Feasibility Study of Language Lateralization using Thai Version of Language Paradigm for Functional MRI in Clinical Service

Jitsupa Wongsripuemtet MD*, Oragarn Wongfukiat MD*, Yudthaphon Vichianin PhD**, Chanon Ngamsombat MD*, Theerapol Witthiwej MD***, Bunpot Sitthinamsuwan MD***, Thaweesak Aurboonyawat MD***, Ekawut Chankaew MD***, Orasa Chawalparit MD*

** Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Department of Radiological Technology, Faculty of Medical Technology, Mahidol University, Bangkok, Thailand*
**** Department of Neurosurgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Objective: *To evaluate the concordance of language lateralization between functional magnetic resonance imaging (fMRI) using Thai version of language paradigm and Wada test or awake surgery with direct cortical brain stimulation (DCS).*
Material and Method: *Retrospective study of thirteen patients (3 males and 10 females with mean age of 33.9 years old) with epilepsy (7 cases) or brain tumor (6 cases) was performed. Every patient underwent both fMRI (word generation, verb generation, naming picture, and sentence completion tasks) and Wada test or awake surgery with DCS (defined as the gold standard). The lateralization index (LI) of fMRI was automatically calculated by using the LI-toolbox on SPM8. The hemispheric lateralization was also evaluated visually. The concordance between fMRI and gold standard were analyzed.*
Results: *The concordance between the lateralization of fMRI by visual assessment and gold standard was 92.3%. Concordance between the calculated LI by fMRI and gold standard was varied along with the task and regional calculation method. The concordance was good in all tasks (except for naming picture task) when using calculated LI from frontal or whole brain excluded cerebellum and occipital lobe (range 76.92 to 88.98% and 76.92 to 92.31%, respectively).*
Conclusion: *There was good concordance between fMRI and gold standard. Regional calculation from frontal lobes and whole brain excluded cerebellum and occipital lobes gave the best results. The results supported feasibility to use the fMRI with Thai language paradigm as an alternative way to determine the language dominant hemisphere in Thai patients. In case of language dominant hemisphere is unclear, further invasive investigation of language mapping such as Wada test or DCS is crucial.*

Keywords: *Functional MRI, Thai, Language, Wada test*

J Med Assoc Thai 2016; 99 (12): 1344-54
Full text. e-Journal: *http://www.jmatonline.com*

Determination of the language areas and hemispheric dominance for language is one of the most important considerations for pre-surgical planning in order to prevent or minimize risk of postoperative functional deficit in surgically treated patients involving language dominant hemisphere. The intracarotid amobarbital test or known as Wada test and direct cortical stimulation (DCS) during awake surgery for cortical mapping are gold standard for assessing the language dominance[1-3]. However, the Wada test is an invasive procedure and has a risk of complications such as carotid artery dissection, stroke, potentiation of seizures, and adverse reaction to contrast agent. The DCS is a method for localizing eloquent area such as sensorimotor and languages during surgery by applying electrical current directly on the cortical surface to temporarily deactivate brain[2,3]. For identification of the language dominance, positive DCS sites confirm the locations of critical language regions within a given hemisphere, but cannot exclude the other essential language areas outside the testing region and in the contralateral hemisphere. Accordingly, the DCS is restricted to the region of the craniotomy and electrode placement and is limited by invasive nature.

The functional magnetic resonance imaging (fMRI) has been developed for assessment of the brain function using blood oxygenation level dependent (BOLD) effect with the basic principle of hemodynamic response during neuronal activation compared with resting stage. During neuronal activation, the regional cerebral blood flow is increased, causing change of the

Correspondence to:
Chawalparit O, M.D, Department of Radiology, Siriraj Hospital, 2 Wanglang Road, Bangkok 10700, Thailand.
Phone: +66-2-4197086, Fax: +66-2-4127785
Email: oak_art@yahoo.com

ratio between oxy- and deoxy-hemoglobin concentration and resulting in signal change on the images[4].

The fMRI has emerged as a noninvasive technique to complement to the Wada test for language lateralization. Many studies demonstrated the concordance between fMRI and Wada test ranging from as high as 100% to as low as 56%[5-14]. The property of the language paradigm or task design is one of the factors influencing the result of functional mapping. The silent word generation task was reported the most robust and best lateralizing paradigm to demonstrate the language related areas[15]. Discordance of patient's native language and one used in the paradigm is another concerned issue[16]. The areas of language activation are different between native and non-native languages and increasing activation of non-dominant hemisphere in people who learn English as a second language was reported[17]. Studies in non-English such as Chinese language reported different cortical language processing areas that were not identical to those in English language processing.

In Thai people, using Thai as a native language may have different brain activity from Western studies. The Thai language paradigm has been developed as "Thai version of language paradigm (SiTP1)" which consists of block paradigm of word generation (WG) from Thai letters, verb generation (VG) from nouns, naming pictures (NP), and sentence completion (SC). The recent study in ten normal right handedness Thai subjects who were native Thai speakers reported localization of the language areas in 90% and left hemispheric lateralization in 100%[18].

The aim of the present study was to evaluate the feasibility of the Thai language fMRI in clinical practice by studying the concodance of language lateralization between fMRI using SiTP1 and Wada test or awake surgery with DCS.

Material and Method

Subjects

This retrospective study was approved by the Institutional Ethic Board of Faculty of Medicine Siriraj Hospital, Mahidol University. The 29 Thai native-speaker patients with epilepsy or brain tumor who underwent fMRI with SiTP1 between January 2012 and September 2014 were enrolled into the study. Five patients were excluded due to non-cooperative fMRI examinations and 11 individuals were excluded due to no available Wada test or DCS.

Finally, 13 patients (3 men and 10 women) were enrolled into the study. Demographic data of each patient such as age, Edinburgh's score, diagnosis, presentation, and duration of symptom was collected from the patients' records.

Functional MRI

The Thai version of language paradigm consisted of 4 tasks: WG from Thai letters, VG from nouns, NP, and SC. All tasks were block design consisting of five pairs of alternating between active and rest blocks with 30 seconds block duration. The patients were briefly informed about the task before the fMRI scanning. Each task started with the instruction slide that specified the category for three seconds. The patients performed silent language generation tasks. Each stimulus (alphabet, word, picture, or sentence) was displayed for three seconds with sequential 10 different stimuli in each active block. The sharp sign (#) was shown on the screen during the rest block. All stimuli and sharp sign were in white on the black background, visually presented by task presentation system for fMRI (ESys, Invivo). The total scan time of each task was five minutes.

The patients were scanned with 3-Tesla scanner (Achieva or Ingenia, Philips Medical systems, Best, NL) and a SENSE-8 head coils. Before the functional tasks, whole brain 3D T1 weighted (T1W) turbo fast echo for structural images was acquired for anatomical reference [voxel size = 1x1x1 mm^3, repetition time (TR) = 7.6 ms, echo time (TE) = 3.6 ms, flip angles = 8°, TFE factor = 144, field of view (FOV) = 230x290 mm^2, matrix = 232x290 mm^2, slice thickness = 1 mm, NEX = 1].

A single shot gradient-echo echo-planar imaging (EPI) was used to acquire BOLD functional image [voxel size = 2x2x4 mm^3, TR = 3,000 ms, TE = 35 ms, flip angles = 90°, FOV = 240x240 mm^2, slice thickness = 5 mm, NEX = 1, dynamic time = 3 seconds, total number of dynamic = 100]. Total scan time was 5 minutes 9 seconds (including a 9 seconds pre-stimulus period excluded from analysis to allow stabilization of the BOLD signal).

Imaging processing and LI analysis

Preprocessing of the EPI images and further analyses were performed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8, Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology, London, UK) running on MATLAB (MathWork Inc., Natick, Maryland, USA, http://www.mathworks.com/) operation on LENUX system.

Briefly, the functional images of each patient were realigned with the first image to reduce movement-related artifacts. Then, the images were co-registered with the T1W structural images using a rigid body transformation and normalized to the standard Montreal Neurological Institute (MNI) space using the ICBM152 template[19], following which they were smoothed by convolving with a Gaussian kernel of 5 mm full-width at half maximum (FWHM).

The activation maps were generated using the first-level subject based on the general linear model (GLM). Each voxel was assigned a T-score revealing the correlation between an expected hemodynamic response function (HRF) and the voxel by voxel BOLD signal response. The first level SPM t-contrast map was generated for each subject at a threshold of $p<0.05$ (uncorrected).

The lateralization index (LI) was calculated based on:

LI = (sum[activation left] - sum[activation right])/
(sum[activation left] + sum[activation right])

The LI value was between -1 and 1. The value of nearly -1 was preferred right hemispheric dominance while nearly 1 was preferred left hemispheric dominance. The LI between -0.2 and 0.2 was defined as bilateral or ambiguous lateralization[20].

In the present study, the automated calculation of LI using the LI-toolbox, which is add-on software on SPM8, was performed[21]. The LI-toolbox is freely available and can be downloaded from a website at http://www.fil.ion.ucl.ac.uk/spm/ext/#LI.

The image analysis of each patient was performed according to workflow in the SPM manual[22]. Then, an additional workflow for LI calculation was done in these following steps. First, the image of t-value map of each subject was assigned to the LI-tool in the SPM. This image resulted from running SPM mapping on the subject that usually ends with spmT_xxx.img where xxx is a running number automatically assigned by the SPM. Then, a selected volume mask of the brain volume in question was applied (i.e., frontal lobe, parietal lobe, temporal lobe, occipital lobe, cingulate, central gray matter, cerebellum, or all lobes). Midline region (10 mm) was excluded from the LI calculation. As a result, the LI-tool automatically generated all results in separate windows plotting LI curves and displaying LI indices against various threshold values.

Example of the LI analysis curve and SPM result were shown in Fig. 1 and 2.

Visual assessment of language lateralization

The individual fMRI results for each task were further evaluated visually by an experienced neuroradiologist (Wongsripuemtet J) who blinded to the calculated LI results. Language lateralization was classified as left, right, or bilateral.

The Wada test and awake-surgery with DCS

The Wada test and awake surgery with DCS used as gold standard were performed by the neurosurgeons. Briefly, the Wada test was used to evaluate the function of each cerebral hemisphere by injecting the propofol (Diprivan®) into one of the internal carotid arteries via the intra-arterial catheter. The propofol introduced temporal anesthesia. When the drug reached the side of the brain, the patient would lose all strength on the side of the body opposite to the injection. Then, the function of brain opposed to the injection was assessed. To test the patient's speech, the patient was asked to count, read words, identify objects, and response to the verbal command. If the patient could not produce the speech, the injected side of the brain was the language hemispheric dominance. The awake surgery with DCS was performed by applying electrical stimulation on the surface of the cerebral cortex directly while the patient awake in order to induce temporary deactivation of the brain function. For assessment of the language area and hemispheric dominance, the patient was asked to count, read words,

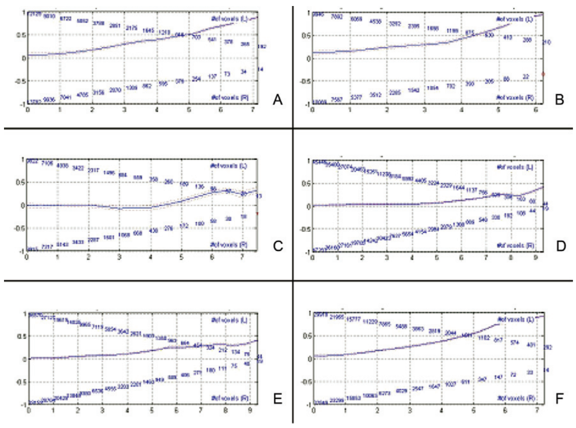

Fig. 1 Forty-eight years old female with right mesial temporal sclerosis and left hemisphereic lateralization by fMRI and Wada test. The LI curve from word generation paradigm calculated from activation areas in frontal lobe (A), parietal lobe (B), temporal lobe (C), whole brain (D), whole brain excluded cerebellum (E), and whole brain excluded cerebellum and occipital lobe (F).

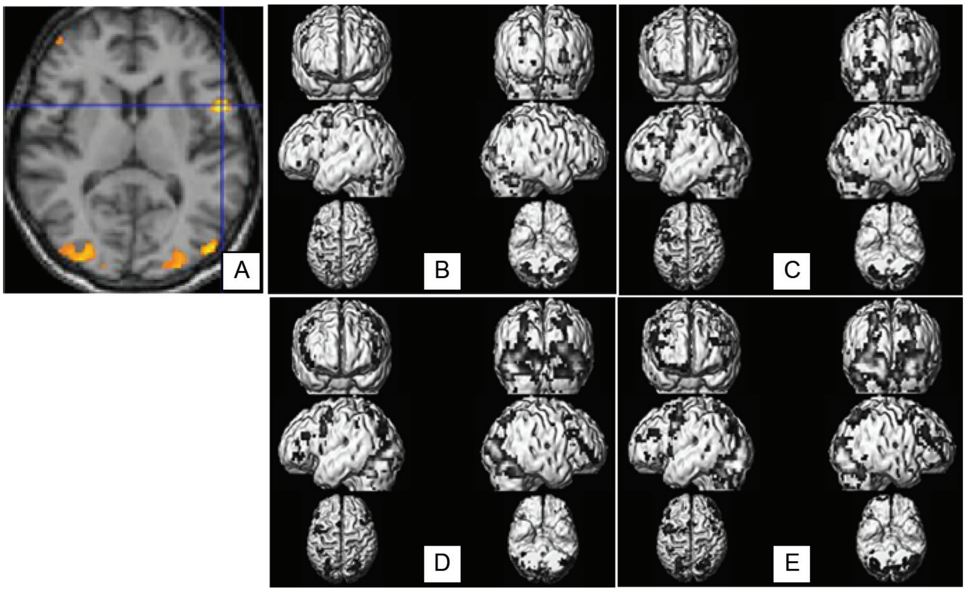

Fig. 2 Same patient with Fig. 1. In verb generation paradigm, activation was demonstrated at Broca area of left inferior frontal gyrus (A). Activated areas on SPM overlying with volume rendering T1W were seen from word generation (B), verb generation (C), naming picture (D), and sentence completion (E) tasks of fMRI.

identify objects, and response to the verbal command while the language cortex was stimulated intermittently with the electrode. A location in which stimulation reproducibly interrupted speech or counting was recorded as the site of speech function or language area.

Twelve patients underwent the Wada test and 1 case underwent awake surgery with DCS.

Statistical analysis

The concordance of language lateralization between fMRI and Wada test or DCS was described in percentage (SPSS v18.0).

Results

Thirteen cases were three males and 10 females with age ranging from 16 to 54 years old (mean age = 33.9 years old). Twelve of 13 patients (92.3%) were right handed according to Edinburgh's score. Seven cases were epilepsy patients and six were tumor cases. The mean duration of symptom before fMRI study was 218.6 months in epilepsy cases and 5.7 months in tumor cases.

There were nine cases with available fMRI studies in 4 tasks of language paradigm (WG, VG, NP, SC). Four cases had fMRI studies available in three tasks (WG, VG, NP) and one case had two tasks (WG, VG). In conclusion, WG and VG were available in 13 cases, NP in 12 cases (6 epilepsy and 6 tumors) and SC in nine cases (5 epilepsy and 4 tumors). The incomplete language paradigm study cases were the cases in our early experience in fMRI and not well co-operated patients.

Lateralization

Wada test or awake surgery with DCS

Of the 13 cases, 11 (84.6%) were left hemispheric lateralization. One case was right and one was bilateral hemispheric lateralization.

Visual assessment of fMRI (Table 1)

Lateralization by visual assessment of fMRI images went along with gold standard in 12 of 13 patients. Only one tumor case, which was bilateral hemispheric lateralization by gold standard, was determined as right lateralization by fMRI visual assessment. The concordance was 92.3%.

LI calculation from fMRI studies

In tumor cases, 6 had available WG, VG, and NP and 4 with SC fMRI studies. Good concordance between calculated LI from fMRI and gold standard were demonstrated when using WG and VG (Table 2). Calculating LI of VG fMRI from activated areas on frontal, parietal lobe and whole brain excluded cerebellum, and occipital lobe gave the best result (100% concordance).

In epilepsy cases, seven had available WG and VG, six with NP, and five with SC fMRI studies. Good concordance between calculated LI from fMRI and gold standard were found when using VG and SC (Table 3). The best result with 100% concordance was LI calculated from VG (whole brain excluded

Table 1. Demographic data and hemispheric lateralization

No.	Sex	Age (years)	LI (Edinburgh's score)	Diagnosis	Location	Duration of symptom*	Gold standard	fMRI (visual assessment)
1	M	16	+100	Epilepsy	Left medial temporal lobe	108	Left	Left
2	F	53	-100	Epilepsy	Left cerebral hemisphere	600	Right	Right
3	F	27	+100	Epilepsy	Left medial temporal lobe	204	Left	Left
4	F	19	+100	Epilepsy	Left hippocampus	84	Left	Mild left
5	F	48	+100	Epilepsy	Right medial temporal lobe	120	Left	Left
6	F	26	+100	Epilepsy	Bilateral hippocampi	18	Left	Left
7	F	36	+70	Epilepsy	Right medial temporal lobe	396	Left	Left
8	M	30	+100	Tumor	Left frontal lobe	0.07	Left	Left
9	M	17	+100	Tumor	Right amygdala	12	Left	Left
10	F	48	+100	Tumor	Right amygdala	7	Left	Left
11	F	42	+100	Tumor	Right temporal and insular lobe	2	Left	Left
12	F	25	+100	Tumor	Left insular and frontal lobe	1	Right	Bilateral
13	F	54	+100	Tumor	Left insular lobe	12	Left	Left

LI = lateralization index; fMRI = functional magnetic resonance imaging; M = male; F = female
* Number in months, Wada test or awake surgery with direct cortical stimulation (DCS) was defined as gold standard

Table 2. Concordance between fMRI and gold standard in tumor group

Region of interest	Concordance (%)			
	WG (n = 6)	VG (n = 6)	NP (n = 6)	SC (n = 4)
Frontal	5 (83.33)	6 (100.00)	4 (66.67)	3 (75.00)
Parietal	5 (83.33)	6 (100.00)	4 (66.67)	1 (25.00)
Temporal	3 (50.00)	5 (83.33)	2 (33.33)	3 (75.00)
Whole brain	3 (50.00)	4 (66.67)	2 (33.33)	2 (50.00)
Whole brain excluded cerebellum	4 (66.67)	5 (83.33)	2 (33.33)	2 (50.00)
Whole brain excluded cerebellum and occipital	5 (83.33)	6 (100.00)	5 (83.33)	2 (50.00)

WG = word generation; VG = verb generation; NP = naming picture; SC = sentence completion
Wada test or awake surgery with DCS was defined as gold standard

Table 3. Concordance between fMRI and gold standard in epilepsy group

Region of interest	Concordance (%)			
	WG (n = 7)	VG (n = 7)	NP (n = 6)	SC (n = 5)
Frontal	5 (71.43)	5 (71.43)	4 (66.67)	4 (80.00)
Parietal	5 (71.43)	5 (71.43)	3 (50.00)	5 (100.00)
Temporal	2 (28.57)	6 (85.71)	4 (66.67)	1 (20.00)
Whole brain	2 (28.57)	5 (71.43)	2 (33.33)	3 (60.00)
Whole brain excluded cerebellum	4 (57.14)	7 (100.00)	2 (33.33)	4 (80.00)
Whole brain excluded cerebellum and occipital	5 (71.43)	6 (85.71)	2 (33.33)	5 (100.00)

WG = word generation; VG = verb generation; NP = naming picture; SC = sentence completion
Wada test or awake surgery with DCS was defined as gold standard

cerebellum) and SC (parietal and whole brain excluded cerebellum and occipital lobe).

Discussion

Currently, the fMRI is widely clinical use as a potential replacing the Wada test or awake surgery with DCS in determination of the language hemispheric dominance for pre-surgical planning. Many studies reported the concordance between the fMRI and Wada test ranging from 56 to 100%[5-14]. However, those studies are based on English language, which is not suitable for Thai patients who are native Thai speakers. Thai language is tonal language like the Mandarin Chinese, which has differences in vocal fold vibration for identical phonemes to distinguish between different words in the lexicon from each other. Unlike the non-tonal language as English, pitch variation is not used to differentiate word meaning. The nature of tonal language of Thai may imply more cortical brain activation especially the non-dominant hemisphere (as reported in music task)[23,24]. The previous pilot study in ten normal native Thai speakers demonstrated the feasibility of fMRI using Siriraj Thai language paradigm (SiTP1) for language localization and lateralization[18].

The LI calculation in fMRI can be performed by many methods and each may have different results depending on many factors such as any threshold-dependent, region of interest and tasks. Our study used the calculated LI from LI-toolbox add-on program in SPM8 and bootstrap analysis, which was the robust, stable, and reliable method for LI assessment[25]. Our pilot study in ten normal native Thai speakers showed good left lateralization of the fMRI using SiTP1 and the regional calculation from the frontal lobe gave the best result. The present study showed good concordance in all tasks (except for NP task) when using frontal and whole brain excluded cerebellum and occipital lobe to calculate the LI (range 76.92 to 88.98% and 76.92 to 92.31%, respectively), but poor concordance when using whole brain to calculate the LI in all tasks. These findings were similar to the previous studies reported that the regional LI within the frontal lobe gave the better concordance than other temporoparietal regions and whole brain[26-28]. The calculated LI using temporal lobe and whole brain have poor concordance that might be from the crossed language dominance or interhemispheric dissociation of frontal and temporal language regions as reported in a healthy subject and in patients with focal epilepsy[29,30] and from crossed cerebro-cerebellar activation[31-33]. As mentioned in previous study, the activation in occipital lobes and midline regions often influenced the calculated LI, especially in visual paradigm[13,14]. In the present study, we found similar result and after excluded occipital lobes from the whole brain analysis the better concordance was given. The occipital lobes are not normally expected to have lateralized function. The recent literatures revealed that the reading mechanism initiated activation at the left ventral occipito-temporal cortex known as visual word form area, which is a specific location for learning to recognize word form, and then projected dorsally to posterior parietal lobe and contributing to the inferior frontal activity by different fiber tract[34,35]. The secondary visual cortex, which is located in the occipital lobe, has an important role in visual memory. All patients in the present study were trained and orientated to the paradigms before performed the fMRI, so the patients might have some learning and memory effects on the fMRI.

Previous studies suggested that the cerebral space occupying lesions such as large hemispheric tumors could be either increased or decreased BOLD effect. BOLD activation was reduced in the ipsilateral hemisphere as compared to the contralateral side. The probably mechanisms were tumor-induced neurovascular uncoupling that altered the coupling between neuronal activity and cerebral blood flow and impaired vascular autoregulation. Reduced activation in the left hemisphere resulted in increased the right hemispheric weighting and falsely interpreted right hemispheric dominance[36-38]. On the other hand, the neuronal plasticity induced by slow-growing tumor might be a compensatory mechanism of the brain to preserved the communicative function, might impact on the language lateralization with a shifting to the contralesional hemisphere in the patients with brain tumor located at language area[39,40]. We found discordance in the patient No. 12 who had low grade glioma at left insular and frontal operculum and bilateral hemispheric dominance determined by Wada test. LI calculation from fMRI gave varying results. The tumor might influence the language lateralization and resulting in discordance between the fMRI and Wada test (Fig. 3).

There has been reported that the injury to the left hemisphere in early childhood often results in shifting of the language function to the contralateral hemisphere and tends to be stronger as a consequence of early lesion as compared to late lesion. The neuronal plasticity gradually declined with age[41,42]. In patient No. 2 who developed epilepsy at 3 years of age and had profound left cerebral hemispheric atrophy, it had the right hemisphere lateralization (Fig. 4). The early onset of disease might lead the language reorganization to the right hemisphere and the cerebral atrophy may result in cerebrovascular alteration, which also affects the BOLD activation.

The present study showed that the VG and WG tasks gave the better concordance than the SC and NP tasks. Only single task might be inadequate to give lateralization. Previous studies demonstrated that using a combination of multiple tasks or conjoint analysis of all tasks gives a more effective and robust result for hemispheric lateralization[43,44].

There were several limitations in the present study: the first was retrospective study in nature. The second was small sample size including small number of patients with atypical or bilateral hemispheric lateralization. Finally, the BOLD technique of the fMRI may influence the calculated LI due to the potential disturbance of the BOLD activation by the lesions, cerebrovascular alteration, and susceptibility artifact such as hemorrhage, hemosiderin or metallic material, which would impair the validity of fMRI. Further prospective study with larger sample size is needed for clinical validation and generalization.

In conclusion, there was good concordance of language lateralization between fMRI using SiTP1 and Wada test or DCS. Regional calculation from frontal lobes and whole brain excluded cerebellum and occipital lobes gave the best results. All tasks and calculated LI of each task should be assessed together for the accurate lateralization. The result supported feasibility to use the fMRI with Thai language paradigm as alternative investigation to determine the language dominant hemisphere in native Thai patients. In case of language dominant hemisphere was unclear, further invasive investigation of language mapping such as Wada test or DCS was crucial.

What is already known on this topic?

The fMRI has emerged as a noninvasive technique to complement to the Wada test for language

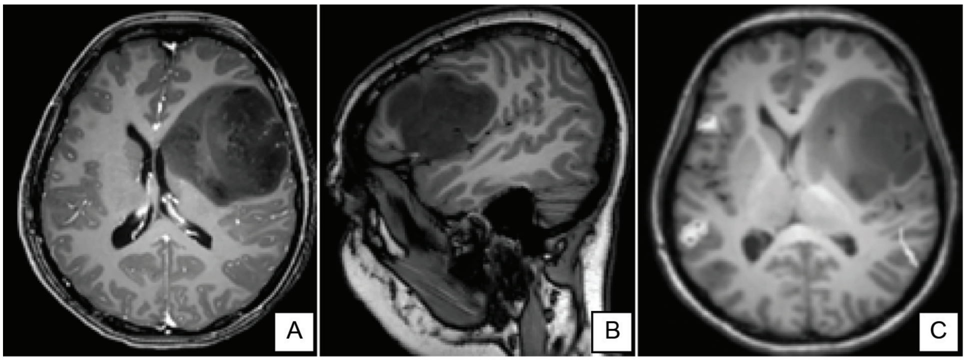

Fig. 3 Twenty-five years old female with low grade glioma at left insular and frontal operculum (A, B) and right hemispheric lateralization on fMRI. In SC task, the Broca area at right inferior frontal gyrus and Wernicke area at right superior temporal gyrus were activated (C).

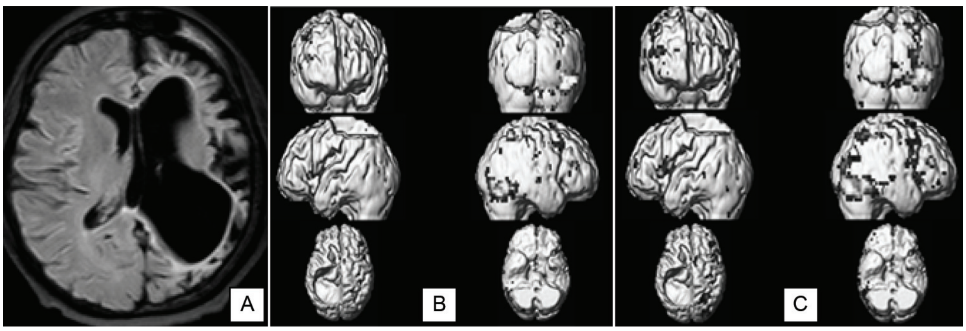

Fig. 4 Fifty-three years old female with left cerebral atrophy (A), and right hemispheric lateralization on fMRI. Activated area on SPM overlying with volume rendering T1W demonstrated more activation on the right hemisphere than the left side from WG (B) and VG (C) task fMRI.

Supplementary Table 1. Hemispheric lateralization by calculated LI

No.	Diagnosis (gold standard)	LI calculation (weight mean)				
		Region of interest	WG	VG	NP	SC
1	Epilepsy (left)	Frontal	L (0.28)	L (0.53)	NA	NA
		Parietal	B (-0.02)	B (-0.17)	NA	NA
		Temporal	L (0.45)	L (0.64)	NA	NA
		WB	B (0.18)	L (0.41)	NA	NA
		WB excluded cerebellum	L (0.34)	L (0.52)	NA	NA
		WB excluded cerebellum and occipital	L (0.31)	L (0.51)	NA	NA
2	Epilepsy (right)	Frontal	B (-0.054)	B (-0.09)	R (-0.58)	NA
		Parietal	R (-0.9)	R (-0.9)	R (-0.86)	NA
		Temporal	R (-0.74)	R (-0.78)	R (-0.82)	NA
		WB	R (-0.68)	R (-0.72)	R (-0.78)	NA
		WB excluded cerebellum	R (-0.69)	R (-0.72)	R (-0.78)	NA
		WB excluded cerebellum and occipital	R (-0.55)	R (-0.58)	R (-0.72)	NA
3	Epilepsy (left)	Frontal	L (0.34)	L (0.7)	R (-0.29)	B (0.045)
		Parietal	L (0.62)	L (0.88)	B (0.091)	L (0.52)
		Temporal	B (0.15)	L (0.35)	L (0.3)	L (0.86)
		WB	L (0.56)	L (0.44)	B (0.095)	L (0.49)
		WB excluded cerebellum	L (0.63)	L (0.45)	B (0.017)	L (0.51)
		WB excluded cerebellum and occipital	L (0.46)	L (0.74)	B (0.14)	L (0.57)
4	Epilepsy (left)	Frontal	B (0.17)	L (0.3)	B (-0.11)	L (0.45)
		Parietal	B (-0.073)	B (0.14)	R (-0.38)	L (0.44)
		Temporal	B (-0.013)	L (0.38)	L (0.26)	B (0.18)
		WB	R (-0.26)	B (-0.16)	B (0.014)	B (-0.0026)
		WB excluded cerebellum	B (0.18)	L (0.41)	B (0.19)	L (0.54)
		WB excluded cerebellum and occipital	B (0.14)	L (0.36)	B (0.048)	L (0.4)
5	Epilepsy (left)	Frontal	L (0.54)	L (0.67)	L (0.42)	L (0.41)
		Parietal	L (0.56)	L (0.59)	L (0.35)	L (0.4)
		Temporal	B (0.13)	L (0.56)	L (0.33)	L (0.48)
		WB	B (0.18)	L (0.41)	L (0.32)	L (0.38)
		WB excluded cerebellum	L (0.24)	L (0.51)	L (0.31)	L (0.38)
		WB excluded cerebellum and occipital	L (0.58)	L (0.61)	L (0.25)	L (0.41)
6	Epilepsy (left)	Frontal	L (0.38)	L (0.46)	L (0.37)	L (0.31)
		Parietal	L (0.46)	L (0.53)	L (0.24)	L (0.24)
		Temporal	R (-0.59)	L (0.42)	B (-0.0057)	B (0.11)
		WB	R (-0.41)	L (0.22)	B (0.056)	B (0.049)
		WB excluded cerebellum	R (-0.41)	L (0.3)	B (0.1)	B (0.052)
		WB excluded cerebellum and occipital	B (-0.0068)	L (0.54)	B (0.19)	L (0.29)
7	Epilepsy (left)	Frontal	L (0.5)	B (0.18)	L (0.36)	L (0.72)
		Parietal	L (0.63)	L (0.32)	B (0.14)	L (0.7)
		Temporal	B (0.083)	B (0.056)	R (-0.38)	B (0.2)
		WB	B (-0.098)	B (0.18)	B (-0.095)	L (0.54)
		WB excluded cerebellum	B (0.067)	L (0.22)	B (-0.0048)	L (0.69)
		WB excluded cerebellum and occipital	L (0.51)	B (0.051)	R (-0.21)	L (0.73)
8	Tumor (left)	Frontal	L (0.63)	L (0.44)	L (0.3)	NA
		Parietal	L (0.62)	L (0.71)	L (0.38)	NA
		Temporal	B (0.1)	B (0.041)	B (0.063)	NA
		WB	L (0.51)	L (0.33)	B (0.18)	NA
		WB excluded cerebellum	L (0.6)	L (0.33)	B (0.17)	NA
		WB excluded cerebellum and occipital	L (0.6)	L (0.52)	L (0.53)	NA
9	Tumor (left)	Frontal	L (0.67)	L (0.34)	L (0.35)	NA
		Parietal	L (0.42)	L (0.79)	L (0.46)	NA
		Temporal	R (-0.29)	L (0.59)	L (0.32)	NA
		WB	L (0.45)	L (0.41)	L (0.31)	NA
		WB excluded cerebellum	L (0.45)	L (0.45)	L (0.48)	NA
		WB excluded cerebellum and occipital	L (0.61)	L (0.53)	L (0.22)	NA
10	Tumor (left)	Frontal	L (0.25)	L (0.58)	B (0.15)	L (0.49)
		Parietal	L (0.66)	L (0.7)	L (0.28)	L (0.61)
		Temporal	L (0.28)	L (0.54)	L (0.45)	L (0.47)
		WB	L (0.36)	L (0.51)	B (-0.025)	L (0.46)
		WB excluded cerebellum	L (0.37)	L (0.57)	B (-0.032)	L (0.49)
		WB excluded cerebellum and occipital	L (0.39)	L (0.63)	L (0.27)	L (0.54)
11	Tumor (left)	Frontal	L (0.74)	L (0.88)	L (0.66)	L (0.42)
		Parietal	L (0.76)	L (0.84)	B (0.18)	B (0.022)
		Temporal	L (0.62)	L (0.25)	B (0.2)	L (0.42)
		WB	B (-0.086)	B (-0.082)	B (0.18)	L (0.25)
		WB excluded cerebellum	L (0.41)	L (0.75)	B (0.14)	L (0.25)
		WB excluded cerebellum and occipital	L (0.77)	L (0.86)	L (0.52)	L (0.25)
12	Tumor (bilateral)	Frontal	R (-0.58)	B (0.0035)	B (-0.024)	R (-0.54)
		Parietal	R (-0.37)	B (-0.038)	R (-0.28)	R (-0.38)
		Temporal	R (-0.49)	B (-0.12)	L (0.48)	B (0.031)
		WB	R (-0.41)	L (0.28)	B (-0.12)	R (-0.3)
		WB excluded cerebellum	R (-0.43)	L (0.25)	B (0.15)	R (-0.28)
		WB excluded cerebellum and occipital	R (-0.44)	B (-0.097)	B (-0.17)	R (-0.36)
13	Tumor (left)	Frontal	L (0.49)	L (0.66J)	R (-0.45)	L (0.24)
		Parietal	L (0.49)	L (0.72)	L (0.57)	R (-0.36)
		Temporal	L (0.29)	L (0.76)	B (0.12)	B (-0.065)
		WB	B (-0.043)	L (0.55)	R (-0.26)	R (-0.29)
		WB excluded cerebellum	B (-0.078)	L (0.65)	R (-0.34)	R (-0.32)
		WB excluded cerebellum and occipital	L (0.46)	L (0.71)	R (-0.32)	B (-0.11)

WG = word generation; VG = verb generation; NP = naming picture; SC = sentence completion; WB = whole brain; L = left; R = right; B = bilateral; LI = lateralization index; NA = not applicable

Wada test or awake surgery with DCS was defined as gold standard lateralization. Many studies demonstrated the concordance between fMRI and Wada test ranging from as high as 100% to as low as 56%[5-14]. The property of the language paradigm or task design is one of the factors influencing the result of functional mapping.

In Thai people, using Thai as a native language may have different brain activity from Western studies. The Thai language paradigm has been developed as "Thai version of language paradigm (SiTP1)". The recent study in ten normal right handed Thai subjects who were native Thai speakers reported localization of the language areas in 90% and left hemispheric lateralization in 100%.

What this study adds?

There was good concordance of language lateralization between fMRI using SiTP1 and Wada test or DCS. Regional calculation from frontal lobes and whole brain excluded cerebellum and occipital lobes gave the best results. All tasks and calculated LI of each task should be assessed together for the accurate lateralization. The result supported feasibility to use the fMRI with Thai language paradigm as alternative investigation to determine the language dominant hemisphere in native Thai patients.

Acknowledgements

This study was supported by Chalermphrakiat Grant, Faculty of Medicine Siriraj Hospital, Mahidol University and received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors would like to thank the Faculty of Medicine Siriraj Hospital for supporting in article submission and publishing.

Potential conflicts of interest

None.

References

1. Branch C, Milner B, Rasmussen T. Intracarotid sodium amytal for the lateralization of cerebral speech dominance; observations in 123 patients. J Neurosurg 1964; 21: 399-405.
2. Ojemann GA. Individual variability in cortical localization of language. J Neurosurg 1979; 50: 164-9.
3. Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. 1989. J Neurosurg 2008; 108: 411-21.
4. Norris DG. Principles of magnetic resonance assessment of brain function. J Magn Reson Imaging 2006; 23: 794-807.
5. Desmond JE, Sum JM, Wagner AD, Demb JB, Shear PK, Glover GH, et al. Functional MRI measurement of language lateralization in Wada-tested patients. Brain 1995; 118 (Pt 6): 1411-9.
6. Binder JR, Swanson SJ, Hammeke TA, Morris GL, Mueller WM, Fischer M, et al. Determination of language dominance using functional MRI: a comparison with the Wada test. Neurology 1996; 46: 978-84.
7. Bahn MM, Lin W, Silbergeld DL, Miller JW, Kuppusamy K, Cook RJ, et al. Localization of language cortices by functional MR imaging compared with intracarotid amobarbital hemispheric sedation. AJR Am J Roentgenol 1997; 169: 575-9.
8. Hertz-Pannier L, Gaillard WD, Mott SH, Cuenod CA, Bookheimer SY, Weinstein S, et al. Noninvasive assessment of language dominance in children and adolescents with functional MRI: a preliminary study. Neurology 1997; 48: 1003-12.
9. Yetkin FZ, Mueller WM, Morris GL, McAuliffe TL, Ulmer JL, Cox RW, et al. Functional MR activation correlated with intraoperative cortical mapping. AJNR Am J Neuroradiol 1997; 18: 1311-5.
10. Lehericy S, Duffau H, Cornu P, Capelle L, Pidoux B, Carpentier A, et al. Correspondence between functional magnetic resonance imaging somatotopy and individual brain anatomy of the central region: comparison with intraoperative stimulation in patients with brain tumors. J Neurosurg 2000; 92: 589-98.
11. Adcock JE, Wise RG, Oxbury JM, Oxbury SM, Matthews PM. Quantitative fMRI assessment of the differences in lateralization of language-related brain activation in patients with temporal lobe epilepsy. Neuroimage 2003; 18: 423-38.
12. Benke T, Koylu B, Visani P, Karner E, Brenneis C, Bartha L, et al. Language lateralization in temporal lobe epilepsy: a comparison between fMRI and the Wada Test. Epilepsia 2006; 47: 1308-19.
13. Arora J, Pugh K, Westerveld M, Spencer S, Spencer DD, Todd CR. Language lateralization in epilepsy patients: fMRI validated with the Wada procedure. Epilepsia 2009; 50: 2225-41.
14. Janecek JK, Swanson SJ, Sabsevitz DS, Hammeke TA, Raghavan M, Rozman E, et al. Language lateralization by fMRI and Wada testing in 229 patients with epilepsy: rates and predictors of

discordance. Epilepsia 2013; 54: 314-22.
15. Zaca D, Jarso S, Pillai JJ. Role of semantic paradigms for optimization of language mapping in clinical FMRI studies. AJNR Am J Neuroradiol 2013; 34: 1966-71.
16. Pillai JJ, Araque JM, Allison JD, Sethuraman S, Loring DW, Thiruvaiyaru D, et al. Functional MRI study of semantic and phonological language processing in bilingual subjects: preliminary findings. Neuroimage 2003; 19: 565-76.
17. Kim KH, Relkin NR, Lee KM, Hirsch J. Distinct cortical areas associated with native and second languages. Nature 1997; 388: 171-4.
18. Chawalparit O, Manochiopinig S, Vichianin Y, Wongsripuemtet J, Siwasattayanon P, Ngamsombat C, et al. Siriraj Thai language paradigm for functional MRI: A pilot study in normal volunteers. Siriraj Med J 2015; 67: 181-6.
19. Mazziotta JC, Toga AW, Evans A, Fox P, Lancaster J. A probabilistic atlas of the human brain: theory and rationale for its development. The International Consortium for Brain Mapping (ICBM). Neuroimage 1995; 2: 89-101.
20. Springer JA, Binder JR, Hammeke TA, Swanson SJ, Frost JA, Bellgowan PS, et al. Language dominance in neurologically normal and epilepsy subjects: a functional MRI study. Brain 1999; 122 (Pt 11): 2033-46.
21. Wilke M, Lidzba K. LI-tool: a new toolbox to assess lateralization in functional MR-data. J Neurosci Methods 2007; 163: 128-36.
22. Statistical parametric map (SPM) (www.fil.ion.ucl.ac.uk/spm/)
23. Kaan E, Barkley CM, Bao M, Wayland R. Thai lexical tone perception in native speakers of Thai, English and Mandarin Chinese: an event-related potentials training study. BMC Neurosci 2008; 9: 53.
24. Ethofer T, Anders S, Erb M, Herbert C, Wiethoff S, Kissler J, et al. Cerebral pathways in processing of affective prosody: a dynamic causal modeling study. Neuroimage 2006; 30: 580-7.
25. Wilke M, Schmithorst VJ. A combined bootstrap/histogram analysis approach for computing a lateralization index from neuroimaging data. Neuroimage 2006; 33: 522-30.
26. Lehericy S, Cohen L, Bazin B, Samson S, Giacomini E, Rougetet R, et al. Functional MR evaluation of temporal and frontal language dominance compared with the Wada test. Neurology 2000; 54: 1625-33.
27. Spreer J, Arnold S, Quiske A, Wohlfarth R, Ziyeh S, Altenmuller D, et al. Determination of hemisphere dominance for language: comparison of frontal and temporal fMRI activation with intracarotid amytal testing. Neuroradiology 2002; 44: 467-74.
28. Deblaere K, Boon PA, Vandemaele P, Tieleman A, Vonck K, Vingerhoets G, et al. MRI language dominance assessment in epilepsy patients at 1.0 T: region of interest analysis and comparison with intracarotid amytal testing. Neuroradiology 2004; 46: 413-20.
29. Baciu MV, Watson JM, McDermott KB, Wetzel RD, Attarian H, Moran CJ, et al. Functional MRI reveals an interhemispheric dissociation of frontal and temporal language regions in a patient with focal epilepsy. Epilepsy Behav 2003; 4: 776-80.
30. Jansen A, Deppe M, Schwindt W, Mohammadi S, Sehlmeyer C, Knecht S. Interhemispheric dissociation of language regions in a healthy subject. Arch Neurol 2006; 63: 1344-6.
31. Hubrich-Ungureanu P, Kaemmerer N, Henn FA, Braus DF. Lateralized organization of the cerebellum in a silent verbal fluency task: a functional magnetic resonance imaging study in healthy volunteers. Neurosci Lett 2002; 319: 91-4.
32. Jansen A, Floel A, Van Randenborgh J, Konrad C, Rotte M, Forster AF, et al. Crossed cerebro-cerebellar language dominance. Hum Brain Mapp 2005; 24: 165-72.
33. Gelinas JN, Fitzpatrick KP, Kim HC, Bjornson BH. Cerebellar language mapping and cerebral language dominance in pediatric epilepsy surgery patients. Neuroimage Clin 2014; 6: 296-306.
34. Price CJ. The anatomy of language: a review of 100 fMRI studies published in 2009. Ann N Y Acad Sci 2010; 1191: 62-88.
35. Bouhali F, Thiebaut de Schotten M, Pinel P, Poupon C, Mangin JF, Dehaene S, et al. Anatomical connections of the visual word form area. J Neurosci 2014; 34: 15402-14.
36. Holodny AI, Schulder M, Liu WC, Maldjian JA, Kalnin AJ. Decreased BOLD functional MR activation of the motor and sensory cortices adjacent to a glioblastoma multiforme: implications for image-guided neurosurgery. AJNR Am J Neuroradiol 1999; 20: 609-12.
37. Schreiber A, Hubbe U, Ziyeh S, Hennig J. The influence of gliomas and nonglial space-occupying lesions on blood-oxygen-level-dependent contrast enhancement. AJNR Am J Neuroradiol 2000; 21:

1055-63.
38. Ruff IM, Petrovich Brennan NM, Peck KK, Hou BL, Tabar V, Brennan CW, et al. Assessment of the language laterality index in patients with brain tumor using functional MR imaging: effects of thresholding, task selection, and prior surgery. AJNR Am J Neuroradiol 2008; 29: 528-35.
39. Desmurget M, Bonnetblanc F, Duffau H. Contrasting acute and slow-growing lesions: a new door to brain plasticity. Brain 2007; 130: 898-914.
40. Partovi S, Jacobi B, Rapps N, Zipp L, Karimi S, Rengier F, et al. Clinical standardized fMRI reveals altered language lateralization in patients with brain tumor. AJNR Am J Neuroradiol 2012; 33: 2151-7.
41. Muller RA, Rothermel RD, Behen ME, Muzik O, Chakraborty PK, Chugani HT. Language organization in patients with early and late left-hemisphere lesion: a PET study. Neuropsychologia 1999; 37: 545-57.
42. Fakhri M, Oghabian MA, Vedaei F, Zandieh A, Masoom N, Sharifi G, et al. Atypical language lateralization: an fMRI study in patients with cerebral lesions. Funct Neurol 2013; 28: 55-61.
43. Ramsey NF, Sommer IE, Rutten GJ, Kahn RS. Combined analysis of language tasks in fMRI improves assessment of hemispheric dominance for language functions in individual subjects. Neuroimage 2001; 13: 719-33.
44. Niskanen E, Kononen M, Villberg V, Nissi M, Ranta-Aho P, Saisanen L, et al. The effect of fMRI task combinations on determining the hemispheric dominance of language functions. Neuroradiology 2012; 54: 393-405.

การศึกษาความเป็นไปได้ในการใช้แบบทดสอบภาษาไทยในการตรวจหาสมองข้างเด่นของผู้ป่วยด้วย functional MRI (fMRI)

จิตสุภา วงศ์ศรีภูมิเทศ, อรกานต์ วงษ์ฟูเกียรติ, ยุทธพล วิเชียรอินทร์, ชนน งามสมบัติ, ธีรพล วิทธิเวช, บรรพต สิทธินามสุวรรณ, ทวีศักดิ์ เอื้อบุญญาวัฒน์, เอกวุฒิ จันแก้ว, อรสา ชวาลภาฤทธิ์

วัตถุประสงค์: *เพื่อเปรียบเทียบการบอกสมองข้างเด่นด้วย fMRI กับการตรวจด้วย Wada test หรือ กระตุ้นสมองขณะผ่าตัด*
วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังในผู้ป่วย 13 ราย (ชาย 3 ราย หญิง 10 ราย อายุเฉลี่ย 33.9 ปี) ที่มาด้วยอาการลมชัก 7 ราย หรือ เนื้องอกในสมอง 6 ราย ทุกรายได้รับการตรวจ fMRI ขณะทำแบบทดสอบภาษาไทย และ Wada test หรือ กระตุ้นสมองขณะผ่าตัด (วิธีมาตรฐาน) ข้อมูลจาก fMRI ถูกวิเคราะห์เพื่อหาดัชนีสมองข้างเด่นด้วยโปรแกรม SPM และโดยการวิเคราะห์จากภาพโดยรังสีแพทย์ ข้อมูลจาก fMRI ถูกนำมาหาร้อยละของผลไปทางเดียวกันกับการตรวจด้วยวิธีมาตรฐาน*
ผลการศึกษา: *การหาสมองข้างเด่นในผู้ป่วยโดยรังสีแพทย์ไปทางเดียวกับวิธีมาตรฐาน (ร้อยละ 92.3) ค่าดัชนีสมองข้างเด่นด้วยโปรแกรม SPM ไปทางเดียวกับวิธีมาตรฐาน เมื่อคำนวณบริเวณที่ถูกกระตุ้นจากสมองกลีบหน้า (frontal lobe) (ร้อยละ 76.92-88.98) หรือ สมองทั้งหมดไม่รวมสมองน้อย และสมองกลีบท้ายทอย (occipital lobe) (ร้อยละ 76.92-92.31)*
สรุป: *การใช้แบบทดสอบภาษาไทยในการตรวจการกระตุ้นสมองด้วย fMRI ในผู้ป่วยสามารถใช้แทนการตรวจด้วยวิธีมาตรฐานเพื่อบอกสมองข้างเด่น เพื่อลดการเสี่ยงต่อผลแทรกซ้อนจากการตรวจมาตรฐานในผู้ป่วยที่ผลการตรวจ MRI ไม่สามารถสรุปได้ แพทย์ยังสามารถใช้การตรวจมาตรฐานเพิ่มเติมได้*
