

## **Interaction Between Brain Regions During Semantic Processing in Chinese Adults\***

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Using functional magnetic resonance imaging (fMRI) and dynamic causal modeling (DCM) methods, we investigated the neural correlates of meaning processing in different brain regions and calculated the inter-connection among these regions during semantic judgments to visual Chinese characters. Twenty-five healthy Chinese adults were asked to indicate if character pairs were related in meaning. Experimental stimuli were character pairs that included semantically-related and semantically-unrelated pairs. The behavioral results showed that reaction times were significantly faster for the related condition than the unrelated condition. fMRI analyses showed greater activation in left inferior frontal gyrus (IFG, BA 45, 47), left posterior middle temporal gyrus (MTG, BA 21) and left fusiform gyrus (FG, BA 37) for the related versus baseline condition, and in left inferior parietal lobule (IPL, BA 39, 40) for the related versus unrelated condition. Effective connectivity from DCM analyses showed modulatory effects from left inferior frontal gyrus to left posterior middle temporal gyrus, suggesting top-down influences of the frontal cortex on retrieval of semantic representations. Effective connectivity analyses also showed modulatory effects from left posterior middle temporal gyrus to left inferior frontal gyrus, suggesting the role of MTG on providing relevant associations in verbal semantic memory for IFG to perform retrieval. We also found significant modulatory effects from left fusiform gyrus to left posterior middle temporal gyrus, suggesting bottom-up orthographic influences on semantic representations. These findings suggest dynamic interaction between brain regions during semantic processing to written characters in Chinese adults.

Key words: semantics, orthography, effective connectivity

### **1. Introduction**

Most psycholinguistic theories of word identification in reading propose that at least three distinct computational systems are engaged by a printed word: orthographic,

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phonological, and lexical-semantic systems. In previous reading studies, processing words in context can be separated into two major components: finding the semantic lexicon and accessing the representations (Badre et al. 2005, Booth et al. 2006, Lau et al. 2008). Combining lesion deficit with imaging studies, three major brain regions have been suggested to be associated with semantic processing as a complicated network. These three brain regions include: left posterior temporal cortex, left anterior temporal cortex, and left inferior frontal cortex (Lau et al. 2008). In addition to these regions, some studies have shown other regions such as left angular gyrus in left inferior parietal lobe that may be involved in integrating semantic information (Booth et al. 2006, Lau et al. 2008). The left anterior temporal cortex was involved in semantic processing during sentence processing (Lau et al. 2008). In this study, we focus on three critical brain regions, which were associated with semantic processing to words.

The first critical region for semantic processing is the left posterior temporal cortex. This region is considered as the crucial area for the storage of conceptual features that are associated with lexical representations (Hickok et al. 2007, Martin 2007). Some studies also showed greater activity in this region during the semantic tasks (Gitelman et al. 2005, Gold et al. 2006). Greater activation in this region has been implicated in the representation of verbal semantic information (Booth et al. 2002a, Chou et al. 2006a). Another study focused on aphasia patients with lesions in this region, showing that they had deficits in semantic comprehension (Hart et al. 1990). These studies suggest that the left posterior temporal cortex is related to store long-term semantic knowledge (Badre et al. 2005).

The second critical region for semantic processing is the left inferior parietal lobule (IPL). This region has been suggested to support the integration of lexical input into the larger units during semantic processing (Lau et al. 2008). Some studies have interpreted the left inferior parietal lobule as related to feature integration and semantic categorization to form a coherent concept so that semantic relationships between words can be determined (Chou et al. 2006a). Stronger semantic association pairs may involve more 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 activation in left inferior parietal lobule has also been interpreted as evidence of semantic integration (Thompson et al. 2007), as supported by a larger N400 wave in this region following errors of semantic integration during ERP (event-related potential) measures (Hagoort et al. 1999).

The final main region is the left inferior frontal gyrus (IFG) that has been proposed to play an important role in on-line semantic search during semantic processing (Fletcher et al. 2000, Gaillard et al. 2003, Schlaggar et al. 2002). This region can be divided into two sub-parts with different cognitive functions: anterior ventral and mid

posterior parts (Badre et al. 2005, Badre & Wagner 2007). Recent studies have demonstrated that the anterior ventral of the IFG is associated with controlling semantic retrieval, and the mid-posterior IFG is related with selection processes (Lau et al. 2008). Altogether, these studies suggest that left inferior frontal gyrus is involved in effortful semantic processing, particularly when there are increased demands on the process of selecting relevant semantic knowledge or on the retrieval of semantic knowledge (Thompson-Schill et al. 1999, Chou et al. 2006b). Regarding the connection between this frontal cortex and posterior semantic representational systems, the IFG has been suggested to support generation of semantic associations between words (Addis & McAndrews 2006) or to select semantic representations from a posterior region in left middle temporal gyrus (Badre et al. 2005, Badre & Wagner 2007).

English has an arbitrary relationship between orthography and semantics at a mono-morphemic level, whereas many Chinese characters are derived from pictures representing meanings or encode meanings by including a semantic radical (Booth et al. 2006). There are approximately 200 semantic radicals in Chinese and these units of characters give a clue to the meaning of the character (e.g., category). Thus, Chinese has a more direct mapping between orthography and semantics than English. In support of this, evidence from event-related potential measures suggests earlier involvement of semantics in Chinese compared to English (Zhang et al. 2006). Despite differences between Chinese and English in the nature of mapping between orthography and semantics, neuroimaging studies have revealed substantial similarities across the two languages using a variety of semantic tasks in Chinese visual character/word comprehension. These studies include judging whether two characters are semantically related (Dong et al. 2005, Tan et al. 2001), semantic judgment of association strength (Booth et al. 2006), semantic categorization (Ding et al. 2003, Liu et al. 2006), silent word generation (Tan et al. 2000), and high-conflict versus low-conflict semantic judgment (Zhang et al. 2004) and matching characters in meaning to corresponding English words (Chee et al. 2000). These studies have reported common activated regions in left inferior frontal gyrus (BA 47, 45) and left posterior temporal areas (BA 21, 37) in Chinese.

Although many studies have identified the functional connectivity involved in semantic processing, few studies have examined the dynamic interaction (i.e., effective connectivity) between brain regions. A study has shown the functional connectivity between left ventral inferior frontal gyrus and left temporal cortex for words that have high semantic valence (Bokde et al. 2001). Bokde proposed that left ventral inferior frontal gyrus is associated with selection of semantic information from a set of competing alternatives. Moreover, Bokde proposed that a functional link between left ventral inferior frontal gyrus and posterior temporal cortex, enabling appropriate semantic

representations to be accessed. Some studies also suggested the anterior and mid-posterior of the inferior frontal gyrus with different cognitive functions. The anterior ventral of the IFG is important for controlling semantic retrieval, and the mid-posterior IFG seems to be associated with selection processes (Lau et al. 2008). However, these hypotheses were based on non-directional evidence. Little is known about the directional interaction between brain regions during semantic processing.

Previous fMRI studies usually identified brain activations with a variety of cognitive tasks, measuring the hemodynamic response of brain tissues to investigate the functional connectivity, which can display task-dependent activations within a network and is in a non-directional fashion (Pugh et al. 2000, Chaminade et al. 2003, Homae et al. 2003). However, the complicated cognitive functions are subserved by large-scale distributed networks whereby individual components may act as nodal points for integrating and distributing information among other regions in a network (Bitan et al. 2005). Thus, effective connectivity methods such as Dynamic Causal Modelling (DCM) now aim to estimate the directional influence that one brain cortical area has on another. DCM is a nonlinear method that uses Bayesian estimation to calculate effective connectivity (the directional influence that one brain region has on another) between neural systems and experimental conditions (Friston et al. 2003). In DCM, three sets of parameters are estimated: the direct influence of stimuli on regional activity, the intrinsic or latent connections between regions and the changes in the intrinsic connectivity between regions induced by the experimental design (modulatory effects) (Mechelli et al. 2003). The aim of DCM is to estimate and to make inferences about the influence that one neural system exerts over another and how this is affected by the experimental context (Friston et al. 2003). Therefore, the significant modulatory effects of DCM only show the changes among brain regions induced by the experimental design. The findings of effective connectivity may not necessarily reflect anatomical connections (Sonty et al. 2007).

In the current study, we used effective connectivity to examine the interaction between brain regions during semantic processing. Particularly, we would like to focus on the directional influence between left IFG and left posterior middle temporal gyrus (MTG) because previous connectivity studies have demonstrated a functional link between left IFG and posterior temporal cortex, enabling appropriate semantic representations to be accessed (Bokde et al. 2001). In this study, participants were given visual character pairs to make semantic judgments. The first goal of the current study is to examine the bidirectional influences between left IFG and left posterior MTG. Second, this study is to evaluate the bidirectional connections between a visual word form area (VWFA) in fusiform gyrus and a meaning-based area in left middle temporal gyrus, as semantic processing needs to link visual word forms with distributed networks

that provide meanings (Booth et al. 2002b, Mesulam 1998). Therefore, this study further examines the interactions between left posterior MTG and fusiform gyrus.

## **2. Material and methods**

### **2.1 Participants**

Twenty-five healthy adults (mean age = 20.9, 13 females) participated in this study. All participants were right-handed, native Mandarin-Chinese speakers. All participants were free of neurological disease or psychiatric disorders and did not have a history of language or reading disabilities. After receiving the detailed information of experimental purpose and administration, informed consent was obtained. The informed consent procedures were approved by the Institutional Review Board at the National Taiwan University Hospital.

### **2.2 Stimuli and procedures**

Character pairs were divided into semantically related and unrelated conditions (Chou et al. 2009). Forty-eight character pairs were semantically related according to their free association values (mean = 0.14, SD = 0.13, ranging from 0.73 to 0.01) (Hue et al. 2005). Twenty-four character pairs were semantically unrelated with zero association values. Several lexical variables were controlled across the related and unrelated conditions. First, all characters were monosyllabic. Second, the first and second character did not share radicals. Third, the first and second character together did not form a word (Wu & Liu 1987, Sinica Corpus 1998). Fourth, characters were matched for visual complexity (in terms of strokes per character) across conditions. Fifth, characters were matched for frequency across conditions (Wu & Liu 1987). Sixth, the number of nouns (48%-50%), verbs (23%), and adjectives (21%-27%), based on their most frequent usage in Academia Sinica balanced corpus (Sinica Corpus 1998), was matched across conditions. The correlation of character frequency or the measure semantic relation (Lee et al., in press) with association strength was not significant indicating that association effects should not be due to frequency or semantic relation differences.

In the meaning judgment task, after a 500-ms solid square, two visual Chinese characters were presented sequentially. The participant had to determine whether the character pairs were related in meaning. The duration of each character was 800 msec followed by a 200 msec blank interval. After the second character, the participant needed to make a response during the presentation of the second character. The participant was instructed to quickly and accurately press with their right hand the yes

button to the related pairs and the no button to the unrelated pairs.

There were two kinds of control tasks. The perceptual control had 24 pairs of non-characters. Non-characters were created by replacing radicals of real characters with other radicals that did not form real Chinese characters such as “𠄎”, “𠄎”, and “𠄎” (Wu & Chen 2000). For the perceptual controls, trials consisted of a solid square (500 ms), followed by the first non-character (800 ms), a 200 ms blank interval, and the second non-character (3000 ms). Participants determined whether the pair of stimuli were identical or not by pressing a yes or no button. In the perceptual task, the non-characters were presented in a different font size in order to encourage participants to perform the task based on the recognition of low level visual similarity (Chou et al. 2009). The second control task involved 24 baseline events. The participant was instructed to press a button when a solid square (1300 ms) at the center of the visual field turned to a hollow square (3000 ms) after a blank interval (200 ms).

### **2.3 Image acquisition**

Participants lay in the scanner with their head position secured. An optical response box was placed in the participants' right hand. The head coil was positioned over the participants' head. Participants viewed visual stimuli projected onto a screen via a mirror attached to the inside of the head coil. Each participant performed two functional runs. Each run took 4.7 minutes.

Images were acquired using a 3 Tesla Siemens Trio scanner, using the 8-channel head coil with echo planar imaging method. The scanning parameters were the following: repetition time (TR) = 2000 ms; echo time (TE) = 24 ms; flip angle = 90°; matrix size = 64 × 64; field of view = 25.6cm; slice thickness = 3 mm; number of slices = 34. Two runs of 9 min (272 images) were acquired. A high-resolution, T1-weighted three dimensional image was also acquired (Magnetization Prepared Rapid Gradient Echo, MP-RAGE; TR = 1560 ms; TE = 3.68 ms; flip angle = 15°; matrix size = 256 × 256; field of view = 25.6cm; slice thickness = 1 mm). The task was administered in a pseudorandom order for all subjects, in which the order of related, unrelated, perceptual, and baseline trials was optimized for event-related design (Burock et al. 1998). We used the Optseq script for randomized event-related design (<http://surfer.nmr.mgh.harvard.edu/optseq>, written by D. Greve, Charlestown, MA) that implemented Burock et al. (1998)'s approach. This script allowed us to determine an optimized event-related design for this study. Forty-eight character pairs and 113 TRs were included in the related condition; twenty-four character pairs and 53 TRs were included in the unrelated condition; twenty-four non-character pairs and 53 TRs were included in the perceptual condition and twenty-four baseline events and 53 TRs were included in the null condition (the second control task).

### 3. Data analysis

#### 3.1 Conventional 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 mm of movement in any plane. Co-registered images were normalized to the MNI (Montreal Neurological Institute) average template. Statistical analyses were calculated on the smoothed data (10 mm isotropic Gaussian kernel), with a high pass filter (128 seconds cutoff period) in order to remove low frequency artifacts. 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 (Hemodynamic Response Function). 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). We compared the related and unrelated pairs separately to the baseline condition, and the related to the unrelated pairs. All reported areas of activation were significant using  $p < .05$  corrected for FDR (false discovery rate) for multiple comparisons at the voxel level with a cluster size greater than or equal to 10 voxels.

#### 3.2 Effective connectivity analysis

Four left hemisphere regions of interest (ROIs) were chosen in the visual semantic task, using the same contrasts as in a previous English study with an identical design (Chou et al. 2006a), with a threshold of FDR  $p < .05$  and containing a cluster size greater than or equal to 10 voxels (Table 1). These include the fusiform gyrus (FG), inferior frontal gyrus (IFG), middle temporal gyrus (MTG), and inferior parietal lobule (IPL). All ROIs were 6 mm radius spheres centered on the most significant voxel in the individual's activation map within 20 mm from the group maximum (Cao et al. 2008). We constrained the individual peaks to be within the following anatomical masks and BAs in SPM2 (IFG: within left inferior frontal gyrus in BA 44, 45, 46, 47; MTG: within left middle temporal gyrus or superior temporal gyrus in BA 21, 22; IPL: within left inferior parietal lobule in BA 40; FG: within left fusiform gyrus, inferior temporal gyrus or middle occipital gyrus in BA 19, 37). A weaker peak was chosen in individuals where the distance between the centers of different ROIs was less than 20 mm apart when the strongest peak was located more than 20 mm apart from the center of ROI.

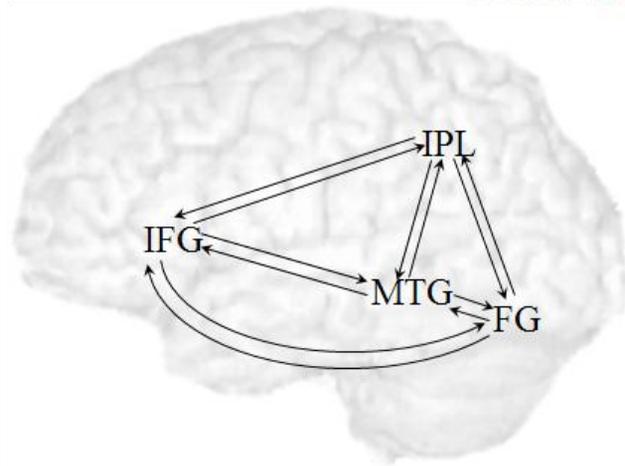
**Table 1:** Regions of interest (ROIs) used for the effective connectivity analysis

Condition	ROI	BA	x	y	z
Related-Null	Inferior Frontal Gyrus	47	-42	30	-3
	Middle Temporal Gyrus	21	-54	-51	-3
	Fusiform Gyrus	37	-42	-60	-12
Related-Unrelated	Inferior Parietal Lobule	39/40	-42	-54	33

Note: These regions were all in the left hemisphere. BA: Brodmann's Area. Coordinates are given in the MNI stereotactic space (x,y,z).

In DCM, three sets of parameters are estimated: the direct influence of stimuli on regional activity; the intrinsic or latent connections between regions in the absence of modulating experimental effects; and the changes in the intrinsic connectivity between regions induced by the experimental design (modulatory effects) (Mechelli et al. 2003). Our analysis adopted a two-stage procedure that is formally identical to the summary statistic approach used in random effects analysis of neuroimaging data. The parameters from the subject-specific, first level DCM models were taken to a second, between-subject level using the random effects approach (Bitan et al. 2005). Subject-specific DCMs were fully and reciprocally connected (resulting in 12 connections), with modulatory (bilinear) effects of the related and the unrelated conditions specified on coupling among all regions (Figure 1). In the visual semantic task, the direct input of the 'visual' condition (including related, unrelated and perceptual conditions) was specified on the fusiform gyrus.

The second level analysis was done on the modulatory effects of related and unrelated conditions for the visual semantic task. Based on previous semantic studies (Bokde et al. 2001, Duffau et al. 2005), our apriori connections of interest were bidirectional connections between left inferior frontal gyrus and middle temporal gyrus, as well as bidirectional connections between left middle temporal gyrus and fusiform gyrus. Therefore, the bidirectional connections between left inferior frontal gyrus and middle temporal gyrus are reported at a significance level of  $p < .025$  ( $p < .05$  corrected for 2 comparisons). In addition, the bidirectional connections between left middle temporal gyrus and fusiform gyrus are reported at a significance level of  $p < .025$  ( $p < .05$  corrected for 2 comparisons). All other connections are reported at the level of  $p < .006$  ( $p < .05$  corrected for 8 comparisons).



**Figure 1:** The connectivity path model tested with modulatory (bilinear) effects of the related and the unrelated conditions specified on coupling among all regions for the visual semantic task (IFG: inferior frontal gyrus, MTG: middle temporal gyrus, IPL: inferior parietal lobule, FG: fusiform gyrus).

## 4. Results

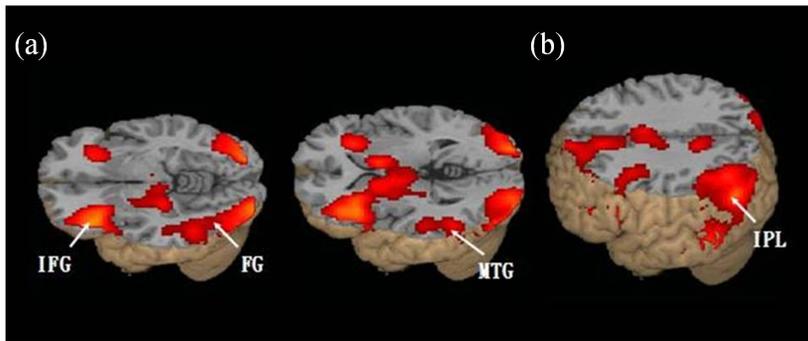
### 4.1 Behavioral results

Accuracy (mean  $\pm$  SD) for the related and unrelated conditions was  $97 \pm 3\%$ , and  $98 \pm 2\%$ , with no significant difference, a paired  $t(24) = 2.068$ ,  $p = .05$ . The reaction times (mean  $\pm$  SD) for the related and unrelated conditions were  $780 \pm 143$ ms, and  $836 \pm 148$  ms, with the related condition being significantly faster than the unrelated condition, a paired  $t(24) = 2.944$ ,  $p < .01$ .

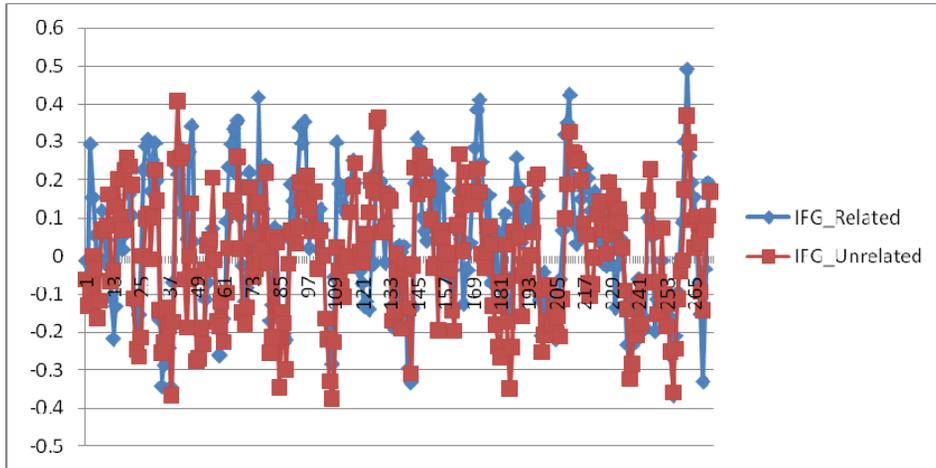
### 4.2 fMRI conventional analysis

Figure 2 presents regions which were active for the related versus baseline contrast and the related versus unrelated contrast. The related versus baseline contrast produced greater activation in left inferior frontal gyrus (BA 45, 47), left posterior middle temporal gyrus (BA 21) and left fusiform gyrus (BA 37) (See Figure 2a). The related versus unrelated contrast produced greater activation in left inferior parietal lobule (BA 40) (See Figure 2b). We used these regions to compute effective connectivity across 272 time series (i.e., 272 volumes). In addition, Figure 3 and Figure 4 show the time course of hemodynamic response function (HRF) amplitude. For the inferior frontal gyrus, the HRF amplitude (mean  $\pm$  SD) for the related and unrelated conditions was  $0.0324 \pm$

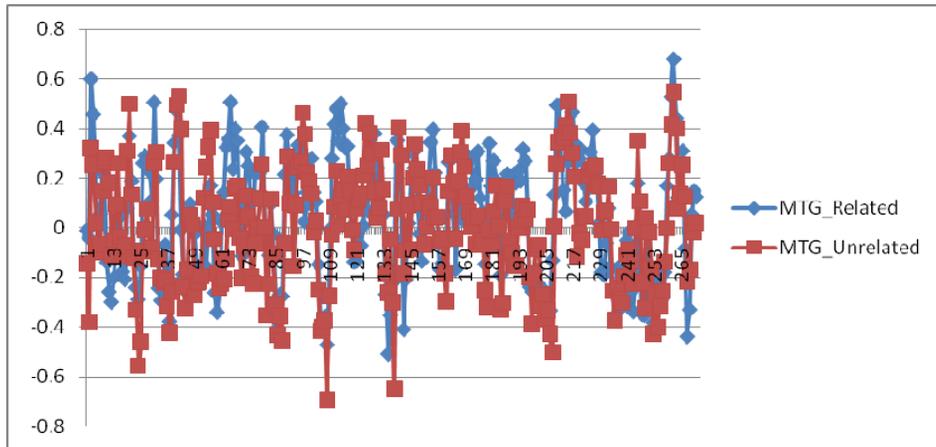
0.175 and  $0.0012 \pm 0.165$  respectively, with the related condition being significantly greater than the unrelated condition, a paired  $t(271) = 4.254, p < .001$ . For the posterior middle temporal gyrus, the HRF amplitude (mean  $\pm$  SD) for the related and unrelated conditions was  $0.0459 \pm 0.247$  and  $0.0001 \pm 0.237$  respectively, with the related condition being significantly greater than the unrelated condition, a paired  $t(271) = 4.161, p < .001$ .



**Figure 2:** (a) For the related versus baseline contrast, regions of interest included the left inferior frontal gyrus (IFG, BA 45/47), fusiform gyrus (FG, BA37) and middle temporal gyrus (MTG, BA 21). (b) For the related versus unrelated contrast, region of interest included the left inferior parietal gyrus (IPL, BA 40). [ $p < 0.05$  FDR (false discovery rate) corrected, only clusters greater than or equal to 10 are presented.]



**Figure 3:** Hemodynamic response function (HRF) amplitude in left inferior frontal gyrus (IFG, MNI coordinates [-42, 30, -3]). The blue line indicates the related condition, and the red line indicates the unrelated condition.



**Figure 4:** Hemodynamic response function (HRF) amplitude in left posterior middle temporal gyrus (MTG, MNI coordinates [-54, -51, -3]). The blue line indicates the related condition, and the red line indicates the unrelated condition.

### 4.3 Effective connectivity analysis

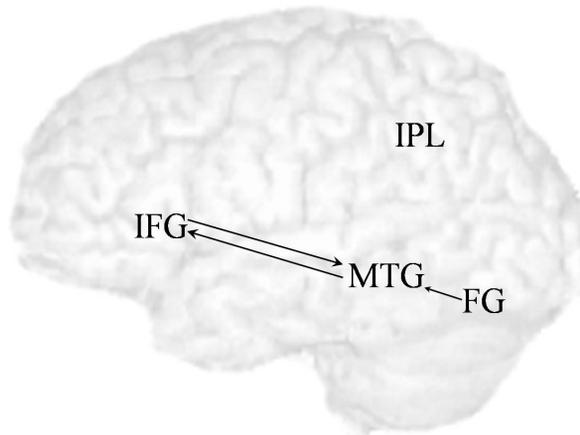
The intrinsic connections between regions showed the interregional influences in the absence of modulating experimental effects (Friston et al. 2003), for example lack of modulation on meaning judgments in this study. We restricted the results of intrinsic connections significant at a level of  $p < .05$  (corrected for 12 comparisons), tested in a 1-sample t-test (Bitan et al. 2005). All intrinsic connections were significant (Table 2). However, in this study we focused on the modulatory effects, which would be proper to reflect the experimental task (Friston et al. 2003), for example the interregional influences on meaning judgments in this study. Table 3 shows the modulatory effects for the related and the unrelated conditions between ROIs. Figure 5 shows the significant modulatory effects for the related versus unrelated condition. Based on our apriori hypotheses, we calculated a 2 condition (related, unrelated) x 2 direction (MTG-IFG, IFG-MTG) ANOVA. The main effect of condition was significant,  $F(1, 24) = 6.323$ ,  $p = .019$ , with stronger effects for the related compared to the unrelated condition. The main effect of direction was not significant,  $F(1, 24) = 1.298$ ,  $p = .266$ . The interaction was not significant,  $F(1, 24) = 1.930$ ,  $p = .178$ . Figure 6 shows a significant difference ( $p$  corrected for 2 comparisons  $< .05$ ) between the related and unrelated condition for the MTG-IFG connection ( $t(24) = 2.420$ ,  $p = .023$ ), and for the IFG-MTG connection ( $t(24) = 2.516$ ,  $p = .019$ ).

**Table 2:** All intrinsic connections between regions of interest are significant for the visual semantic tasks.

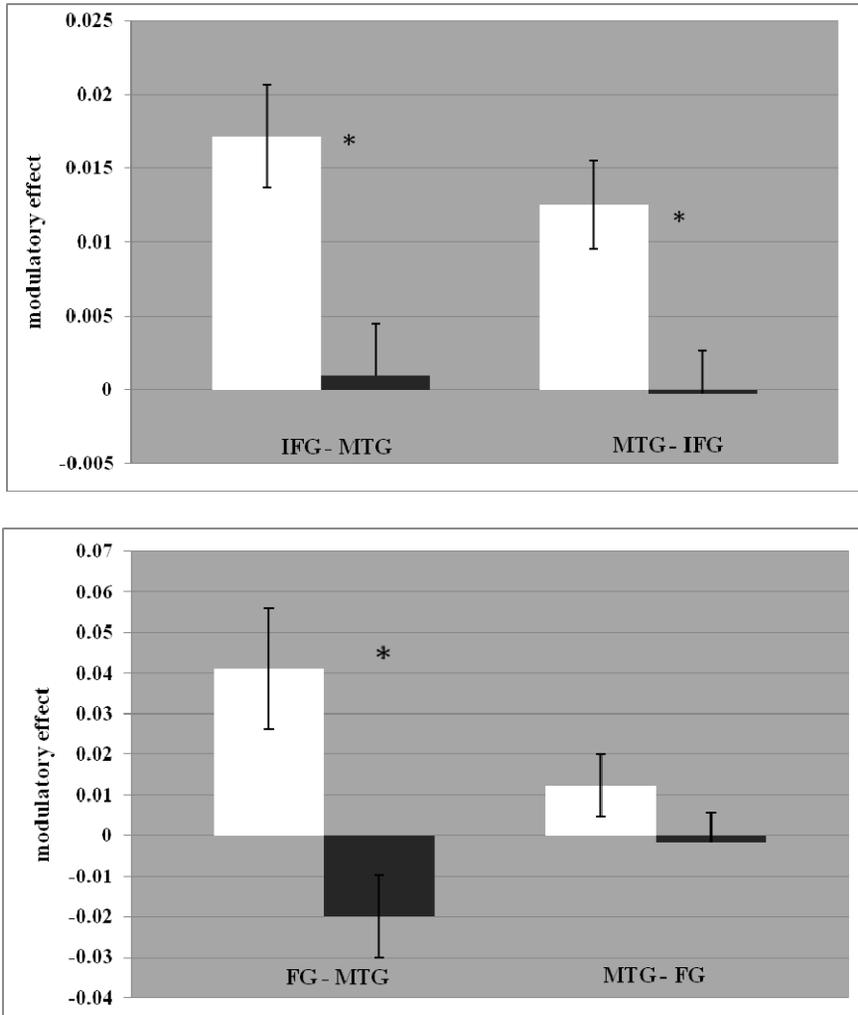
	Intrinsic
IFG→IPL	0.0342
IPL→IFG	0.0465
IFG→MTG	0.0795
MTG→IFG	0.0829
IFG→FG	0.0375
FG→IFG	0.0668
IPL→MTG	0.0395
MTG→IPL	0.0363
IPL→FG	0.0292
FG→IPL	0.0427
MTG→FG	0.0336
FG→MTG	0.0461

**Table 3:** Modulatory effects between regions of interest for the visual semantic tasks. Significant modulatory effects are in bold (\*: corrected for 2 comparisons based on apriori hypotheses).

	Related	Unrelated
IFG→IPL	0.0132	0.0025
IPL→IFG	0.0088	0.0023
IFG→MTG*	<b>0.0204</b>	0.0110
MTG→IFG*	<b>0.0145</b>	0.0113
IFG→FG	0.0175	0.0053
FG→IFG	0.0506	0.0133
IPL→MTG	0.0035	0.0013
MTG→IPL	0.0115	0.0034
IPL→FG	0.0016	0.0001
FG→IPL	0.0271	-0.0011
MTG→FG*	0.0139	0.0054
FG→MTG*	<b>0.0582</b>	-0.0019



**Figure 5:** Connections which are differentially modulated by the related versus the unrelated condition during Chinese semantic processing. Arrows indicate significant effects ( $p < .025$ ).



**Figure 6:** Connections which are differentially modulated by the related versus the unrelated condition. Bar charts are presented for the related (white bars) and the unrelated (grey bars) conditions. Significant modulatory effects on the connection between left inferior frontal gyrus (IFG) and left middle temporal gyrus (MTG), and from left fusiform gyrus (FG) to MTG. \* indicates significant difference between the related and unrelated condition.

In addition, we calculated a 2 condition (related, unrelated) x 2 direction (FG-MTG, MTG-FG) ANOVA. The main effect of condition was significant,  $F(1, 24) = 8.190$ ,  $p = .009$ , with stronger effects for the related compared to the unrelated condition. The main effect of direction was not significant,  $F(1, 24) = 0.156$ ,  $p = .696$ . The interaction was significant,  $F(1, 24) = 6.656$ ,  $p = .016$ , showing that the effect of condition was stronger for the FG-MTG connection as compared to the MTG-FG connection. Figure 6 shows a significant difference ( $p$  corrected for 2 comparisons  $< .05$ ) between the related and unrelated condition for the FG-MTG connection ( $t(24) = 2.824$ ,  $p = .009$ ), but a non-significant difference for the MTG-FG connection ( $t(24) = 2.155$ ,  $p = .041$ ). There were no significant differences between the related and unrelated condition for all other connections.

In the related versus unrelated condition, there were significantly negative correlations ( $p$  corrected for 2 comparisons  $< .05$ ) with reaction times on the connection from IFG to MTG ( $r(24) = -.48$ ,  $p = .014$ ), and on the connection from MTG to IFG ( $r(24) = -.53$ ,  $p = .007$ ). There were no significant correlations with accuracy for the related versus unrelated condition. There were no significant correlations between behavioral performance (reaction time/accuracy) and modulatory effects for the related or the unrelated condition.

## 5. Discussion

The current study examined effective connectivity during semantic processing in Chinese adults. Participants were asked to determine if pairs of characters were associated in meaning. We used conventional fMRI analysis methods to identify brain areas activated in left inferior frontal gyrus (BA 45, 47), left posterior middle temporal gyrus (BA 21), left fusiform gyrus (BA 37), and left inferior parietal lobule (BA 40) in the visual semantic task (Figure 2). We then used dynamic causal modeling (DCM) to examine the interaction among these four brain regions (Figure 5). The fusiform gyrus (FG) served as a process of visual word forms. Both the inferior frontal gyrus (IFG) and the posterior middle temporal gyrus (MTG) were considered as important nodes in the semantic network. There were three significantly effective connections within this network: the connection from IFG to posterior MTG, the connection from posterior MTG to IFG, and the connection from FG to posterior MTG in the left hemisphere.

The first major finding of our study was regarding top-down influences from left IFG to left posterior MTG. Previous English studies have suggested a ventral semantic system connecting left ventral IFG and left posterior MTG, via the inferior fronto-occipital fasciculus (Duffau et al. 2005). Our findings in Chinese adults are consistent with previous functional connectivity studies, showing that the activity in left IFG

predicts activity in left posterior MTG in language tasks (Stamatakis et al. 2005). The role of left IFG has also been suggested to support generation of semantic associations between words (Addis & McAndrews 2006) or to select semantic representations from a posterior region in MTG (Badre et al. 2005). Thus, in the context of our study, the significant modulatory effect from left IFG to left posterior MTG suggests that the frontal region may be involved in a search of posterior representations to seek for existing semantic associations stored in verbal semantic memory.

The second major finding was significantly modulatory connection from left posterior MTG to left IFG. Two recent studies propose that the left posterior MTG was emerging through fast bottom-up mechanism, triggering by a cue to activate associated representations from semantic memory automatically, and this automatic retrieval processing was mediated by left ventrolateral frontal cortex (Badre et al. 2005, Badre & Wagner 2007). The role of left posterior MTG is involved in semantic information (Montaldi et al. 1998) or in providing more efficient access to semantic representations (Chou et al. 2006a). In addition, previous studies have shown that the ventral region of left IFG is involved in semantic tasks that require retrieval of semantic representations (Fiez 1997) or generation of semantic associations between items/words (Addis & McAndrews 2006). Altogether, task-relevant representations may be retrieved in semantic memory in the temporal region, providing relevant associations for IFG to perform retrieval. Thus, the significant modulatory effect from left posterior MTG to left IFG suggests that the posterior MTG may activate the task-relevant representations to provide the retrieval which is mediated by left IFG.

Finally, the significant connection from left FG to left posterior MTG is thought to be associated with bottom-up orthographic influences on semantic representations. Previous English studies have suggested the fusiform gyrus (FG) involved in visual word form recognition (Sonty et al. 2007). Another study also proposes that the FG may affect the visual-orthographic word recognition, and the middle temporal regions may be engaged by lexico-semantic processing (Richlan et al. 2009). Moreover, the left MTG has been suggested to play a role in storing conceptual features that are associated with lexical representations (Hickok & Poeppel 2007, Martin 2007). Thus, in our study this significant connection from left posterior FG to MTG implies that the orthographic word forms are encoded in FG then sent to the posterior MTG for linking with their semantic representations (Mesulam 1998, Booth et al. 2002a).

In the theoretical ground, it is important to discuss whether reading in Chinese is unique in terms of brain activity and connectivity as compared to English. This question, however, is beyond the scope of this study, as addressing this issue requires researchers to directly compare Chinese with English findings in the same study. In the future, parallel designs across scripts will be helpful to draw a substantial conclusion in this

issue. A second point to make is the lack of effective connectivity between inferior parietal lobule and other regions. The null effect may be due to the situation that in this study the related pairs were not arranged in a continuous variable according to association strength. This parametric manipulation allows for a more precise determination of the role of the left inferior parietal lobule in processing meaning (Chou et al. 2009). A third point is regarding top-down versus bottom-up processing. Our definition was based on the use of the fusiform gyrus as the input to calculate bidirectional connections (Cao et al. 2008) and of the top-down modulation from the inferior frontal cortex (Bitan et al. 2006).

In conclusion, four critical brain regions were identified in Chinese semantic processing, and interactions between these brain regions were found in the DCM analysis. The first significant connection from left IFG to left posterior MTG suggests the top-down modulation, showing that IFG may be involved in retrieving semantic knowledge stored in the posterior MTG. The second significant connection is from left posterior MTG to IFG, suggesting that MTG may provide the task-relevant representations for IFG to perform retrieval. The final significant connection is from left FG to left posterior MTG, suggesting that the orthographic processing in fusiform cortex may influence the semantic representations in posterior MTG during visual semantic judgments. These findings are taken as evidence to show how different brain regions interact during semantic processing in Chinese adults.

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## 中文成人語意處理的腦區間的交互影響

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本研究利用功能性磁共振造影 (fMRI) 及動態因果推論模型 (DCM)，探討中文語意處理的神經機制，並計算不同腦區之間的動態連結。中文成人需要判斷以視覺呈現的中文字對在意義上是否相關。本實驗採用兩種刺激字對，分別是語意相關組與語意無關組。在行為表現上，語意相關組的反應時間顯著地快於無關組。在功能性磁共振造影結果，針對語意相關組與對照組的差異得到較大的活化區，分別位於左腦下額葉 (IFG, BA 45, 47)，左腦中顳葉 (MTG, BA 21) 及左腦梭狀回 (FG, BA 37)；而針對語意相關組與無關組的差異，得到較大的活化區在左腦下頂葉 (IPL, BA 39, 40)。在動態因果推論模型推論出的有效性連結，發現從左腦下額葉到左腦中顳葉的顯著調節效果 (modulatory effects)，推論為左下額葉負責從上到下提取語意表徵的歷程。同時，從左腦中顳葉到左腦下額葉的顯著調節效果，推論左腦中顳葉負責提供語意記憶中相關的表徵連結，協助左下額葉進行提取。最後，從左腦梭狀回到左腦中顳葉的顯著調節效果，推論左梭狀回將字形訊息藉由從下到上的歷程，傳送至左腦中顳葉處理語意表徵訊息。本研究的結果顯示成人進行中文語意處理的腦區間的動態交互作用。

關鍵詞：語意，字形，有效連結