

Language Lateralization of Chinese–English Bilingual Patients With Temporal Lobe Epilepsy: A Functional MRI Study

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Functional MRI was used to examine language lateralization of Chinese characters and English words associated with temporal lobe epilepsy (TLE) in Chinese–English bilinguals with left or right TLE. The results suggest that the neural basis of processing Chinese and English seems to be different, as normal controls demonstrated left hemispheric lateralization in reading English words but bi-hemispheric lateralization in reading Chinese characters. This difference in the neural bases of Chinese and English processing was found to affect the patterns in change-of-language processing associated with TLE. That is, whereas left-TLE patients were more likely than right-TLE patients to demonstrate a bi-hemispheric language involvement in reading English, both left- and right-TLE patients demonstrated primarily bilateral hemispheric involvement for reading Chinese characters.

Keywords: functional MRI, temporal lobe epilepsy, language, Chinese, bilingualism

It is generally recognized that language processing is primarily mediated by the left hemisphere (Beeson & Rapesak, 1998; D. F. Benson, 1985; Rasmussen & Milner, 1977). Whereas patients with temporal lobe epilepsy (TLE) may have some language deficits (Davey & Thompson, 1991; Hermann, Seidenberg, Haltiner, & Wyler, 1992; Howell, Saling, Bradley, & Berkovic, 1994; Sass et al., 1992), the phenomenon of left-hemisphere language dominance does not seem to be significantly changed by the disorder. Specifically, by using the intracarotid amobarbital procedure (IAP; Loring, Meador, & Lee, 1992), most TLE patients were found to have left-hemisphere language dominance, with an incidence ranging from 63% to 96% (Helmstaedter, Kurthen, Linke, & Elger, 1997; Loring et al., 1990; Risse, Gates, & Fangman, 1997; Springer et al., 1999). With the advancement of brain imaging techniques, Binder et al. (1996) compared the performance of TLE patients on the IAP with the results from functional magnetic resonance imaging (fMRI), using a semantic decision task, and found that most patients (18/22) demonstrated strongly left-lateralized language. Similar results have been reported in other fMRI

studies with different verbal paradigms, such as verb generation, verbal fluency, or sentence repetition (R. R. Benson et al., 1999; Desmond et al., 1995; Gaillard et al., 2002, 2004; Lehericy et al., 2000; Springer et al., 1999), and the majority of TLE patients showed left-hemisphere language dominance. The specific areas in the left hemisphere activated during fMRI were identified; these included the left inferior and middle frontal gyri, left premotor areas, left superior temporal gyrus, fusiform gyrus, and bilateral anterior cingulate gyri (Adcock, Wise, Oxbury, Oxbury, & Matthews, 2003; Binder et al., 1996; Springer et al., 1999).

Our current knowledge about the language lateralization in TLE patients is mainly drawn from a population whose first language is English. To our knowledge, no empirical data have yet been reported on the language lateralization of TLE patients whose first language is Chinese. Given that some empirical data suggested that the neural processing of Chinese characters and English words seems to be different (Chan et al., 2002; Cheung, Cheung, & Chan, 2004; Tan et al., 2000; Tan, Feng, Fox, & Gao, 2001; Tan, Liu, et al., 2001), we speculated that the pattern of language lateralization of Chinese-speaking patients with TLE would be different from that of English speakers. Specifically, our recent study on the spontaneous naming by Chinese-speaking patients with either left, right, or bilateral temporal lobe lesions (Cheung et al., 2004) showed that whereas patients with left-sided lesions demonstrated language impairment as expected, patients with right-sided lesions also demonstrated a similar degree of impairment when processing Chinese characters. As most studies on Caucasian patients reported language impairments after left, but not right, temporal lesions (Howell et al., 1994; Sandson & Albert, 1987), these findings were novel and led us to speculate that Chinese characters may be processed more bilaterally than English words. Each hemisphere may be involved in a coherent system of neural processing for Chinese characters. In fact, some fMRI studies have found that the processing of Chinese characters is associated with activations in both the left and right hemispheres, including the right inferior and middle frontal gyrus (Chan et al., 2002; Cheung et al., 2004; Tan, Feng, et al., 2001; Tan, Liu, et al., 2001; Tan et al., 2000). Because the language representation of Chinese- and English-speaking pa-

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tients with TLE may be different, the primary purpose of the present study was to examine, through fMRI, the language lateralization of Chinese-speaking patients with either left or right TLE.

Whereas left-hemispheric language lateralization is observed in most TLE patients, previous studies suggested greater variability of language lateralization in TLE patients compared with normal controls. Specifically, fewer than 2% of normal controls have right-hemispheric language lateralization (Loring et al., 1990; Mastronardi et al., 1994), but the proportion of either bilateral or right-hemispheric language lateralization in TLE patients can range from 4 to 37% (Brazdil, Zakopcan, Kuba, Fanfrdlova, & Rektor, 2003; Risse et al., 1997; Springer et al., 1999). A recent study (Adcock et al., 2003) further reported that left-TLE patients had a higher proportion of bilateral or right-hemispheric language lateralization (33%) than did right-TLE patients (all of whom had left-hemispheric language lateralization). More activation in the right hemisphere, specifically in the inferior (BA 20) and middle temporal (BA 21 and BA 37) gyri, was observed in the left-TLE patients when processing English. However, predominantly left hemisphere activation was observed in the right-TLE patients, similar to the activation pattern of the normal controls. The location of the lesion is thus found to have different effects on language lateralization, suggesting distinct neuroplasticity patterns of language processing in left- and right-TLE patients. Specifically, pathological involvement in the left hemisphere may lead to a more bilateral or right-hemispheric language lateralization (Adcock et al., 2003; Brazdil et al., 2003). It should be noted that this phenomenon is observed in the processing of English, which is primarily mediated by the left hemisphere. If Chinese is processed by both hemispheres, it is conceivable that TLE patients with Chinese as their first language will show a different pattern of language representation from the phenomenon observed with English-speaking TLE patients as a result of the pathological involvement. Therefore, the second purpose of the study was to examine the neuroplasticity of language processing in Chinese-speaking TLE patients and possible factors associated with the change.

Although we speculated that the differences in language representation in English and Chinese are due to the differences between the Chinese (a logographic language) and English (an alphabetic language) language systems, the diverse ethnic groups may be a confounding factor. In other words, the difference in representation may be due to the population (that is, Chinese vs. Caucasian participants). To examine this issue, the TLE patients in the present study were examined with an additional English word reading task in addition to the Chinese reading task. If their English processing was consistent with that of Caucasian samples, then ethnicity could effectively be ruled out.

Method

Participants

Twenty-one right-handed preoperative patients with TLE who were candidates for surgical treatment of refractory TLE were recruited from the Prince of Wales Hospital, Hong Kong. Thirteen of them had left TLE (mean age = 25.54 years, $SD = 10.34$), and the other 8 had right TLE (mean age = 27.50 years, $SD = 7.15$). No significant difference was found in their age of onset, $F(1, 19) = 0.07, p > .05$, or duration of illness, $F(1, 29) = 0.76, p > .05$. The pre-surgical evaluation of the epileptic patients included fMRI, video electroencephalogram (EEG) monitoring, compre-

hensive neuropsychological assessment, routine brain MRI, and the intracarotid amobarbital procedure (IAP). Information on the neurological history for each patient with TLE is presented in Table 1.

The normal control group consisted of 23 healthy, right-handed normal individuals with no previous history of neurological or psychiatric disorder. The normal participants and the two groups of TLE patients did not differ in age, $F(2, 41) = 1.78, p > .05$; level of education, $F(2, 41) = 3.35, p > .05$; or gender, $\chi^2(2, N = 44) = 3.43, p > .05$. Demographic information is summarized in Table 2.

All participants were native Chinese speakers who had begun to learn English before the age of 6 years and had at least 10 years of education in English. They all participated voluntarily and gave informed consent according to institutional guidelines. The study was ethically approved by the Clinical Research Ethics Committee of The Chinese University of Hong Kong.

Activation Paradigm

A block design with three epoch cycles was used. Each cycle consisted of a 20-s experimental task (covert word reading) and a 20-s visual fixation task. The stimuli were presented through a notebook computer with E-prime (Psychological Software Tools, Pittsburgh, 2002) and projected on a screen placed in front of the scanner bed. The participants viewed the stimuli through a reflective mirror fixed on the head coil. In the Chinese reading paradigm, the experimental stimuli consisted of 18 two-character Chinese words, with 6 words in each epoch. Participants were instructed to read the words covertly. The control stimulus consisted of a cross, similar in size to the Chinese characters displayed in the center of the screen continuously for 20 s in each epoch. Participants were instructed to visually fixate silently on the cross. In the English reading paradigm, similar procedures were used except that the presented words were in English. In order to make sure that the participants were able to see and read the words during scanning, they were instructed to read both the Chinese characters and the English words to the experimenter in a post-scanning session.

fMRI Data Acquisition

MRI was performed on a 1.5-tesla (1.5-T) MRI scanner (Gyrosan ACS-NT, Philips Medical Systems, The Netherlands) with a circularly polarized head coil. Before the fMRI activation tasks, 3-D Fast Field Echo T1-weighted (axial) high-resolution structural images covering the whole brain were acquired with a T1-weighted gradient echo sequence [repetition time (TR) = 30 ms, echo time (TE) = 5 ms, flip angle (FA) = 40°, slice thickness = 2 mm, acquisition matrix = 256 × 256]. This anatomical scan was later co-registered with the functional images.

The functional images were obtained with a gradient-echo, echo-planar imaging sequence [TE = 40 ms, TR = 2000 ms, FA = 90°, acquisition matrix = 128 × 128, field of view = 230 × 230 mm]. During each functional scan, a brain volume composed of 16 contiguous 5-mm-thick axial images covering the whole brain and parallel to the anterior-posterior commissure lines was obtained. Each functional scan consisted of 60 sequential echo-planar volumes, producing a total of 960 images for each participant.

fMRI Data Analysis

Data analyses were performed with the fMRI software package Brain-Voyager 2000 version 4.9.6 (<http://www.brainvoyager.com>, Brain Innovation, Maastricht, Holland). Before statistical analysis, motion corrections were conducted by aligning the time series of functional images for each slice to minimize the signal variations due to small movements of the participants during image acquisition. Gaussian filtering was applied in spatial domain (full-width-half-maximum [FWHM] = 4 mm). Linear trend removal and 0.016-Hz temporal high-pass filtering were also performed on

Table 1
Clinical Information on Temporal Lobe Epilepsy (TLE) Patients

Patient	Gender	Age (years)	Age at onset (years)	Duration of Epilepsy (years)	EEG	MRI	IAP
Left temporal lobe epilepsy							
1	M	28	20	8	L TL	Cavernous hemangioma in L TL	L
2	F	26	16	10	B FL	Low-grade glioma in L TL	L
3	F	40	10	30	L TL	L MTS	L
4	F	26	10	16	L TL	L MTS	L
5	F	13	12	1	L TL	DNET in L TL	L
6	F	23	13	10	L TL	Cyst in L TL	L
7	F	48	47	1	N	Low-grade glioma in L TL	L
8	F	14	12	2	L TL	L MTS	L
9	M	15	1	14	L TL	L MTS	L
10	F	27	4	23	L TL	L MTS	L
11	F	16	12	4	L TL	L MTS	L
12	M	23	19	4	R TL	Cavernous hemangioma in L TL	L
13	M	33	13	20	L TL	Low-grade glioma in L TL	L
Right temporal lobe epilepsy							
1	F	29	16	13	R TL	Small cyst in the R hippocampus	L
2	F	26	17	9	R TL	R MTS	B
3	M	30	20	10	R TL	Cyst in R TL	L
4	F	23	14	9	R TL	Lesion in the R middle TL, N hippocampus	L
5	M	28	6	22	R TL	R MTS	L
6	M	14	12	2	R TL	Astrocytoma in R anterior hippocampus	L
7	M	31	15	16	R TL	N hippocampus	L
8	M	39	25	14	R TL	Low-grade glioma in R anterior hippocampus	L

Note. MRI = magnetic resonance imaging; EEG = electroencephalogram; IAP = intracarotid amobarbital procedure; M = male; F = female; L = left; R = right; B = bilateral; TL = temporal lobe; FL = frontal lobe; MTS = mesial temporal sclerosis; DNET = dysembryoplastic neuroepithelial tumor; N = normal.

the data. The complete functional data set for each participant was then transformed into Talairach space. The individual brain image was aligned by rotation in the anterior commissure (AC)–posterior commissure (PC) plane, and coordinates of each brain were transformed to the coordinates of the Talairach brain (Talairach & Tournoux, 1988). Realigned images were then co-registered to the high-resolution structural images.

Data were analyzed both on the group and individual levels. On the group level, the activation pattern for normal controls was first obtained. A group-based general linear model (GLM) with fixed effects analysis was applied to compute the pooled activation maps, according to the boxcar model with the hemodynamic response (Boynton, Engel, Glover, & Heeger, 1996). The signal change between the experimental (i.e., either English words or Chinese characters) and control (that is, fixation) stimuli resulted in activation maps for Chinese characters and

English words, respectively. A three-dimensional statistical map was then generated for each condition, by associating each voxel with the F value for the specified set of predictors, and calculated on the basis of the least-mean-square solution of the GLM. The effect was only considered significant when the t value for group analysis was greater than 4.85 at $p < .05$ (corrected for whole-brain multiple comparisons with the Bonferroni method) and when the threshold of the activated regions consisted of at least 300 voxels. This strict threshold was applied to pooled activation maps to avoid Type I error associated with multiple comparisons. Clusters not reaching this statistical threshold were not displayed. Talairach-transformed group data were finally displayed on a volume-rendered brain of an individual from the cohort. Regions of interest (ROIs) were first identified in the normal control as areas having a significant activation in the frontal and temporal lobes in the group analysis for English words and Chinese characters, respectively (Table 3), which included the inferior frontal gyrus, middle frontal gyri, and precentral gyrus in the frontal lobe, the middle temporal gyrus, and the medial temporal gyrus in the temporal lobe. Similar group analysis was done for the patients' group except that the threshold of the ROIs consisted of at least 6 voxels.

On the individual level, the functional images were co-registered with each individual's own brain image in the identification of ROIs. The data were also analyzed with single-study GLM across the reading and fixation sessions, adopting an uncorrected threshold of $p < .0001$, corresponding to a t value greater than 4.

To assess the relative lateralization for language processing, we computed the total number of activated voxels in the ROIs identified as having a significant activation in the group analysis in the left (L) and right (R) hemispheres, respectively. A laterality index (LI) was calculated for each subject with the formula $[LI = (L - R)/(L + R) \times 100]$. A positive LI

Table 2
Demographic Information on Normal Controls and Epileptic Groups

Variable	Normal controls ($n = 23$)	Left TLE ($n = 13$)	Right TLE ($n = 8$)
	M (SD)	M (SD)	M (SD)
Age (years)	31.26 (8.81)	25.54 (10.34)	27.50 (7.15)
Education (years)	13.22 (2.84)	11.31 (2.71)	10.63 (3.02)
Gender (male/female)	14/9	4/9	5/3

Note. TLE = temporal lobe epilepsy.

Table 3

*Localization of Activated Regions in Reading English Words and Chinese Characters, Corresponding Brodmann Areas, Number of Voxels, and Their *t* Values for Normal Controls*

Regions activated	Brodmann areas	English words vs. fixation			Chinese characters vs. fixation		
		Coordinate	<i>t</i> (1334)	Voxel no.	Coordinate	<i>t</i> (1334)	Voxel no.
Left hemisphere							
Frontal							
Inferior frontal gyrus	44	(-52, +8, +19)	5.83	386			
	45	(-54, +14, +12)	2.20	353	(-50, +25, +4)	6.08	1,076
	46				(-47, +33, +8)	6.13	425
	47				(-47, +24, -1)	5.81	806
Middle frontal gyrus	9	(-50, +7, +27)	5.55	1,679	(-42, +6, +28)	6.22	560
	9	(-48, +12, +31)	5.03	591	(-40, +6, +33)	7.31	1,091
Precentral gyrus	44				(-56, +11, +6)	7.14	693
	6	(-45, 0, +32)	8.35	1,599	(-43, 0, +32)	6.40	764
Temporal							
Middle temporal gyrus	37	(-46, -58, -2)	6.11	453			
Superior temporal gyrus	22	(-54, +10, 0)	6.39	427			
Fusiform gyrus	20	(-34, -40, -19)	7.84	786	(-35, -39, -18)	11.04	1,007
	36	(-41, -40, -23)	9.61	583	(-41, -40, -23)	9.43	638
	37	(-40, -53, -15)	11.83	5,367	(-39, -53, -15)	12.65	5,551
Parahippocampal gyrus	36				(-36, -33, -22)	6.62	315
Occipital							
Lingual gyrus	17	(-18, -86, 0)	8.53	610	(-17, -84, +1)	8.79	613
	18	(-17, -78, -10)	10.51	3,311	(-16, -78, -9)	10.71	4,151
Fusiform gyrus	18	(-21, -83, -16)	11.74	478	(-21, -82, -17)	11.77	451
	19	(-31, -72, -13)	14.74	4090	(-30, -71, -13)	13.58	4,387
Right hemisphere							
Frontal							
Inferior frontal gyrus	45				(+50, +20, +5)	5.37	346
Middle frontal gyrus	46				(+45, +36, +24)	5.65	470
	9	(+45, +28, +30)	6.01	521	(+47, +28, +33)	6.01	1,704
Precentral gyrus	6	(+42, 0, +37)	6.90	465			
	9	(+39, +7, +34)	6.21	319			
Temporal							
Middle temporal gyrus	37	(+44, -58, 0)	6.57	350			
Fusiform gyrus	20	(+34, -39, -17)	6.27	928	(+34, -39, -18)	7.97	1,037
	37	(+38, -52, -14)	8.56	4,578	(+38, -52, -14)	7.92	4,872
Parahippocampal gyrus	36				(+32, -32, -18)	8.28	457
Occipital							
Lingual gyrus	17	(+19, -84, 0)	7.41	303	(+17, -83, +1)	10.13	496
	18	(+20, -76, -8)	8.58	3,298	(+18, -76, -8)	10.18	3,968
Fusiform gyrus	19	(+27, -71, -3)	5.87	229	(+28, -70, -2)	6.89	341

value (defined as $LI > 20$) indicates strong left-hemispheric language dominance, whereas a negative LI value ($LI < -20$) shows strong right-hemispheric language dominance. An LI between 20 and -20 was viewed as bilateral involvement.

Results

Language Lateralization of Chinese Characters and English Words in Normal Controls

Table 3 shows the localization of group activation produced by the covert Chinese character and English word reading tasks for the normal controls. For English word reading, activations were found primarily over the left frontal lobe (Figure 1A), including

the inferior frontal gyrus (BA 44, BA 45, and BA 9), the middle frontal gyrus (BA 9), the precentral gyrus (BA 6), and the left temporal fusiform gyrus (BA 20 and BA 37). Right frontal activation was only observed in the precentral gyrus (BA 6 and BA 9) and the right fusiform gyrus (BA 20 and BA 37). Activated regions on the left hemisphere observed in the present study were consistent with results from previous studies on the brain activations associated with processing English words in English speakers (Adcock et al., 2003; Binder et al., 1996; Springer et al., 1999).

Activation patterns were somewhat different during the covert Chinese character reading task, in which significant bilateral activations were found in the frontal lobe (Figure 1B), including the inferior frontal gyrus (BA 45), the middle frontal gyrus (BA 9), the

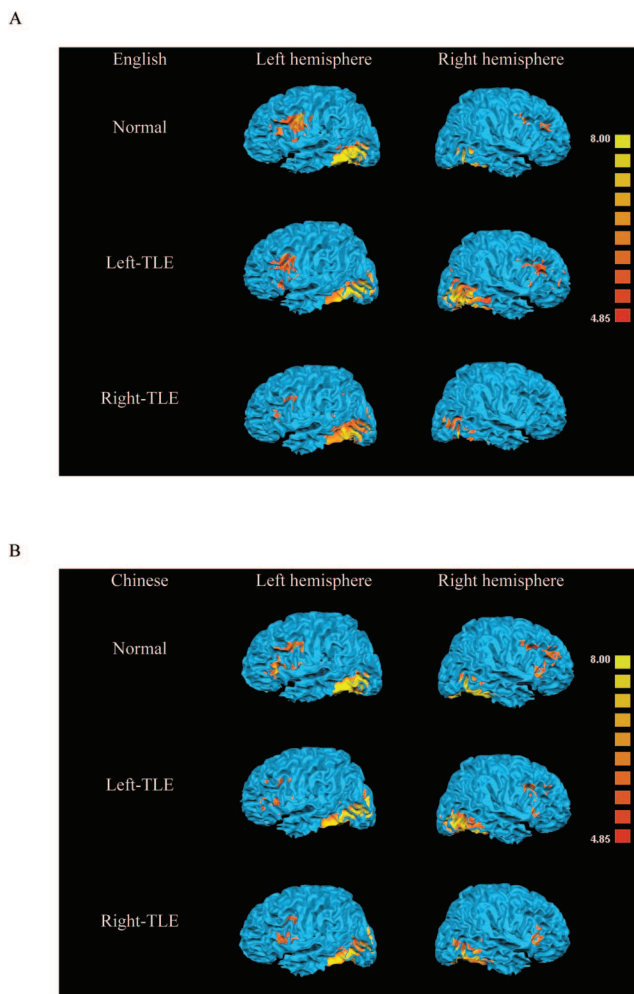


Figure 1. Activation associated with reading (A) English words and (B) Chinese characters versus fixation for normal controls and patients with left and right temporal lobe epilepsy (TLE), displayed at a threshold of $p < .05$, corrected for multiple comparisons. Both normal controls and the right-TLE patients showed activation predominantly in the left frontal and temporal lobes, whereas the left-TLE patients had a more bihemispheric activation in reading English words. For Chinese characters, symmetric activation in both hemispheres was found in the three groups of participants.

fusiform gyrus (BA 20 and BA 37), and the parahippocampal gyrus (BA 36) in the temporal lobe. In addition to these gyri, activation in the left frontal lobe, including the inferior frontal gyrus (BA 46 and BA 47), the middle frontal gyrus (BA 9), and the precentral gyrus (BA 44 and BA 6) was also found.

To determine language lateralization, we calculated a laterality index (LI) for each participant by summing the activated voxels in the ROIs in the left and right hemispheres, following the suggestion by Binder et al. (1996); the LIs are presented in Figure 2A and 2B. The majority of the normal control participants (70%) showed left-hemispheric lateralization in processing English (mean LI = 43.57, $SD = 38.82$). However, the distribution of language lateralization in processing Chinese characters seemed to be more heterogeneous (mean LI = 14.95, $SD = 53.05$). Twelve

(52%) control participants showed left-hemispheric lateralization, whereas 11 (48%) showed non-left lateralization, that is, either bilateral (5 cases) or right-dominant (6 cases). Overall, the mean LI for English words and Chinese characters was significantly different with the normal controls, $t(22) = -2.98, p < .01$. Therefore, the Chinese–English bilinguals in the present study demonstrated a similar distribution of left-hemisphere dominance for processing English as did English speakers. On the other hand, a higher percentage of participants showed bilateral or right-hemispheric language lateralization in processing Chinese characters.

Language Lateralization of English Words in Chinese–English Bilingual TLE Patients

Figure 1A shows the activation pattern of English words in the left- and right-TLE patients. Consistent with the normal controls, both groups of patients demonstrated frontal activation in the left hemisphere, including the inferior frontal gyrus (BA 9), the middle frontal gyrus (BA 9), and the precentral gyrus (BA 6). However, the left-TLE patients, unlike the normal controls and the right-TLE patients, had activation in the right middle frontal lobe (BA 46).

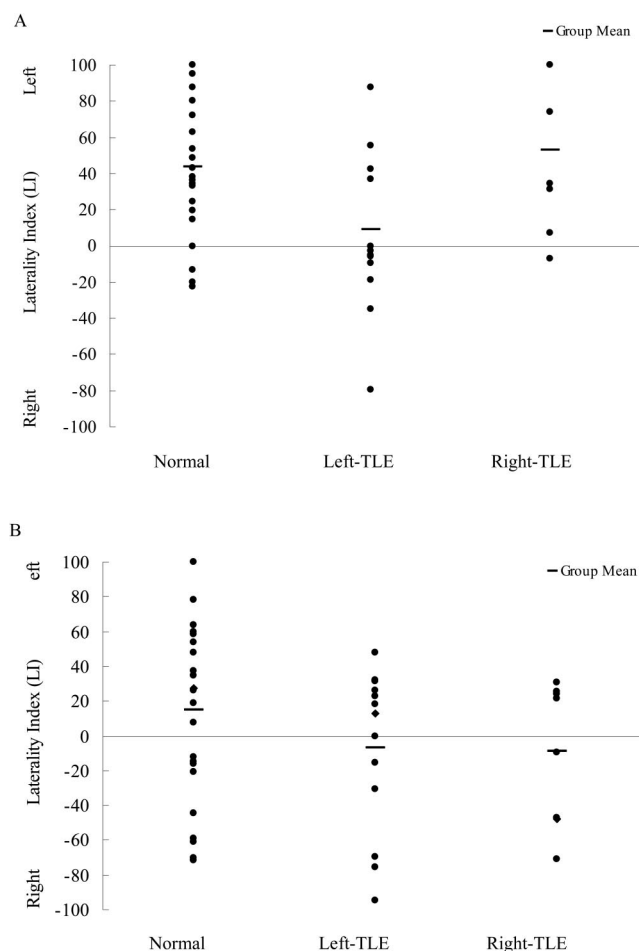


Figure 2. Laterality index (LI) in normal controls and patients during silently reading (A) English words and (B) Chinese characters.

Because the Chinese–English bilingual controls demonstrated left lateralization in processing English just as the English speakers did, we examined the language lateralization for TLE patients in processing English. Analysis of the lateralization in processing English revealed that the majority (75%) of the right-TLE patients (mean LI = 52.69, $SD = 41.74$), similar to normal controls, demonstrated left-hemispheric language dominance in processing English (Figure 2A). However, a greater proportion of left-TLE patients (62%) showed either right- or bilateral-hemispheric lateralization, and the LI (mean LI = 8.81, $SD = 44.03$) for English word reading of the left-TLE patients, as shown by analysis of variance (ANOVA), was significantly different from those of the normal controls and right-TLE patients, $F(2, 41) = 3.92, p < .05$, partial eta squared = 0.16. In fact, the proportion of left-TLE patients (62%) having non-left lateralization, either bilateral or right-dominant, was twice that of normal controls (30%). In sum, the present findings on Chinese–English bilinguals were consistent with the findings on English-speaking TLE patients (Adcock et al., 2003; Brazdil et al., 2003), in which left-, but not right-, TLE patients demonstrated a higher proportion of a shift in language lateralization when processing English.

Language Lateralization of Chinese Characters in Chinese–English Bilingual TLE Patients

Figure 1B shows the group mean in the brain activation pattern of Chinese character reading in the left- and right-TLE patients. Unlike the findings in English word reading, bilateral activation was observed in both groups of patients. Specifically, activation was found in bilateral inferior frontal gyrus (BA 45) and middle frontal gyrus (BA 46 and BA 9), fusiform gyrus (BA 20 and BA 37), and parahippocampal gyrus (BA 36) in the temporal lobe in both left- and right-TLE patients.

The findings on Chinese language lateralization in the present patient sample were somewhat different from their English language lateralization. Whereas more left- but not right-TLE patients tended to have bi-hemispheric or right-hemispheric language lateralization in processing English, the language lateralization in processing Chinese characters for left-TLE (mean LI = -7.25 , $SD = 46.59$) and right-TLE (mean LI = -9.24 , $SD = 40.76$) patients was quite similar and not significantly different from that of the normal controls, $F(2, 41) = 1.20, p > .05$, partial eta squared = 0.06; Figure 2B. That is, similar to the normal controls, patients showed both left and non-left language lateralization. Whereas 5 left-TLE patients had left-hemispheric language lateralization, the other 8 had non-left language lateralization. For the right-TLE patients, 4 showed left and 4 showed non-left language lateralization. The distribution of language lateralization of the two groups of patients was not significantly different from that of the normal controls, $\chi^2(2, 44) = 0.65, p > .05$.

Factors Affecting Language Lateralization of Chinese Characters

Among the normal controls, there was no significant difference between the mean LIs of men and women for Chinese characters. Simple correlation analysis found that age and education were not correlated with LI for Chinese characters. However, there was a positive correlation between the LIs for Chinese character reading

and English word reading among the normal controls, $r(23) = 0.53, p < .01$ (see Figure 3), suggesting that participants who demonstrated a left-hemispheric language lateralization in Chinese characters tended to show left-hemispheric language lateralization in English words.

The effects of age, education, gender, age of onset, and duration of seizure on the language lateralization was examined in the epileptic group. Similar to the normal controls, the LIs for Chinese character reading did not show significant correlation with age, education, gender, or age of onset for either the left- or the right-TLE patients ($p > .05$). No significant correlation was found between the LIs for Chinese character reading and English word reading. On the other hand, for the left-TLE patients, there was a negative correlation between the LI for Chinese character reading and duration of seizure, $r(13) = -0.58, p < .05$, with longer duration having more bi-hemispheric or right-hemispheric involvement. When the patients were divided into two groups according to their duration of illness, we found that 7 patients had a relatively shorter duration of less than 10 years (mean duration = 3.43, $SD = 2.44$), and 6 had at least 10 years of illness (mean duration = 16.67, $SD = 7.55$). A significantly greater proportion of the patients with relatively longer duration of illness had right-hemispheric dominance, as determined using categorized LIs, $\chi^2(2, 13) = 8.98, p < .05$ (Figure 4A). For right-TLE patients, 4 out of 5 patients whose duration of illness was 10 years or more had a more left or bilateral language lateralization, although the effect of duration of illness was not significant, $\chi^2(2, 8) = 1.96, p > .05$ (Figure 4B).

Discussion

Language Lateralization in Chinese–English Bilinguals

The present findings on the normal control participants showed that reading Chinese characters was more associated with bilateral

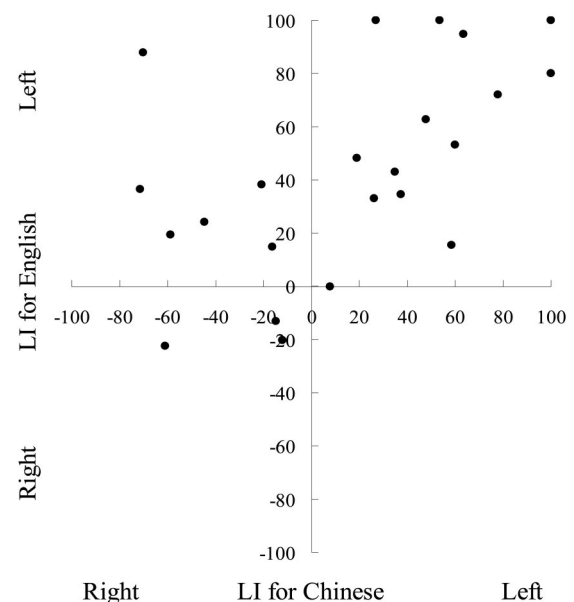


Figure 3. Scatterplot between laterality indexes (LIs) for English words and Chinese characters among normal controls.

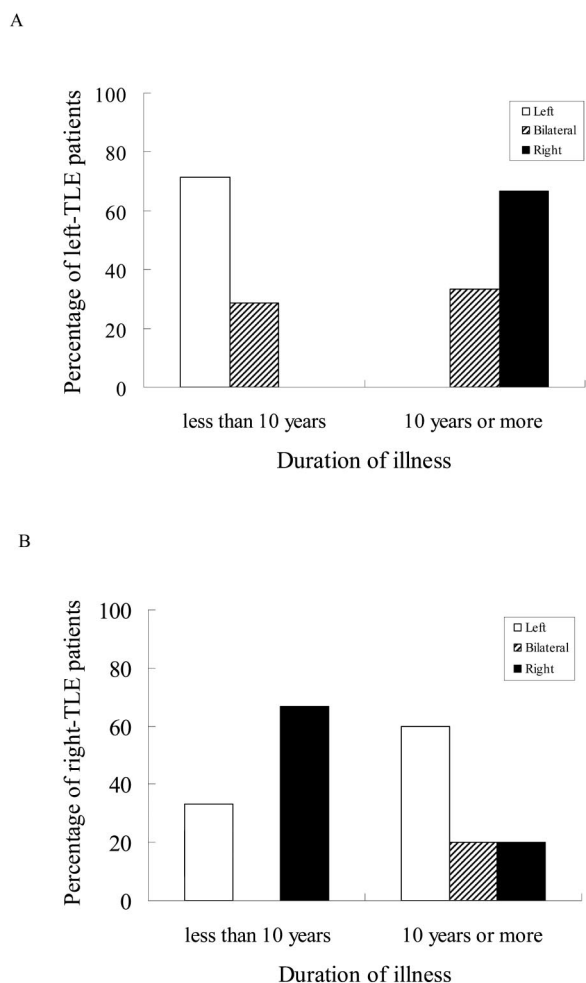


Figure 4. Effect of duration of illness on the frequency distribution of language lateralization determined by laterality index (LI) for (A) left-TLE and (B) right-TLE patients in reading Chinese characters. TLE = temporal lobe epilepsy.

activation and that reading English words was primarily associated with activation in the left hemisphere. These findings supported the previous hypothesis that reading Chinese characters and English words seems to be mediated by different neural mechanisms (Chan et al., 2002; Cheung et al., 2004; Tan et al., 2000; Tan, Feng, et al., 2001; Tan, Liu, et al., 2001). Furthermore, the present study showed that the variability of LI for Chinese character reading in normal control participants was found not to be related to age, gender, or education. Instead, it was related to the variability of LI for English word reading. That is, if a person tends to use the left hemisphere to process English, he or she will also tend to use the left hemisphere in processing Chinese. On one hand, this finding leads to speculation that there is some degree of overlap for the neural processing of the two languages. On the other hand, it is interesting to note that as compared with the LI for English word reading (range = 100 to -25.50), the LI for Chinese character reading is more widely distributed from strongly left lateralization (LI = 100) to strongly right lateralization (LI = -71.34). In fact, among the 23 normal control participants, we found that only 1

participant had right-hemispheric language lateralization in English word reading, whereas 6 of the participants had relatively right-hemispheric language lateralization in Chinese word reading. Therefore, though an overlap in the neural processing for the two languages is conceivable, Chinese may still have its own distinct neural processing mechanism associated with greater activation in the right hemisphere. In fact, these findings were consistent with previous studies in which more right-hemispheric regions are activated in reading Chinese, compared with reading English, and are involved in analysis of visual-spatial information required by the Chinese logographs (Chan et al., 2002; Tan, Liu, et al., 2001).

Language Lateralization in TLE Patients

The cortical activation pattern associated with covert reading of English words and Chinese characters in the left- and right-TLE patients revealed different patterns of language lateralization for two languages associated with epilepsy. For English word reading, the results on Chinese-English bilingual TLE patients were consistent with previous findings on English-speaking patients, in which right-TLE patients showed significant activations mainly over the left hemisphere (Adcock et al., 2003; Brazdil et al., 2003). Common activation regions included the inferior frontal gyrus (BA 9 and BA 44), the middle frontal gyrus (BA 46), the precentral gyrus (BA 6), and the temporal fusiform gyrus (BA 20 and BA 37). Again, consistent with the findings on English-speaking patients, the change in language lateralization of English was more commonly found in left-TLE patients than right-TLE patients, and a higher percentage of left-TLE patients showed bi-hemispheric or right-hemisphere language lateralization (Adcock et al., 2003; Brazdil et al., 2003).

However, the results on the cortical activation patterns involved in processing Chinese were somewhat different. Whereas left-, but not right-, TLE patients showed more bilateral activation in reading English, the left- and right-TLE patients demonstrated bilateral activation of frontal and temporal regions during the covert Chinese character reading task. Activated regions in both hemispheres included the inferior frontal gyrus (BA 45), the middle frontal gyrus (BA 46 and BA 9), the fusiform gyrus (BA 20 and BA 37) and the parahippocampal gyrus (BA 36) in the temporal lobe.

Thus, the present results supported our hypothesis that the difference in neural bases in the processing of the two languages seems to be a significant factor that affects the neuroplasticity of language processing associated with pathological change. Because processing Chinese tends to involve both hemispheres, pathological involvement in either hemisphere may affect Chinese processing. Therefore, variability of language lateralization was not only found in left-, but also in right-, TLE patients in the present study. It should be noted that the present study was consistent with a previous study in our laboratory on the naming impairment of patients with left, right, or bilateral temporal lobe lesions (Cheung et al., 2004). That is, consistent with findings in the West (Sandson & Albert, 1987), Chinese-speaking patients with left-hemisphere damage showed naming impairment. However, the Chinese patients (unlike the English-speaking patients) with either right or bilateral temporal damage also showed a similar level of naming impairment. As a result, damage in either hemisphere seems to disrupt the neural processing of Chinese, affecting language performance. Thus, on the basis of the present fMRI findings and

previous neuropsychological results on Chinese patients, caution is recommended in applying the language model developed with English-speaking patients to understand the influence of pathological change on Chinese language processing.

Factors Affecting Language Lateralization of Chinese Characters in TLE Patients

Although bilateral hemispheric activation was found in both left- and right-TLE patients in processing Chinese, a shift in language lateralization was still observed, and the duration of illness was found to be a significant factor affecting the variability of language lateralization of Chinese character reading in the TLE patients. Specifically, among the left-TLE patients, those with a longer duration of illness tended to show more right-hemispheric involvement in processing Chinese. This shift was not obvious in patients with shorter duration of illness (less than 10 years), who tended to have more left-hemispheric language lateralization. For the right-TLE patients, we also found that 4 out of 5 patients (80%) with a longer duration of illness tended to have bilateral or left-hemispheric language lateralization; that is, pathological involvement in the right hemisphere of right-TLE patients seems to affect the relative language dominance by shifting to the left hemisphere. Therefore, the tendency of a shift in language dominance as a result of pathological involvement is still observed in the Chinese right-TLE patients and was related to the duration of illness. Though the distribution of language lateralization was not significant between shorter and longer duration of illness among the right-TLE patients, which may be due to small sample size, the pattern found in right-TLE patients in the present study deserves further investigation with a larger sample size. In addition, if the duration of illness really has a causal effect in affecting the language lateralization of Chinese, the causation may be explored through more longitudinal studies.

Using a larger sample of patients ($n = 50$), Springer et al. (1999) found that atypical language representation was associated with an earlier age of seizure onset. Specifically, atypical language representation is more frequently observed in patients having an onset before the age of 6 years. However, we did not find any statistical correlation in our sample between lateralization and the age of seizure onset, $r(21) = .33, p > .05$. One possible explanation may be the comparatively small sample size in our study. In addition, in our sample, the majority of the patients had an onset after the age of 9 years (19 out of 21 TLE patients), so the effect of early onset of seizure on language lateralization might have gone undetected. Besides, because the language lateralization for Chinese participants tended to involve both hemispheres, it is also conceivable that the relationship between the laterality index and the age of seizure onset may not be linear, as has been found in studies of Western samples.

Language Lateralization of Chinese and Clinical Implications

The determination of language lateralization in TLE patient populations has traditionally been determined by the IAP, which has been regarded as the "gold standard" (Loring, Meador & Lee, 1992). More recently, the noninvasive method of fMRI (Adcock et al., 2003; Baxendale, 2002; Carpentier et al., 2001; Matthews et al., 2003) has also been used. Empirical studies have demonstrated that there is good agreement between results from the IAP and fMRI (Binder et al., 1996; Desmond et al., 1995; Gaillard et al., 2004; Lehericy et al., 2000; Springer et al., 1999; Weormann et al., 2003). However, results from the present study were somewhat different. Whereas the majority of our bilingual TLE patients were found to show left-lateralized speech output when assessed with the IAP (Table 2), results from the fMRI suggest that both hemispheres were involved in processing Chinese. Hence, for TLE patients, using Chinese as their first language, the results from the IAP and fMRI seemed to provide information on different aspects in Chinese processing. The IAP may be an indicator on the hemispheric dominance for speech output, whereas the fMRI may reflect more fine-grained information regarding the specific regions in the brain being activated during language processing. It is still open to question whether the neural pathway, especially those regions in the right hemisphere, as revealed by fMRI for Chinese processing, is an essential or adjunctive component. Considering that TLE patients are faced with the risk of language impairment after surgery, however, a detailed evaluation of the language performance through both neuropsychological assessment and fMRI should be considered essential for Chinese-English bilingual left- and right-TLE patients.

Limitations of the Study

In the present study, a more bilateral language lateralization was observed for reading Chinese characters than for reading English words. However, it should be noted that previous research conducted with other paradigms, such as rhyme decision (Tan et al., 2003), demonstrated more left-lateralized brain activations. Therefore, it is possible that different levels of Chinese processing may involve distinct systems of neural networks, resulting in task-related brain activity. Further studies conducted with different stimuli paradigms as well as systematic comparison of the observed activation patterns for different paradigms are recommended. Language lateralization in processing Chinese and English for each individual in the current study was based on analyses of regions of interest (ROIs) found in the group analysis that exceeded a certain p value and threshold level. One possible limitation of this approach is that activated regions with voxels smaller than this criterion or that are not identified in the targeted ROIs may be overlooked. However, there is no standardized way to address the issue of laterality of activation, and different studies may use different threshold levels to determine the activated regions and compare the results on a voxel-by-voxel basis (Gaillard et al., 2002, 2004). Yet, this post hoc regions-based analysis is often considered a common method for analyzing the language lateralization in TLE patients (Binder et al., 1996; Carpentier et al., 2001; Lehericy et al., 2000; Springer et al., 1999) and normal control participants (Tan et al., 2000; Tan, Liu, et al., 2001).

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