

Modulation of Neural Connectivity During Tongue Movement and Reading

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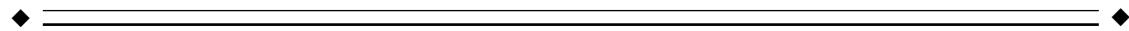
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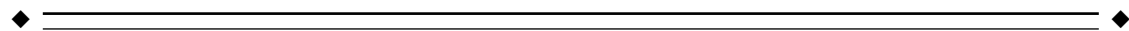
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Abstract: In a functional magnetic resonance imaging (fMRI) study, a novel connectivity analysis method termed within-condition interregional covariance analysis (WICA) was introduced for investigation into brain modulation during tongue movement and reading Chinese pinyins and logographic characters. We found that performing a horizontal tongue movement task generated a specific brain module with hierarchical orders of neural computation. Such functional modularity was further examined during both overt and silent Chinese reading tasks. Our results showed that overt pinyin reading was associated with the following distributed regions involved in tongue movement: the primary motor cortex (M1), the supplementary motor area (SMA), Broca's area, and Wernicke's area. Furthermore, we have used the WICA and demonstrated task-dependent covariance patterns that are strongly associated with the M1 mouth/tongue region, in which the Broca-Wernicke pathway is implicated in a meaning access procedure based on assembled phonology, while the SMA-Broca pathway is implicated in a meaning access procedure based on addressed phonology. Our functional connectivity analysis of the neural pathway involved in language processing may provide a basis for future studies of the dynamic neural network associated with language learning and reading in both developmental and disease conditions. *Hum. Brain Mapping* 18:222–232, 2003. © 2003 Wiley-Liss, Inc.

Key words: brain circuits; fMRI; motor function; Chinese learning; Pin-Yin; phonological processing



INTRODUCTION

Motor function of tongue movement plays an important role in the control of a variety of human be-

haviors such as mastication, swallowing, whistling, and speech. The representation of tongue movement in the primary motor cortex (M1) was documented by direct neurosurgical stimulation on the exposed scalp in humans [Foerster, 1936; Penfield, 1938]. In these early studies, the function of tongue movement was mapped onto the inferior part of the M1 near the lateral fissure. Recently, functional neuroimaging, including both positron emission tomography (PET) and fMRI, has shown consistent findings [Grafton et al., 1991; Wildgruber et al., 1996]. However, in neuroimaging studies, a tongue movement task may not just activate the M1 but also involve extensive cortical and subcortical structures [Corfield et al., 1999]. Although

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a potential cortical–subcortical interaction was shown during tongue contraction for the control of respiratory activity [Corfield et al., 1999], the cortical interconnections have not yet been demonstrated for tongue movement involved in the processes of language learning and speech, especially in terms of functional connectivity.

While the human language system critically depends upon distributed regions within the left cerebral hemisphere, very little is known about the connectivity of these cortical regions [Di Virgilio and Clarke 1997]. As shown in lesion studies, deficits in speech production seem to be associated with the posterior portion of the inferior frontal gyrus, Broca's area (corresponding to Brodmann's areas [BAs] 44 and 45), whereas deficits in language comprehension are associated with the temporoparietal junction, Wernicke's area (BA 22, BA 39, BA 40) [Geschwind, 1965]. However, how these brain areas are functionally organized during language processing remains unclear [Horwitz et al., 1998; Pugh et al., 2000]. We propose that although speech or reading aloud involves different aspects of tongue muscle activities (e.g., orientation, tension, sensory feedback, etc.), it may embody a common module or computation consisting of the M1 mouth/tongue region, Broca's area, Wernicke's area, and the SMA. Based on the effective connectivity concept [Friston, 1994; Horwitz et al., 1992], the goal of the present study is to first establish interregional covariance analysis approaches, focusing on functional modularity instead of individual activated regions specific to a tongue movement task. Then, we use these approaches to further examine brain activation during various Chinese reading tasks.

In the past few years, the neural mechanism underlying orthographic and semantic processing of written Chinese has been investigated in a number of brain-mapping studies [Chee et al., 2000; Chen et al., 2002; Fu et al., 2002; Hsieh et al., 2001; Kansaku et al., 1998; Kuo et al., 2001; Tan et al., 2000, 2001a]. The neuro-anatomical basis for phonological processing of the Chinese language, however, remains far from clear [but see Chen et al., 2002; Fu et al., 2002; Tan et al., pages 158–166, this issue]. In Chinese, two kinds of visual forms can be used to decode speech: logographic characters and phonemic pinyins. Logographic characters have a square configuration that maps onto monosyllables rather than phonemes in the spoken language. Thus, they have to be read aloud by recourse to the direct retrieval of lexical level phonological units represented in the brain. In the psycholinguistic literature, this kind of phonology is termed

addressed phonology. Contrary to Chinese characters, pinyins use alphabetic letters as sound symbols (for Chinese characters) that follow letter-to-sound conversion rules. Therefore, pinyins can be read out by assembling fine-grained phonemic units, *assembled phonology*. For instance, to express “thank you,” Chinese students may use logographic characters 谢谢 or pinyin “xiexie.” The two visual/graphic forms present a sharp contrast in their mapping units at the phonological level.

In Mainland China, all school-age children (starting from age 6 to 7 years or earlier) are required to master pinyin knowledge in the first 8 weeks of grade 1. Although pinyin may no longer be used as an aid for character learning by adults, it is still broadly used in looking up a Chinese dictionary, in computer keyboard typing for inputting Chinese characters, and in name-spelling for overseas Chinese from the Mainland. Cognitive studies of reading development indicate that children's pinyin knowledge is a powerful predictor of their reading ability [Siok and Fletcher, 2001]. Neuroimaging research has implicated brain regions common to both visual forms as well as brain regions in which activation is dependent on word forms [Chen et al., 2002; Fu et al., 2002]. Pinyin is taught as an assistance tool in Chinese language education for learning new words and their pronunciations.

The present fMRI experiment intended to examine distributed cortical regions involved in reading aloud of pinyins (and Chinese characters) and their interconnections in the neural network. The involvement of overt vocal response in fMRI experiments may produce profound motion artifacts that are difficult to control. Therefore, our current work took advantages of fMRI study using a tongue movement task to control motion effects in pinyin speech tasks, given some degree of similarity among these tasks. In addition, speech-related brain modulation may be built on a common neural computation associated with simple tongue movement.

METHODS

Subjects and tasks

Eighteen healthy subjects (6 men, 12 women; 22–54 years old, right-handed) were recruited. Six of them participated in both pinyin and tongue movement fMRI scans. These six subjects all are China-born females (native language: Mandarin; age: 27–43 years; years of living in the United States: 1–3.5 years; edu-

cation level: college plus; years of learning English: 10 years plus at the time of participation). The remaining 12 subjects participated only in tongue movement fMRI study.

Horizontal tongue movement task

During the tongue movement task, the participant was instructed to move the tongue with the mouth slightly open. The task performance was guided by visual cues switching between “◀▶” (for repeatedly moving tongue *left* and *right*) and “▲▼” (for repeatedly moving tongue *forward* and *backward*), which were randomly presented for 200 msec. The task lasted for 60 sec (or 30 sec for the subjects participating in Chinese reading tasks) and repeated twice in an fMRI run interleaving with control tasks.

Chinese word and pinyin reading tasks.

Both reading aloud and silent reading tasks were used. The Chinese words or pinyins were selected from the Chinese language textbook for Grade 1 of the primary school in China. The following five tasks were devised: (1) Reading aloud of pinyins without meaning (e.g., xiji, which consisted of two single-tone syllables that could not form a two-syllable word). (2) Reading aloud of pinyins that have varied tones and could form a legitimate word of meanings (e.g., xiao3niao3, meaning *little bird*. The number following each pronunciation represents tone). (3) Reading aloud of Chinese orthographic words that are composed of two characters (e.g., 闹钟 meaning *clock*). (4) Silent reading of Chinese orthographic words (e.g., 桌子 meaning *table*). (5) Silent reading of pinyins that have varied tones and could form a legitimate word of meanings (e.g., da4xiang4, meaning *elephant*.)

The exposure duration of a stimulus in the overt reading task was controlled by the experimenter according to the time required for reading out the stimulus. A stimulus for silent reading was presented for 1.5 sec. Each reading task was repeated twice (with different words or syllables) in an fMRI run and interleaved with control tasks.

Control tasks

Frequently used visual symbols, such as “<< ¶” were used for the partial control of visual effect. During the control scan, subjects passively viewed two symbols exposed for 1.5 sec on each trial. A fixation

task with a crosshair (+) presented at the screen center was used as an experimental resting baseline.

fMRI protocol and image acquisition

The experiment was performed on a 3.0 Tesla GE/Signa MRI whole-body scanner (GE Medical Systems) with a dome-shaped head coil (MRI Devices, Inc.). An EPIBOLD sequence was used for functional scanning of 22–24 axial slices covering the whole brain (TR = 2.5 sec (or 3.0 sec for the study of tongue movement only), TE = 25 msec, flip-angle = 90 degrees, FOV = 240 mm, matrix size = 64 × 64, and slice-thickness = 6 mm without gap). For each subject, a 3D fast SPGR pulse sequence (flip angle = 25 degrees; FOV = 240 mm; matrix size = 256 × 256; slice thickness = 1.5 mm) was used to acquire anatomical MRIs for structural co-registration of functional images. A spin-echo sequence (TR = 800 msec; TE = 7.9 msec; matrix size = 256 × 256) with the same FOV and slice thickness as those in functional scanning was also used to acquire T1-weighted MRIs for mediating the above co-registration.

During the fMRI experiment, the subject was positioned supine inside the magnet and the head was restricted in the coil using cushion padding for reducing motion artifact. The instructions and visual stimulation were delivered to a mirror screen mounted on the head coil by back projection using a LCD projector. An MRI-compatible auditory system (Resonance Technology, Inc.) with stereo earphones and a microphone (connected to a digital voice recorder) was used for recoding subjects' vocal responses, which were used to constrain the temporal analysis of brain activation.

Six fMRI runs were conducted for the subjects performing both tongue movement and Chinese reading tasks in a time-locked block design. Each subject was given instruction on the screen before the beginning of each run. Each run lasted for 2 min consisting of four task blocks: two target task (e.g., reading aloud pinyins of semantics) blocks plus two control task (e.g., viewing visual symbols) blocks in a random order. For the subjects in the study of tongue movement only, one run was conducted consisting of four time-locked blocks: two tongue movement task blocks and two fixation control blocks in a random order. The fMRI run lasted for either 2 min (for TR = 2.5 sec) or 4 min (for TR = 3.0 sec).

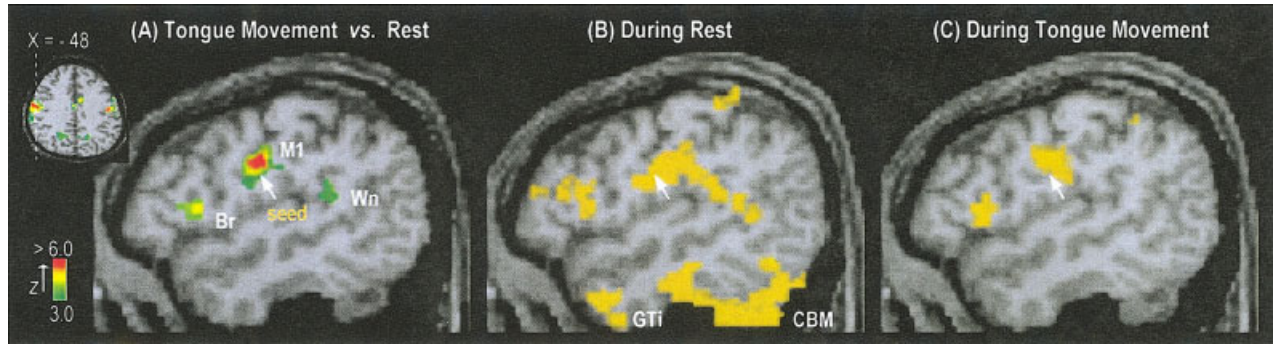


Figure 1.

Functional maps (colored) overlaid on the anatomical MRI of a sagittal brain section (Talairach coordinate $x = -48$). **A:** The mapping of fMRI signal variance changes over two experimental conditions, i.e., tongue movement vs. resting condition. The color bar encodes Z scores, indicating the significant level (with a threshold at $Z > 3.0$ and pixel clustering size = 27) of the mean signal changes. The inlaid presents an axial ($z = 27$) activation map for specifying the location of the sagittal brain section. **B,C:** The mapping of interregional covariance with seeding reference (ar-

row) at the M1 mouth/tongue region *within* an experimental condition, i.e., *tongue movement* (B) or *Rest* (C). The seeding procedure consists of (1) correlating the fMRI time series of all the voxels with that in the M1 (averaged over voxels in the M1 having Z scores larger than 3.0), and (2) thresholding the voxel-wise correlation [at $cc > 0.48$, $P < 0.05$ ($N = 20$)] by color-coding. Br: Broca; Wn: Wernicke; CBM: cerebellum; GTI: inferior temporal gyrus.

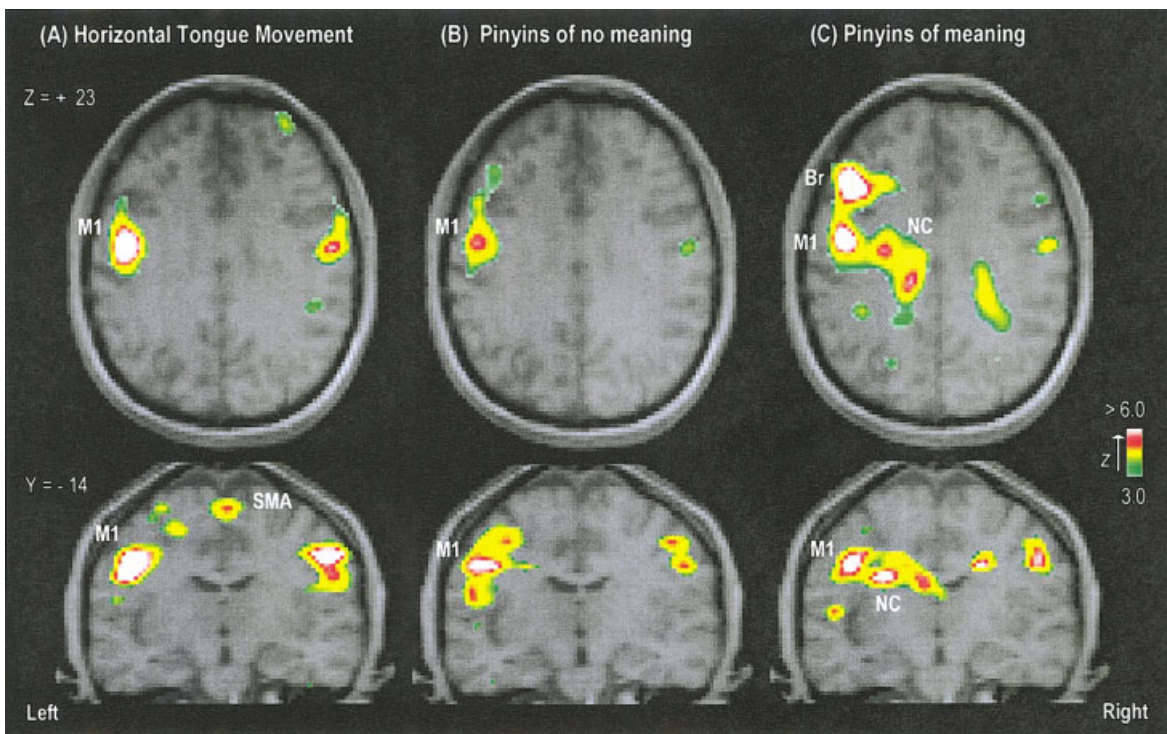


Figure 2.

Comparison of the task-specific activation (vs. the visual control) patterns during **(A)** horizontal tongue movement, **(B)** reading aloud of pinyin without semantics, and **(C)** reading aloud of pinyin with semantic meaning. Both the functional and anatomical images

were normalized to a standard image from one subject by scaling, transformation, and interpolation, and then were averaged across the six subjects participating in the Chinese pinyin speech experiment. NC: caudate nucleus.

Image processing and data analysis

Correction for motion artifact

The fMRI images were first co-registered and aligned using a motion correction program in MEDX and in-house programs coded in MATLAB for linear de-trending [Liu et al., 1999]. The head motion artifact could be a serious problem due to overt reading response. It is important to set strict criteria for eliminating motion artifact from analysis (images rejected if the shift > 0.25 pixel size). We have employed robust methods for motion detection and correction, including non-intensity weighted center of mass and navigator-echo methods, and other techniques used in fMRI language studies [Barch et al., 2000; Phelps et al., 1997; Rosen et al., 2000]. Further strategies used in event-related fMRI processing have been explored [Birn et al., 1999; De Zubicaray et al., 2001; Huang et al., 2002; Palmer et al., 2001].

Mapping brain activation and defining functional clusters

The brain response was first determined individually by voxel-wise t -tests comparing the mean of fMRI intensities between different conditions using a spatial clustering technique [Xiong et al., 1995]. Comparisons were focused on the patterns of brain activation during the tongue movement task and Chinese pinyin speech tasks by averaging the fMRI BOLD response over two same task blocks (vs. visual control blocks) in an fMRI run. The resulting t -score maps were transformed to Z-score maps smoothed using a Gaussian filter (FWHM = 4.5 mm). The statistical parametric maps were then further standardized into Talairach space [Talairach and Tournoux, 1988] using spatial normalization [Lancaster et al., 1998] and averaged over subjects before applying a clustering threshold (a clustering size of 27 voxels with 3-D searching) and a Z-threshold corresponding to a significance level of $P < 0.01$ (Fig. 1A, 2). Functional clusters defined on the averaged functional maps were quantified and used for region of interest (ROI)-based covariance analyses.

Analyses of functional/effective connectivity

The analysis procedures have been described in previous reports on temporal analyses of sensorimotor function [Liu et al., 1999, 2000; Qin et al., 1999] using an fMRI intensity normalization procedure [He et al., 2001] based on a Monte Carlo simulation [Ogawa,

1993]. Briefly, the BOLD signal, b , as a function of time was obtained by normalizing the whole series of MRI signal to the mean of a baseline. The temporal normalization could be done through a log transformation, given the absolute BOLD signal values $|b| \ll 1$ and the mean of BOLD signal during the resting baseline is close to zero [He et al., 2001]. Based on the normalization procedure, we proposed a within-condition inter-regional covariance analysis (WICA) method to examine modulation of neural connectivity. This method consists of three procedures for analyzing different aspects of functional connectivity.

1. *Seeding procedure for analysis of temporal covariance.* WICA correlates the normalized time series, $b(n)$, just within a task time period. This procedure is different from most correlation analyses in which the reference series used for correlation is either a boxcar function or an MRI time series (without temporal normalization) across both task and control conditions [Bandettini et al., 1993]. It has the advantage that it is independent of experimental design effects. The voxel-by-voxel covariance of the time series between two brain areas, namely, BA_a and BA_b , was calculated according to a procedure described previously [Liu et al., 1999]. When a task induces activation signal both at BA_a and BA_b , the relative within-condition covariance between these two regions could be determined as the sum of covariances during the rest (or the baseline) and during a task. Therefore, the calculated relative covariance (or functional connectivity) indicates that the resting covariance between BA_a and BA_b (which has been suggested to reflect the intrinsic pathway between BA_a and BA_b or their anatomical connectivity [Biswal et al., 1995]) can be modulated by a task. If either BA_a and BA_b does not show task-related activity changes as measured by BOLD signal, the covariance between these two regions is zero, meaning that there is no modulation on their connectivity even though these two regions could be anatomically connected.

In the analysis of functional brain circuits associated with the M1 mouth/tongue region, for example, we can specify the M1 as BA_a , which is used as a seeding ROI determined by statistical parametric mapping described above (Fig. 1A), and any other voxel as BA_b so as to do the whole brain voxel-by-voxel covariance analysis (Fig. 1B,C). The voxels having a correlation above a significance level were (color) mapped on group

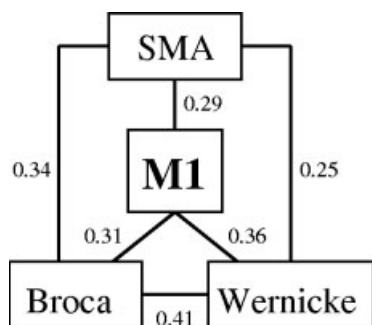


Figure 3.

A functional module consisting of the supplementary motor area (SMA), the M1, Broca's area, and Wernicke's area in the language dominant (left) side of brain. This module was specific to an experimental resting condition; the number around each line indicates interregional correlation (i.e., normalized covariance of fMRI signal changes between the regions of interest [ROIs] defined and measured on the activation maps, Fig. 1A).

average data with a threshold of the same P level used in the individual data [$cc > 0.48$, $P < 0.05$, ($N = 20$)].

2. *ROI-based analysis of effective connectivity.* Functional modulation of brain circuitry was modeled through cross-correlation analysis of BOLD signal or activation index [Liu et al., 1999, 2000] over two task blocks and six subjects performing both pinyin and tongue movement tasks. For simplicity, in the current study we limited our analysis in a basic unit or module involved in tongue movement (Fig. 3). The averaged BOLD signal for each task block was individually calculated for each ROI in a module defined both anatomically and functionally on the activation maps. The between-ROI cross-correlation was then calculated for all the tongue movement and Chinese reading tasks (Fig. 4) and the significance level ($P < 0.05$, $N = 6 \times 2 = 12$) of the correlation between activation magnitudes was determined by one-tail t -tests [Liu et al., 1999, 2000].
3. *Dynamic analysis of the time-dependence of connectivity.* The time courses of functional connectivity were shown by correlating the ROI-based BOLD signals for each individual image time point within a task block and comparing to a resting baseline of connectivity between two selected ROIs [Liu et al., 1999]. In the current study, Broca's and Wernicke's areas were selected for further analysis of the time-dependent changes of effective connectivity specific to the tongue movement task and the overt pinyin reading task

(Fig. 5).

For the correlational analysis of fMRI time series, autocorrelation could be a confounding factor [Purdon and Weisskoff, 1998]. We used a low-pass filter at a cutoff frequency of 0.2 Hz to reduce the autocorrelation of MRI signal and physiological noises such as cardiovascular effects. Note that the covariance was constrained by the above-threshold mean variance between two conditions. In addition, we used different task time lengths and different TRs (varying the temporal resolution) in the tongue movement experiment for eliminating autocorrelation.

RESULTS

The tongue movement task activated bilaterally the M1 mouth/tongue region [note that the M1 activation extended to the primary somatosensory cortex (S1)] and the SMA (Fig. 1A). Interestingly, significant activation was also found unilaterally in the left ($x = -48$) Broca's (primarily at BA 45) and Wernicke's areas. Seeded at the M1, WICA showed extensive covariance at the lateral cerebellum and inferior temporal cortex as well as Broca's and Wernicke's areas during the resting condition (Fig. 1B). However, during the tongue movement task only the Broca response covaried with the reference at the M1, even though both Broca's and Wernicke's areas showed the BOLD signal changes on the activation map (Fig. 1C).

Consistent activation and covariance patterns at these brain regions were found in all our subjects regardless of different TRs and different task lengths used. Based on these results, we defined a functional module simply consisting of the left M1, Broca, Wernicke, and SMA for the analysis of ROI-based covariance, in which no significant difference in connection strengths (as weighted by the normalized interregional covariance) was found for the resting baseline (Fig. 3). Consistent with the covariance map (Fig. 1B), the resting connectivity among those ROIs showed a non-specific pattern in contrast to a task-dependent connectivity pattern during tongue movement (Fig. 4A).

For comparison, we examined the pinyin reading results on the same ROIs involved in the tongue movement task (Figs. 1A, 2A). Reading single tone pinyins without semantic meaning induced a similar activation pattern but with strong lateralization as M1 activation shifted toward the left side (Fig. 2B). In addition, the activation area around the left M1 extended along both z and y directions, although the

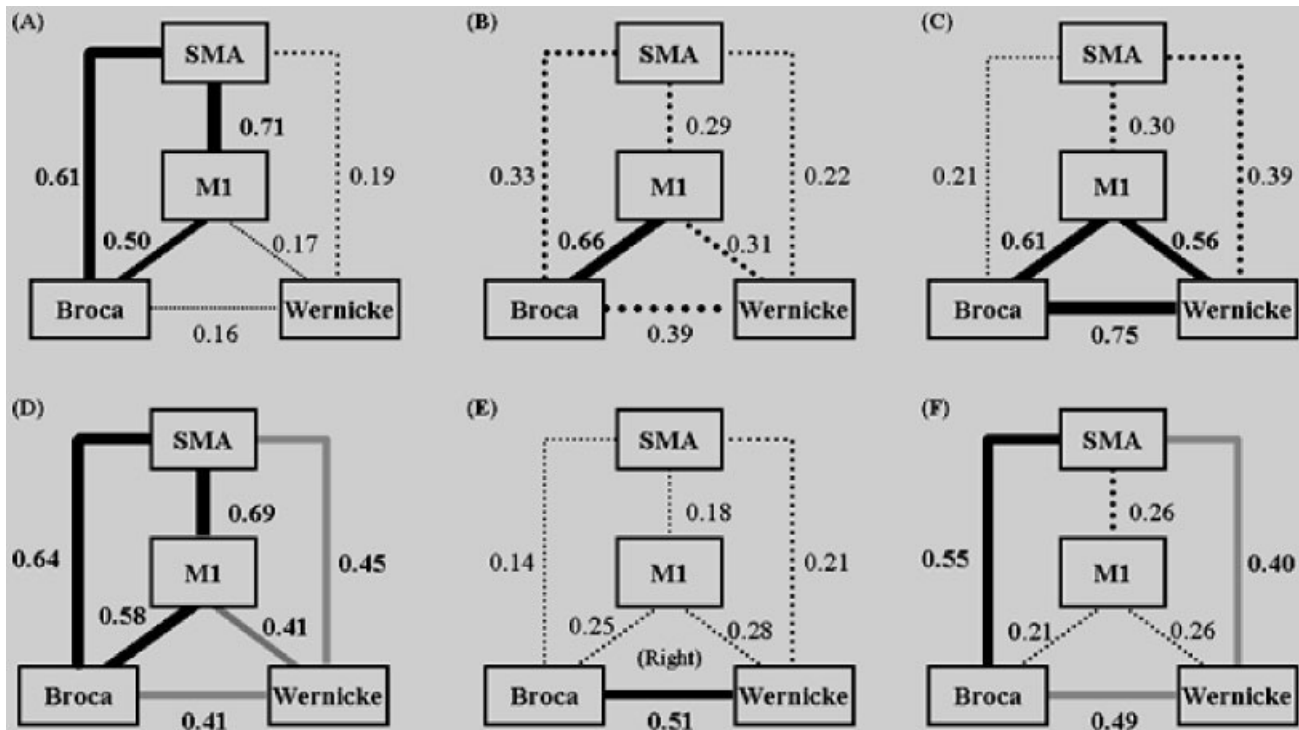


Figure 4.

Comparison of the task-specific modulation of neural connectivity based on a both anatomically and functionally constricted module (refer to Fig. 2). **A:** Horizontal tongue movement; **B:** Reading aloud of pinyins without semantics (e.g., *ji, xi*); **C:** Reading aloud of pinyins with semantic meaning [e.g., *xiao(3) niao(3)*, meaning *little bird*]; **D:** Reading aloud of Chinese orthographic characters [e.g., 闹钟, meaning *clock*]; **E:** Silent reading of Chinese orthographic characters [e.g., 桌子, meaning *table*]; **F:** Silent reading of pinyins of semantics [e.g., *da(4) xiang(4)*, meaning *elephant*]. The strength of ROI-based

functional connectivity was labeled by a number (normalized to a reference, i.e., the covariance between M1 and Br during the tongue movement task) and weighted by lines: (1) solid black (or gray) lines indicate the covariance above a significance level ($P < 0.05$, $N = 6 \times 2 = 12$) and larger (or less) than the reference; (2) dashed lines indicate the covariance below the significance level. Note that F shows the covariance at the right side of brain, since the brain activation during silent reading of Chinese characters was primarily localized at the non-dominant side.

activation intensity at the M1 slightly decreased. Importantly, reading aloud pinyins of semantic meanings induced much stronger activation at Broca's area as well as Wernicke's area, while M1 activation remaining almost the same (Fig. 2C). Furthermore, the caudate nucleus (NC) in the basal ganglia and other regions such as the lateral prefrontal cortex (BA 9), hippocampus, and lateral cerebellum (data not shown) were strongly activated during reading pinyins with semantic meaning. However, the SMA did not show activation during both pinyin reading tasks.

Figure 4 demonstrates differential modulation of the effective connectivity among the selected ROIs during each task. Specifically, all the tasks involving tongue movement were strongly associated with the M1 (Fig. 4A–D), while the silent reading tasks without

tongue movement were not associated with the M1 (Fig. 4E–F). Moreover, the tasks requiring semantic processing involved strong functional connection between Broca's and Wernicke's areas (Br-Wn) (Fig. 4C,F). In contrast to the resting connectivity (Fig. 3) that may represent anatomical connections among these regions, the task-specific interregional covariance may indicate how a task can modulate the neural connectivity. In other words, the task-specific modulation may indicate differential expression of the intrinsic fiber connection.

Finally, the task-specific connectivity between Broca's and Wernicke's areas was time-dependent (Fig. 5). The Br-Wn connectivity became enhanced during the progress of the pinyin reading task (with semantic meanings) as compared to the resting Br-Wn connectivity, implicating a dynamic association between the Br-

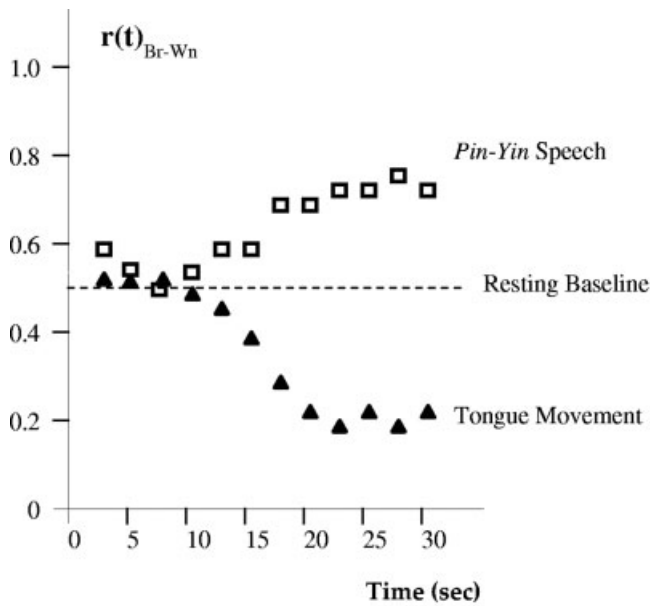


Figure 5.

Dynamic reconfigurations of functional neural pathway between Broca's (Br) and Wernicke's (Wn) areas during Chinese pinyin speech task (open squares) and horizontal tongue movement task (close triangles). Each task block lasted for 30 sec. For every image time point within the task period, the correlation, $r(t)$, was calculated across both (six) subjects and (two) task blocks in an fMRI scan ($n = 6 \times 2 = 12$). The dashed line indicates a baseline correlation averaged over the 12 image time-points during the resting condition.

Wn connection and language comprehension. On the other hand, there was a decrease in the Br-Wn connection during the tongue movement, implying a functional dissociation.

DISCUSSION

Brain modulation during tongue movement

While the motor function involves the M1, our horizontal tongue movement task also activated Broca's and Wernicke's areas, the brain regions primarily responsible for language processing. These results suggest a residual function of these regions for internal verbal monitoring during the task, given their either direct or indirect anatomical connections [Di Vergilio and Clarke, 1997]. However, covariance analyses using WICA showed a more specific temporal coherence of the fMRI signal among the M1, SMA, and Broca's but not Wernicke's area during the tongue movement task, although the resting covariance (with the M1)

extended to many other brain regions including Wernicke's area (Figs. 1B,C, 3, 4A). These results indicate that the Wernicke activation during tongue movement may not be associated with language function per se. This was consistent with the dynamic analysis that within the tongue movement task period there was a temporal dissociation in the Br-Wn connection (Fig. 5). In other words, the Br-Wn connection, which is known to be involved in language comprehension, may not be expressed in the simple motor task.

These data support an integrative view on the central nervous system that the brain function (e.g., the motor function of tongue movement) is implemented by different orders of neural computations and these different orders of computation are built upon hierarchical modules in the brain [Bressler, 1995]. This brain modularity challenges the one-to-one (i.e., function to structure) brain mapping concept, as shown in the "motor homunculus." Nevertheless, functional data can be influenced by processing strategy, task demand, and complexity, and so on. We proposed that there are at least three orders of neural computation in the current study of tongue movement at a system level, on which our connectivity analysis methods were developed.

1. The first order of neural computation is the composition of a module, i.e., the activated brain regions associated with a specific task as identified by fMRI mapping and their potential fiber connections. Such activated regions can be localized and quantified by the standard Talairach coordinates, the intensities and spatial extent (i.e., the volume size). However, this order of computation is not necessarily attributed to a single brain function as argued previously on the human prefrontal cortex [D'Esposito et al., 1998].
2. The second order of neural computation is the interaction or connectivity in the components of a module consisting of distributed brain regions activated by a specific task. While this order of neural computation is constrained by anatomy, the interaction is task-dependent (Fig. 4). The function of a brain module may not be mediated through individual regions in a module but through the information flow or connectivity between them. For example, the control of tongue movement is mediated through the M1-SMA-Br connections but not through the Br-Wn connection in the defined module, even though both Broca's and Wernicke's areas were activated during the task.

3. The third order of neural computation is the dynamics or temporal processing of the interaction in a module. The moment-to-moment change or the time course of effective connectivity may reflect dynamic reconfiguration of brain circuitry for performing a specific task [Liu et al., 1999]. While both task and time-dependent changes as shown in fMRI interregional covariance data are intriguing (Fig. 5), it should be noted that, limited by the hemodynamic properties of BOLD signal and its temporal resolution, these changes may not directly reflect neuronal activity changes. However, for adaptive neural processes such as learning, these temporal changes may provide more information about functional association or dissociation with the structural components in a module during such processes [Buchel et al., 1999; Liu et al., 1999].

Brain modulation during chinese speech

Reading aloud of pinyins elicited extensive left lateralized activation in Broca's area. In particular, reading pinyins of meanings strongly activated regions involved in language comprehension and other cognitive processes such as memory (Fig. 2B,C). These regions included Wernicke's area, the basal ganglia, the inferior temporal gyrus, the hippocampus, and the lateral cerebellum. These results are consistent with recent findings of the processing of alphabetic English words and Chinese pinyins [Chen et al., 2002]. However, reading pinyins without semantic meanings did not involve the regions listed above but induced activations similar to that induced by tongue movement.

Interestingly, SMA activation was significantly decreased during reading aloud pinyins (with and without meanings) (Fig. 2B,C) as compared to tongue movement (Fig. 2A) and overt Chinese logographic word reading (data not shown in this article). This finding seems to indicate that the SMA is relevant to the production of the addressed phonological codes of Chinese characters. In a previous event-related fMRI study, the role of SMA in reading aloud of Chinese logographs has also been identified [Tan et al., 2001b].

Using the covariance analysis model developed in the study of tongue movement, we have further revealed differential functional connectivities in the brain that were task-dependent. In other words, each experimental task modulated the resting connectivity (Fig. 3) and formed a specific connectivity pattern or module (Figs. 4, 5). In sum, our results may indicate

the following two distinct processes associated with Chinese learning and speech production.

1. Modulation of the *M1-Br-Wn* pathways during overt Chinese (pinyin) reading involved a *meaning access* procedure based on assembled phonological codes, i.e., from phonological processing to semantic comprehension. This process was shown by the strength changes in the Br-Wn covariance during the tasks involving different levels of semantic retrieval effort [i.e., Fig. 4: (C) > (D) > (B)]. The strong association of the Br-Wn connection with the M1 mouth/tongue region is further established during the tasks involving tongue movement (i.e., during overt reading) (Fig. 4A–D). This association did not occur during tasks without tongue movement (i.e., during silent reading) (Fig. 4E, F). The learning process was also shown by the time-dependent changes in the Br-Wn connection within the pinyin reading task period (Fig. 5).
2. Modulation of the *M1-SMA-Br* pathways during reading aloud of Chinese characters involved a *meaning access* procedure based on addressed phonological codes, as seen from the enhanced M1-SMA-Br covariance in Figure 4D. For Chinese characters, their phonology must be generated by a direct look-up procedure after the appropriate lexical candidate has been accessed. This is totally different from the phonological processing based on the letter-to-sound conversion rules, which involves the M1-Br-Wn pathway. Thus, our results support the view of dual route models of visual word recognition [Coltheart et al., 2001].

In summary, the present fMRI study of overt reading of Chinese characters and pinyins indicates that functional connectivity is modulated by linguistic features of the tasks. Our long-term goal is to investigate neural processes of language learning and production in both normal and disabled (e.g., impaired processes in SMA-Br-M1 connections in stuttering) children. The methods developed in the current study should be helpful for achieving this goal.

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