontal gyri (BA 10) associated with increased selection demands (unusual vs. usual verbs). Further, it has been shown that identification of weak (i.e., more difficult) vs. strong associations (Wagner, Paré-Blagoev, Clark, & Poldrack, 2001), and encoding of previously otherwise grouped word pairs (i.e., inhibiting previous associations) vs. novel word pairs (Fletcher, Shallice, & Dolan, 2000) activates anterior IFG (BAs 45/47).

Other semantic tasks that may require increased cognitive support have yielded similar results. Activity in BAs 45/47 has been correlated with subsequent retrieval success after semantic encoding (Kirchhoff, Wagner, Maril, & Stern, 2000). Moreover, partial word retrieval has been associated with activation in IFG, suggesting that this region may be involved when word retrieval is most difficult. Kikyo, Ohki, and Miyashita (2002) correlated the degree of participants' reported 'feeling of knowing' after failed word-retrieval with activation during attempted retrieval, identifying increased activation in bilateral BA 47. The authors suggested that these areas might be involved in accessing and screening available information about the target. Further, the degree to which participants can semantically structure learned word-lists has also been correlated with increased activity in inferior (BA 45) and middle (BA 10) frontal gyri (Fletcher, Shallice, & Dolan, 1998a; Savage et al., 2001). In summary, converging evidence suggests that increased task difficulty correlates with activity in inferior and middle frontal gyri.

1.1.2. Between-subjects brain–behavior correlations

Lower performance on semantic tasks across individuals has been associated with higher activation in IFG. Schlaggar et al. (2002) correlated accuracy and reaction time (RT) measures to the signal during word-generation from a visually presented base word, and found that activation in left BAs 45/47 was performance-related, showing greater activation in low-performance children relative to high-performance children and performance-matched adults. Similarly, in a bilingual fMRI study of a semantic association judgment task, Chee, Hon, Lee, and Soon (2001) found that a smaller signal change in

left prefrontal cortex (BA 44, 45) was associated with higher language proficiency and shorter RTs, while a larger signal change was associated with lower language proficiency and longer RTs (also see Hernandez, Martinez, & Kohnert, 2000). Further, lower language proficiency was also associated with right prefrontal activation. The authors suggest that neurons in prefrontal cortex are less ‘well-tuned’ to unfamiliar representational patterns, resulting in more effortful semantic retrieval and manipulation in lower performance individuals (i.e., individuals with less experience).

Further, limited findings suggest a possible correlation between higher performance and activation in temporal regions. Shaywitz et al. (2002) performed correlations across a large continuum of dyslexic to normal performing children on a visual word categorization task. High performers correlated with activation in left occipitotemporal and parietotemporal regions. Low performers, on the other hand, correlated with right occipitotemporal cortex, suggesting the usage of an ‘ancillary system.’ It is especially worth noting that lower performers correlated with less temporal activation, suggesting that higher performers are associated with more elaborated posterior semantic representations.

1.2. Current study

The primary goal of this study was to examine brain–behavior correlations in *both*, frontal and temporal cortices during semantic associative processing. We aimed to (1) expand the limited literature on between-subject brain–behavior correlations, and to (2) specifically build on Shaywitz et al.’s (2002) findings suggesting a possible brain–performance correlation for temporal cortex. We targeted a population (9- to 12-year-old children) that features large variation in performance, which may be particularly suited to revealing brain–performance correlations. Further, the semantic task used by Booth et al. (2002) was employed, where participants were shown, or listened to, three words and had to decide whether the third word was semantically associated to either of the previous two. This task requires a specific feature search to establish a dimension of similarity between words, as well as deep semantic processing of presented words. We reasoned that, based on previous findings, the processing demands of this task were likely to implicate both frontal and temporal cortices.

We hypothesized that if IFG and MFG indeed provide additional cognitive guidance in semantic manipulation tasks, then children who fail more frequently in identifying semantic associations would likely recruit more of these guidance mechanisms and show more activation in IFG/MFG relative to children who identify semantic associations easily. We also expected that children who identified associations easily would have more elaborated semantic representations in MTG and ITG.

2. Methods

2.1. Participants

Sixteen children (M age = 10.7 ($SD = 0.7$) years, range = 9.3–11.8) participated. Behavioral accuracy means were obtained for high association, low association, and unrelated trials of the semantic judgment task. In the auditory modality, one participant performed below two standard deviations from the mean on the unrelated items, and was excluded from analysis on these grounds. This resulted in a mean age of 10.7 ($SD = 0.7$) with 15 participants for the auditory semantics condition. Eight males and eight females participated. All children were right-hand dominant ($M = 75$, range = 20–90, where negative scores indicate left-hand dominance) according to a 10 item likert-scale questionnaire. All children were recruited from private and public schools in the Evanston, Illinois area.

All parents were administered an internal interview. None of the participants had a history of intelligence deficits, reading deficits or oral-language deficits. All participants were native English speakers and had normal hearing and normal or corrected-to-normal vision. All participants were free of neurological diseases or psychiatric disorders and were not taking medication affecting the central nervous system.

2.2. Functional activation tasks

2.2.1. Word judgment tasks

In the word judgment task, three words were presented sequentially and the participant had to determine whether or not the final word was semantically associated to either of the two preceding words. For example, in the sequence *found–tank–lost*, the first and third words are associated, while in the sequence *snap–king–queen*, the second and the third words are associated. Half of the semantically related pairs had a high association and half had a low association (Nelson, McEvoy, & Schreiber, 1999). There was no overlap in free association values for the high associates ($M = .59$) and the low associates ($M = .27$). Half of the correct trials involved a match to the first stimulus (first match) and half involved a match to the second stimulus (second match). If there was a match, the participant pressed a button with the index finger; if there was no match, the participant pressed a different button with the middle finger. Versions of the word judgment task were presented to subjects in both a visual (reading words) and an auditory (hearing words) format. These visual and auditory task versions were comprised of different stimulus lists, which consisted of 50 sets each, and were balanced for word frequency and associability. For details on stimulus characteristics, see Booth et al. (2002).

The word-reading task lasted 9 min and consisted of 10 blocks of 54 s. This included a 4-s introduction screen to each block. The five experimental blocks alternated with the five control blocks. In each trial for the experimental blocks, three consecutive words were presented in lowercase letters with each word presented for 800 ms followed by a 200 ms blank interval. A yellow fixation cross (+) appeared on the screen after the third stimulus was removed, indicating the need to make a response during the subsequent 2000 ms interval. Participants were told that they could respond before the yellow cross (+) appeared on the screen. Participants were encouraged to respond as quickly as possible without making errors. Each trial lasted a total of 5000 ms and there were 10 trials in each block. The timing for the auditory task was the same as for the visual task. All stimuli for this task were recorded in a soundproof booth using a digital recorder and a high quality stereo microphone. A native Chicagoan female spoke each word in isolation so that there would be no contextual effects. All words longer than 800 ms were shortened through linear transformation to this duration (less than 1% of the words). All words were then normalized so that they were of equal amplitude. The stimuli were easily heard through the headphones in the 1.5 T scanner. During the auditory tasks, a white fixation cross (+) was presented during the presentation of the auditory stimuli. As in the visual word tasks, a yellow fixation cross (+) appeared on the screen after the third stimulus was presented. Participants were asked to fixate on the cross during the entire trial.

2.2.2. Control tasks

The control blocks for the visual and auditory tasks were designed to equate the experimental and control blocks in terms of their memory demands and response characteristics. The experimental set-up and timing for the control blocks was exactly the same as for the word blocks. For control blocks in the visual tasks, the three stimuli were abstract, *non-linguistic* symbols consisting of straight lines (e.g., / \ - \ - / \). For control blocks in the auditory tasks, the three stimuli were high (700 Hz), medium (500 Hz), and low frequency (300 Hz) *non-linguistic* pure tones (e.g., 300–500–300). The tones were 600 ms in duration and contained a 100 ms linear fade in and a 100 ms linear fade out.

2.3. Experimental procedure

After informed consent was obtained, participants were administered an informal interview about their developmental history (see above) and given their first practice session in a simulator to acclimate the participant to the scanner environment (Rosenberg et al., 1997). Different stimuli (matched in their stimulus characteristics) were used in the practice and fMRI sessions. Within 3 days, the participant was administered the first

MRI session. Within 2 months, the participant was administered the second practice and MRI session. The auditory and visual tasks were run on separate days with an approximately equal number of participants receiving the visual and auditory modality first.

2.3.1. MRI data acquisition

After screening, the participant was asked to lie down on the scanner bed. The head position was secured with a specially designed vacuum pillow (Bioniz, Toledo, OH) that allowed for the insertion of two earphones (for the auditory sessions). An optical response box (Lightwave Medical, Burnaby, Canada) was placed in the participant's right hand and a compression alarm ball was placed in the left hand. The head coil was positioned over the participant's head and a goggle system for the visual presentation of stimuli (Avotec, Jensen Beach, FL) was secured to the head coil. Each imaging session took less than 1 h.

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 echo planar imaging (EPI) method with blood oxygenation level-dependent (BOLD) was used. The following scan parameters were used: TE = 40 ms, flip angle = 90°, matrix size = 64 × 64, field of view = 22 cm, slice thickness = 4 mm, number of slices = 32. These scanning parameters resulted in a 3.437 × 3.437 × 4 mm voxel size. The acquisition of this volume was repeated every 3 s (TR = 3000 ms) for a total of 9 min per run. This resulted in 90 volumes for each word judgment task and 90 volumes for each non-linguistic control task.

At the end of the functional imaging session, 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). These scanning parameters resulted in a .86 × .86 × 1 mm voxel size. The orientation of this 3D volume was identical to the functional slices.

2.3.2. Image data analysis

Data analysis were performed using SPM-99 (Statistical Parametric Mapping) for motion correction and statistical inference (Friston, Ashburner, et al., 1995; Friston, Holmes et al., 1995; Friston, Jezzard, & Turner, 1994). The functional images were realigned to the last functional volume in the scanning session using affine transformations. No individual runs had more than 2.5 mm maximum displacement (less than the voxel size) from the beginning to the end of the run for any participant in the *x*-plane. All statistical analyses were conducted on these movement-corrected images.

Images were then segmented and the gray-white matter information was used to co-register the structural and functional images. The co-registered images were

normalized to the MNI stereotaxic template (12 linear affine parameters for brain size and position, 8 non-linear iterations and $2 \times 2 \times 2$ non-linear basis functions for subtle morphological differences). The MNI template is similar to the Talairach and Tournoux (1988) stereotaxic atlas (Talairach & Tournoux, 1988) and there are algorithms to convert between coordinate spaces (Calder, Lawrence, & Young, 2001; Duncan et al., 2000). Considering the age of our participants and our voxel size, it is reasonable to normalize all participants into the standard MNI template (Burgund et al., 2002; Kang, Burgund, Lugar, Petersen, & Schlaggar, 2003; Muzik, Chugani, Juhasz, Shen, & Chugani, 2000; Wilke, Schmithorst, & Holland, 2002).

Statistical analyses were calculated on the smoothed data (7 mm isotropic Gaussian kernel) using a delayed boxcar design with a 6-s delay from onset of block to account for the lag in hemodynamic response. A high pass filter was applied equal to two cycles of the experimental and control conditions (216 s) to remove low frequency effects such as signal drift, cardiac, and respiratory pulsations. We used global normalization to scale the mean of each scan to a common value in order to correct for the whole brain differences over time.

3. Results

3.1. Behavioral performance

Average performance levels were high in both the auditory ($M = 89.5\%$ ($SD = 7.4\%$)) and visual ($M = 93.9\%$ ($SD = 3.7\%$)) modalities. Accuracy levels across the two modalities ranged from 72.9 to 100%. We performed a modality (auditory, visual) \times block (baseline, words) \times session (practice, test) repeated measures ANOVA on accuracy. This analysis revealed no significant within-subject effects, suggesting that participants performed with similar accuracy levels in the auditory and visual modalities, on the experimental and baseline tasks, and inside and outside of the scanner. Since accuracy levels were similar inside and outside of the scanner, we only report accuracy data from the scanning sessions. Although no effect of age was expected given the small range in the children's ages (9–12 years), accuracy scores were correlated with participants' ages to rule out age as a contributing factor in the brain-behavior correlation. No accuracy-age correlation was found ($p = .4$), confirming that age may not enter as a factor in the brain-behavior correlation.

3.2. Analysis of fMRI data

Behavioral accuracy measures acquired during the imaging session were correlated with brain activation during the word-judgment tasks (i.e., the experimental

condition) in both modalities. We examined the relation between the continuous measure of behavioral performance and the intensity of activation. A design matrix was created to include all fMRI data from each child, and the preliminary threshold for activation was removed to estimate each voxel's intensity of activation during each condition relative to the global mean intensity. Raw accuracy scores on the tasks were converted into z scores by subtracting each individual's accuracy score from the mean for that subject group. This z score resulted in a mean of 0 with individuals with higher error rates having a positive z score and those with lower error rates having a negative z score. These z scores were entered as a T-contrast in the statistical analysis for the experimental condition of interest. This procedure weights the β estimates of each voxel's signal intensity relative to the global mean by the individual's accuracy, thereby testing for a systematic relationship between voxel intensity and performance. A significant effect in this comparison (positive association) would mean that greater intensity activation was associated with poorer performance (higher error rates). We then reversed the signs of the z scores so that those with lower error rates or reaction times had positive z scores and those with higher error rates had negative z scores. A significant effect in this comparison (negative association) indicated that greater intensity activation was associated with better performance (lower error rates).

The resulting maps were masked with the experimental-control contrast for the whole group at $p = .01$ uncorrected. This was done separately for the auditory and visual modalities. Within our regions of interest, our criteria in reporting areas of significant activation were $p < 0.01$ uncorrected at the voxel level, and a cluster size greater or equal to 10 voxels. The anterior regions of interest were the inferior and middle frontal gyri, and the posterior regions of interest were the middle and inferior temporal gyri.

3.3. Activation associated with high accuracy levels

Table 1A presents significant auditory and visual modality activations that correlate with higher-accuracy. Fig. 1 shows brain activation patterns associated with higher-accuracy across these two modalities. For the auditory modality, higher-accuracy was associated with activation in right middle temporal gyrus (BA 21, 63 voxels). For the visual modality, higher-accuracy was associated with activation in left middle temporal gyrus (BA 37, 37 voxels) and right inferior temporal gyrus (BA 37, 69 voxels).

3.4. Activation associated with low accuracy levels

Table 1B presents significant auditory and visual modality activations that correlate with lower-accuracy.

Table 1

Stereotaxic coordinates (x , y , z) of greater activation associated with higher-accuracy (A) and lower-accuracy (B) performance on the semantic judgment task for the auditory and visual modalities (H = hemisphere, BA = Brodmann's area)

Location		Significance		Coordinate					
							Area	H	BA
(A) High									
Auditory	Middle temporal gyrus	R	21	4.06	63	63	−45	3	
Visual	Middle temporal gyrus	L	37	4.00	37	−54	−60	−3	
	Inferior temporal gyrus	R	37	3.55	69	48	−69	−3	
	Middle frontal gyrus	R	46	3.23	21	48	18	24	
(B) Low									
Auditory	Middle frontal gyrus	L	10	8.88	170	−42	54	−6	
	Inferior frontal gyrus	L	47	3.62	14	−33	30	−18	
Visual	Inferior frontal gyrus	R	47	4.21	84	48	39	−15	
					21	21	33	−9	
	Inferior frontal gyrus	L	47	4.01	27	−15	24	−15	

Within our regions of interest, the number of voxels per activated cluster based on a z test is reported at $p < .01$ uncorrected. Outside these areas, nothing reached significance for $p = .01$ corrected.

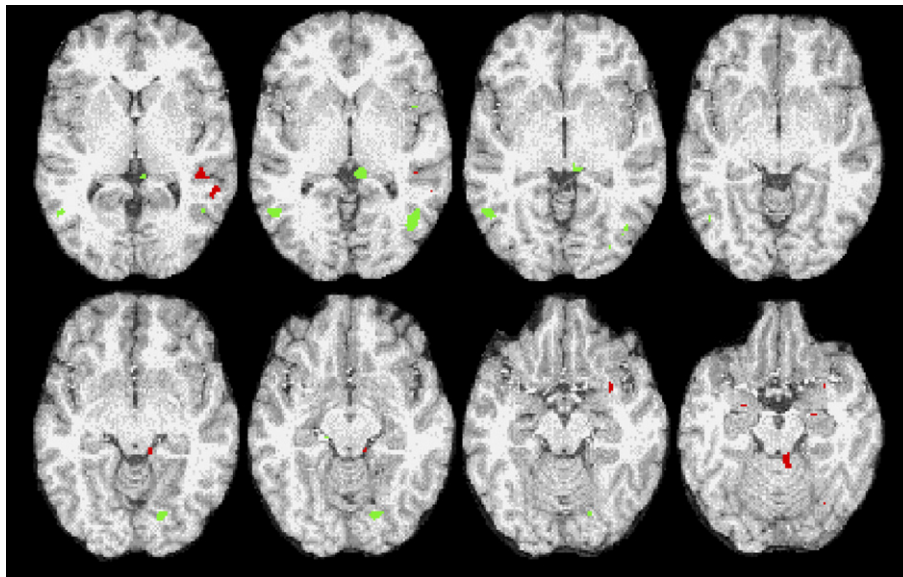


Fig. 1. Neural activation associated with higher-accuracy performance on auditory (red) and visual (green) versions of the semantic judgment task. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this paper.)

Fig. 2 shows brain activation patterns associated with lower-accuracy across these two modalities. For the auditory modality, lower-accuracy was associated with activation in left middle frontal gyrus (BA 10, 170 voxels) and left inferior frontal gyrus (BA 47, 14 voxels). For the visual modality, lower-accuracy was associated with activation in left inferior frontal gyrus (BA 47, 27 voxels) and right inferior frontal gyrus (BA 47, 105 voxels).

4. Discussion

During on-line associative semantic processing, higher-accuracy was associated with more activation in mid-

dle and inferior temporal gyri, while lower-accuracy was associated with more activation in inferior and middle frontal gyri. While processing in both the auditory and visual modalities followed this general pattern, there were modality differences that will be discussed later.

Middle temporal gyrus was positively correlated with higher-accuracy in both modalities. Combined with previous results (Binder et al., 1997; Chee et al., 2000; Pugh et al., 1996; Wise et al., 1991), this suggests that the middle temporal gyrus is central to successful access of semantic content. This finding is consistent with our hypothesis that children who perform more accurately at identifying semantic associations have a more elaborated temporal semantic network at their disposal,

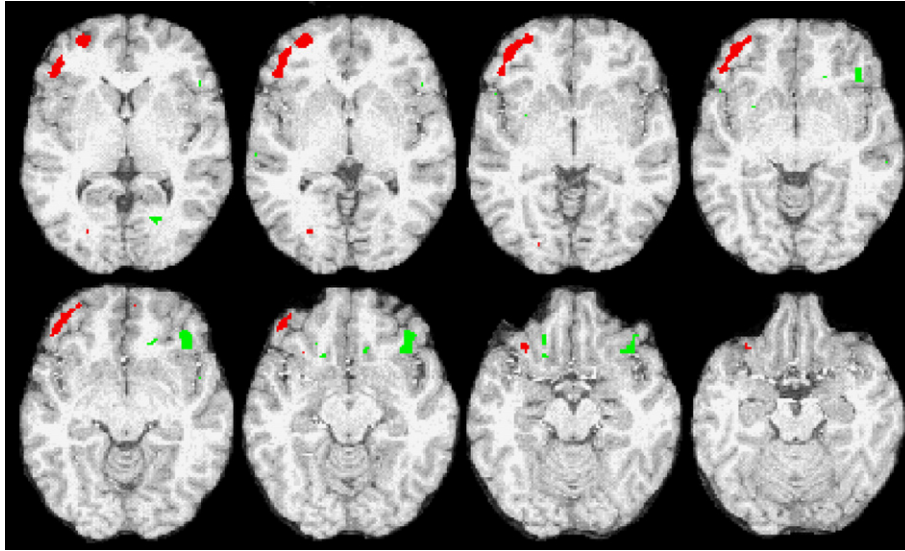


Fig. 2. Neural activation associated with lower-accuracy performance on auditory (red) and visual (green) versions of the semantic judgment task. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this paper.)

which activates more widely. Behavioral findings also suggest that as breadth and depth of vocabulary knowledge increase, the child's semantic system is gradually elaborated as conceptual links are added or strengthened between lexical representations (McGregor & Appel, 2002; McGregor, Friedman, Reilly, & Newman, 2002). With more of these conceptual links available, it becomes increasingly likely that a child who accesses the first and second words of the three-word sequence presented in our task will also automatically activate, and thus prime, semantically associated words (Plaut & Booth, 2000). In such a case, when the third word is presented, appropriate semantic environments have already been activated, resulting in facilitation.

The present finding that more activation in the inferior frontal gyrus (BA 47) is associated with lower-accuracy is consistent with Schlaggar et al. (2002), who showed that activation in BA 45/47 correlates with lower accuracy in children. Further, our finding is consistent with other parametric designs implicating left IFG in more effortful semantic processing (Fletcher et al., 1998a, Fletcher, Shallice, Frith, Frackowiak, & Dolan, 1998b; Kikyo et al., 2002; Seger et al., 2000; Thompson-Schill et al., 1997, 1999; Wagner et al., 2001; Whatmough et al., 2002). Previous studies using processing tasks focusing on the semantic relationship between words also found increased activation in IFG with increased interference (Fletcher et al., 2000; Savage et al., 2001; Wagner et al., 2001). Thus, our between-subjects results contribute to a body of evidence suggesting that IFG is implicated in semantic processing, especially if this processing is effortful or requires manipulations at the feature level.

Although not explicitly addressed in the current study, the dissociation between lower-accuracy and

higher-accuracy performers' anteroventral IFG activation is consistent with previous evidence suggesting that this region is not necessary for accurate semantic processing. For example, Devlin et al. (2003) applied transcranial magnetic stimulation (TMS) to pars orbitalis without reducing accuracy. Moreover, patient SW, who had a lesion in this area, performed within the normal accuracy range on the Palmtrees and Pyramids task (see Devlin et al., 2003). These findings implicate anteroventral IFG as a region that mediates semantic processing, arguably guiding it, without being directly responsible for its content or being the only alternative in successfully accomplishing semantic manipulations. These conclusions are consistent with previous claims that this region is implicated in semantic control processes (Bookheimer, 2002; Price, 2000).

We also found that activation of the middle frontal gyrus (BA 10) was associated with lower-accuracy. It is likely that the low-performing children retrieved semantic associates to presented words differently than the high-performing children. We suggest that the low-performing children did so less automatically, thus requiring more cognitive guidance. BA 10 has previously been implicated with increased processing demands (Savage et al., 2001; Seger et al., 2000; Whatmough et al., 2002), consistent with our hypothesis that lower-accuracy performers had to devote more resources to the search for semantic relationships. The activation of BA 10 only in the auditory modality may be due to a more extensive semantic search in this modality. For the visual modality, more resources may be used in decoding the visual word forms in these relatively inexperienced readers, and therefore, less time is available for semantic search.

4.1. Modality differences

Convergent modality-general activations during semantic judgment tasks have been demonstrated in BAs 45, 46, 47, and 10 (Adams & Janata, 2002; Booth et al., 2002; Chee, O'Craven, Bergida, Rosen, & Savoy, 1999; Michael, Keller, Carpenter, & Just, 2001). Even though regions activated in by the auditory and visual modalities do not overlap in the present findings, they are adjacent to each other. This has also been found in some previous bi-modal studies (Adams & Janata, 2002; Michael et al., 2001) and converges with findings that lesions in ITG or MTG tend to produce multimodal comprehension deficits (Chee et al., 1999). The current finding of left-lateralized auditory and bilateral visual activations in frontal cortex is also consistent with previous findings of semantic activation in adults (Booth et al., 2002).

We found right-lateralized auditory and bilateral visual activations in temporal cortex were associated with higher accuracy. Specifically, 63 voxels were active in right MTG in the auditory modality, whereas in the visual modality, 69 voxels were active in right ITG and 37 voxels were active in left MTG. The finding that higher-accuracy correlates with temporal activation in the left hemisphere is consistent with Shaywitz et al.'s (2002) findings on visual word processing. Shaywitz et al. (2002) found left temporal activation was associated with higher-accuracy, but also found that lower-accuracy correlated with activation in right temporal regions. These inconsistencies with our results may be related to task differences. Shaywitz et al. had their participants perform category decisions, whereas our participants identified relationships between words. This associative semantic processing likely makes demands on wider 'semantic fields,' thus involving the right hemisphere to a larger extent. This interpretation is consistent with the Coarse Semantic Coding Hypothesis (Beeman, Bowden, & Gernsbacher, 2000; Bowden & Beeman, 1998). This hypothesis argues that the right hemisphere is implicated in 'coarse semantic coding,' co-activating large semantic fields which may overlap and thus aid in the generation of distant associations, and is based on strong priming effects for distant semantic associations upon presentation to the left visual field (Beeman et al., 2000; Bowden & Beeman, 1998). Under the assumption of weaker connections and more sparse representations in children compared to adults, we suggest that this right-hemisphere semantic processing component may be particularly relied on in establishing semantic associations.

5. Conclusion

The present study identified brain-behavior correlations showing that more activation in the inferior and

middle frontal gyri (BAs 47, 10) were associated with lower-accuracy in semantic processing, whereas more activation in the middle temporal gyrus (BAs 21, 37) was associated with higher-accuracy in semantic processing in a group of children. Anterior regions in lower-accuracy performers may be recruited when posterior regions that access semantic representations are inadequate or inefficient in providing semantic associative links between concepts. Once recruited, the anterior regions may be involved in feature selection processes needed to identify semantic associations (Seeger et al., 2000; Thompson-Schill et al., 1997, 1999; Wagner et al., 2001). In contrast, higher-accuracy performers with elaborated posterior semantic representations may be able to automatically access semantic environments via spreading-activation mechanisms, providing for a broader semantic context to identify associations between words. Although the correlational nature of the study design does not allow for claims about causality or the involvement of specific mechanisms, this sort of interactive cooperation between frontal and posterior areas has been previously suggested in models of the semantic system, where the anterior component has an executive function and the posterior component stores semantic representations (e.g., see Bookheimer, 2002; O'Reilly & Munakata, 2000).

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References

- Adams, R. B., & Janata, P. (2002). A comparison of neural circuits underlying auditory and visual object categorization. *Neuroimage*, *16*(2), 361–377.
- Beeman, M. J., Bowden, E. M., & Gernsbacher, M. A. (2000). Right and left hemisphere cooperation for drawing predictive and

- coherence inferences during normal story comprehension. *Brain and Language*, 71, 310–336.
- Binder, J. R., Frost, J. A., Hammeke, T. A., Cox, R. W., Rao, S. M., & Prieto, T. (1997). Human brain language areas identified by functional magnetic resonance imaging. *Journal of Neuroscience*, 17, 353–362.
- Bokde, A. L. W., Tagamets, M.-A., Friedman, R. B., & Horwitz, B. (2001). Functional interactions of the inferior frontal cortex during the processing of words and word-like stimuli. *Neuron*, 30, 609–617.
- Bookheimer, S. (2002). Functional MRI of language: New approaches to understanding the cortical organization of semantic processing. *Annual Review of Neuroscience*, 25, 151–188.
- Booth, J. R., Burman, D. D., Meyer, J. R., Gitelman, D. R., Parrish, T. B., & Mesulam, M. M. (2002). Modality independence of word comprehension. *Human Brain Mapping*, 16, 251–261.
- Bowden, E. M., & Beeman, M. J. (1998). Getting the right idea: Semantic activation in the right hemisphere may help solve insight problems. *Psychological Science*, 9(6), 435–440.
- Burgund, E. D., Kang, H. C., Kelly, J. E., Buckner, R. L., Snyder, A. Z., Petersen, S. E., et al. (2002). The feasibility of a common stereotactic space for children and adults in fMRI studies of development. *Neuroimage*, 17(1), 184–200.
- Calder, A. J., Lawrence, A. D., & Young, A. W. (2001). Neuropsychology of fear and loathing. *Nature Reviews Neuroscience*, 2, 352–363.
- Chee, M. W., Hon, L., Lee, H. L., & Soon, C. S. (2001). Relative language proficiency modulates BOLD signal change when bilinguals perform semantic judgments. *Neuroimage*, 13, 1155–1163.
- Chee, M. W., Weekes, B., Lee, K. M., Soon, C. S., Schreiber, A., Hoon, J. J., et al. (2000). Overlap and dissociation of semantic processing of Chinese characters, English words, and pictures: Evidence from fMRI. *Neuroimage*, 12(4), 392–403.
- Chee, M. W., O'Craven, K. M., Bergida, R., Rosen, B. R., & Savoy, R. L. (1999). Auditory and visual word processing studied with fMRI. *Human Brain Mapping*, 7(1), 15–28.
- Demb, J. B., Desmond, J. E., Wagner, A. D., Vaidya, C. J., Glover, G. H., & Gabrieli, J. D. E. (1995). Semantic encoding and retrieval in the left inferior prefrontal cortex: A functional MRI study of task difficulty and process specificity. *Journal of Neuroscience*, 15, 5870–5878.
- Demonet, J. F., Chollet, F., Ramsey, S., Cardebat, D., Nespoulous, J. L., Wise, R., et al. (1992). The anatomy of phonological and semantic processing in normal subjects. *Brain*, 115, 1753–1768.
- Devlin, J. T., Matthews, P. M., & Rusworth, M. F. S. (2003). Semantic processing in the left inferior prefrontal cortex: A combined functional magnetic resonance imaging and transcranial magnetic stimulation study. *Journal of Cognitive Neuroscience*, 15(1), 71–84.
- Duncan, J., Seitz, R. J., Kolodny, J., Bor, D., Herzog, H., Ahmed, A., et al. (2000). A neural basis for general intelligence. *Science*, 289, 457–460.
- Farah, M. J., & McClelland, J. L. (1991). A computational model of semantic memory impairment: Modality specificity and emergent category specificity. *Journal of Experimental Psychology: General*, 120, 339–357.
- Fletcher, P. C., Shallice, T., & Dolan, R. J. (2000). "Sculpting the response space"—An account of left prefrontal activation at encoding. *Neuroimage*, 12, 404–417.
- Fletcher, P. C., Shallice, T., & Dolan, R. J. (1998a). The functional roles of prefrontal cortex in episodic memory: I. Encoding. *Brain*, 121, 1229–1248.
- Fletcher, P. C., Shallice, T., Frith, C. D., Frackowiak, R. S. J., & Dolan, R. J. (1998b). The functional roles of prefrontal cortex in episodic memory: II. Retrieval. *Brain*, 121, 1249–1256.
- Friston, K. J., Ashburner, J., Frith, C. D., Poline, J. B., Heather, J. D., & Frackowiak, R. S. J. (1995). Spatial registration and normalization of images. *Human Brain Mapping*, 2, 1–25.
- Friston, K. J., Holmes, A. P., Poline, J. B., Grasby, P. J., Williams, S. C. R., Frackowiak, R. S. J., et al. (1995). Statistical parametric maps in functional imaging: A general linear approach. *Human Brain Mapping*, 2, 189–210.
- Friston, K. J., Jezzard, P., & Turner, R. (1994). Analysis of functional MRI times-series. *Human Brain Mapping*, 1, 153–171.
- Gourovitch, M. L., Kirkby, B. S., Goldberg, T. E., Weinberger, D. R., Gold, J. M., Esposito, G., et al. (2000). A comparison of rCBF patterns during letter and semantic fluency. *Neuropsychology*, 14(3), 353–360.
- Hernandez, A. E., Martinez, A., & Kohnert, K. (2000). In search of the language switch: An fMRI study of picture naming in Spanish-English bilinguals. *Brain & Language*, 73(3), 421–431.
- Kang, H. C., Burgund, E. D., Lugar, H. M., Petersen, S. E., & Schlaggar, B. L. (2003). Comparison of functional activation foci in children and adults using a common stereotactic space. *Neuroimage*, 19(1), 16–28.
- Kapur, S., Tulving, E., Cabeza, R., McIntosh, A. R., Houle, S., & Craik, F. I. M. (1996). The neural correlates of intentional learning of verbal materials: A PET study in humans. *Cognitive Brain Research*, 4, 243–249.
- Kapur, S., Rose, R., Liddle, P. F., Zipurski, R. B., Brown, G. M., Stuss, D., et al. (1994). The role of the left prefrontal cortex in verbal processing: Semantic processing or willed action? *NeuroReport*, 5, 2193–2196.
- Kikyo, H., Ohki, K., & Miyashita, K. (2002). Neural correlates of feeling-of-knowing: An fMRI parametric analysis. *Neuron*, 36, 177–186.
- Kirchoff, B. A., Wagner, A. D., Maril, A., & Stern, C. E. (2000). Prefrontal-temporal circuitry for episodic encoding and subsequent memory. *The Journal of Neuroscience*, 20(16), 6173–6180.
- Martin, M. (2001). Functional neuroimaging of semantic memory. In R. Cabeza & A. Kingstone (Eds.), *Handbook of functional neuroimaging of cognition* (pp. 153–186). Cambridge: The MIT Press.
- McGregor, K. K., & Appel, A. (2002). On the relation between mental representation and naming in a child with specific language impairment. *Clinical Linguistics and Phonetics*, 16(1), 1–20.
- McGregor, K. K., Friedman, R. M., Reilly, R. M., & Newman, R. M. (2002). Semantic representation and naming in young children. *Journal of Speech, Language, and Hearing Research*, 45(2), 332–346.
- Michael, E. B., Keller, T. A., Carpenter, P. A., & Just, M. A. (2001). fMRI investigation of sentence comprehension by eye and by ear: Modality fingerprints on cognitive processes. *Human Brain Mapping*, 13(4), 239–252.
- Muzik, O., Chugani, D. C., Juhasz, C., Shen, C., & Chugani, H. T. (2000). Statistical parametric mapping: Assessment of application in children. *Neuroimage*, 12(5), 538–549.
- Nelson, D. L., McEvoy, C. L., & Schreiber, T. A. (1999). *The University of South Florida Word Association, Rhyme and Fragment Norms* [Data file]. Available from University of South Florida Web Site, <http://luna.cas.usf.edu/~nelson/>
- O'Reilly, R., & Munakata, Y. (2000). Higher-level cognition. In R. O'Reilly & Y. Munakata (Eds.), *Computational explorations in cognitive neuroscience* (pp. 379–410). Cambridge: The MIT Press.
- Perani, D., Schnur, T., Tettamanti, M., Gorno-Tempini, M., & Cappa, S. F. (1999). Word and picture matching: A PET study of semantic category effects. *Neuropsychologia*, 37(3), 293–306.
- Petersen, S. E., & Fiez, J. A. (1993). The processing of single words studied with positron emission tomography. *Annual Review of Neuroscience*, 16, 509–530.
- Petersen, S. E., Fox, P. T., Posner, M. I., Mintum, M., & Raichle, M. E. (1989). Positron emission tomographic studies of the processing of single words. *Journal of Cognitive Neuroscience*, 1, 153–170.
- Petersen, S. E., Fox, P. T., Posner, M. I., Mintum, M., & Raichle, M. E. (1988). Positron emission tomographic studies of the cortical anatomy of single word processing. *Nature*, 331, 358–389.

- Plaut & Booth (2000). Individual and developmental differences in semantic priming: Empirical and computational support for a single-mechanism account of lexical processing. *Psychological Review*, 107(4), 786–823.
- Poldrack, R. A., A.D Prull, M. W., Desmond, J. E., Glover, J. H., & Gabrieli, J. D. (1999). Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. *Neuroimage*, 10(1), 15–35.
- Price, C. J., Moore, C. J., Humphreys, G. W., & Wise, R. J. S. (1997). Segregating semantic from phonological processes during reading. *Journal of Cognitive Neuroscience*, 9, 727–733.
- Price, C. J. (2000). The anatomy of language: Contributions from functional neuroimaging. *Journal of Anatomy*, 197, 335–359.
- Pugh, K. R., Shaywitz, B. A., Shaywitz, S. E., Constable, R. T., Skudlarski, P., Fulbright, R. K., et al. (1996). Cerebral organization of component processes in reading. *Brain*, 119(4), 1221–1238.
- Ricci, P. T., Zekowicz, B. J., Nebes, R. D., Meltzer, C. C., Mintun, M. A., & Becker, J. T. (1999). Functional neuroanatomy of semantic memory: Recognition of semantic associations. *Neuroimage*, 9, 88–96.
- Rosenberg, D. R., Sweeney, J. A., Gillen, J. S., Chang, S. Y., Varanelli, M. J., O'Hearn, K., et al. (1997). Magnetic resonance imaging of children without sedation: Preparation with simulation. *Journal of the American Academy of Child Adolescent Psychiatry*, 36, 853–859.
- Savage, C. R., Deckersbach, T., Heckers, S., Wagner, A. D., Schacter, D. L., Alpert, N. M., et al. (2001). Prefrontal regions supporting spontaneous and directed application of verbal learning strategies: Evidence from PET. *Brain*, 124, 219–231.
- Schlaggar, B. L., Brown, T. T., Lugar, H. M., Visscher, K. M., Miezin, F. M., & Peterson, S. E. (2002). Functional neuroanatomical differences between adults and school-age children in the processing of single words. *Science*, 296, 1476–1479.
- Seger, C. A., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. E. (2000). Functional magnetic resonance imaging evidence for right-hemisphere involvement in processing unusual semantic relationships. *Neuropsychology*, 14(3), 361–369.
- Shallice, T., Fletcher, P., Frith, C. D., Grasby, P., Frackowiak, R. S., & Dolan, R. J. (1994). Brain regions associated with acquisition and retrieval of verbal episodic memory. *Nature*, 368(6472), 633–635.
- Shaywitz, B. A., Shaywitz, S. E., Pugh, K. R., Mencl, W. E., Fulbright, R. K., Skudlarski, R., et al. (2002). Disruption of posterior brain systems for reading in children with developmental dyslexia. *Society of Biological Psychiatry*, 52, 101–110.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.
- Thompson-Schill, S. L., D'Esposito, M., & Kan, I. P. (1999). Effects of repetition and competition on activity in left prefrontal cortex during word generation. *Neuron*, 23, 513–522.
- Thompson-Schill, S. L., D'Esposito, M., Aguirre, G. K., & Farah, M. J. (1997). Role of left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. *Proceedings of the National Academy of Sciences of the United States of America*, 94(26), 14792–14797.
- Vandenberghe, R., Price, C. J., Wise, R., Josephs, O., & Frackowiak, R. S. J. (1996). Functional anatomy of a common semantic system for words and pictures. *Nature*, 383, 254–256.
- Wagner, A. D., Paré-Blagoev, E. J., Clark, J., & Poldrack, R. A. (2001). Recovering meaning: Left prefrontal cortex guides controlled semantic retrieval. *Neuron*, 31, 329–338.
- Wagner, A. D., Schacter, D. L., Rotte, M., Koutsaal, W., Maril, A., Dale, A. M., et al. (1998). Building memories: Remembering and forgetting of verbal experiences as predicted by brain activity. *Science*, 281, 1188–1191.
- Wagner, A. D., Desmond, J. E., Demb, J. B., Glover, G. H., & Gabrieli, J. D. E. (1997). Semantic repetition priming for verbal and pictorial knowledge: A functional MRI study of left inferior prefrontal cortex. *Journal of Cognitive Neuroscience*, 9(6), 714–726.
- Whatmough, C., Chertkow, H., Murtha, S., & Hanratty, K. (2002). Dissociable brain regions process object meaning and object structure during picture naming. *Neuropsychologia*, 40, 174–186.
- Wilke, M., Schmithorst, V. J., & Holland, S. K. (2002). Assessment of spatial normalization of whole-brain magnetic resonance images in children. *Human Brain Mapping*, 17(1), 48–60.
- Wise, R., Chollet, F., Hadar, U., Friston, K., Hoffner, E., & Frackowiak, R. (1991). Distribution of cortical neural networks involved in word comprehension and word retrieval. *Brain*, 114, 2235–2252.