Siriraj Thai Language Paradigm for Functional MRI: A Pilot Study in Normal Volunteers

Orasa Chawalparit, M.D.*, Sriwimon Manochiopinig, Ph.D., Yudthaphon Vichianin, Ph.D.***, Jitsupa Wongsripuemtet, M.D.*, Praphun Siwasattayanon, M.D.*, Chanon Ngamsombat, M.D.*, Piya Chavalparit, Ph.D.****, Panida Charnchaowanish, B.Sc.*, Prapaporn Pornpunyawuth, B.Sc.*, Suvicha Chaovongphanit, B.Sc.*, Yodchanan Wongsawat, Ph.D.*****, Ngamkae Ruangvaravate, M.D.********

**Department of Radiology, **Department of Rehabilitation Medicine, ****Medical Student, ******Department of Ophthalmology, Faculty of Medicine Siriraj Hospital, ***Department of Radiological Technology, Faculty of Medical Technology, Mahidol University, Bangkok 10700, *****Department of Biomedical Engineering, Faculty of Engineering, Mahidol University, Salaya, Nakhonprathom 73000, Thailand.*

ABSTRACT

Objective: To create a language paradigm in Thai for functional MRI (fMRI) study.

Methods: Ten normal Thai native speakers with right-handedness from Edinburgh's score underwent fMRI study (BOLD on 3T MR scanner) using created Thai version of language paradigm (SiTP1) with block paradigms of word generation (WG) from Thai letters, verb generation (VG) from nouns, naming pictures (NP), and sentence completion (SC). Individual and group analysis was done using SPM8 to obtain activated areas and lateralization index (LI).

Results: Participants were 5 males and 5 females (22 to 37 years old). Eight were post-graduate students, one was a residential training fellow and the other one had grade 12 education. In group analysis (whole brain calculation), WG indicated left lateralized (LI = 0.7). The VG and SC paradigm gave ambiguous result (LI = 0.13 and -0.11 respectively), whereas the NP paradigm gave weakly right lateralization (LI = -0.26). For the frontal and parietal lobe, all paradigms gave strong left LI index. Comparison of LI between frontal lobe and parietal, temporal or whole brain from each paradigm were significantly different ($p<0.05$). For frontal lobe only, no significant difference was found between each paradigm except between VG and NP ($p=0.016$).

Conclusion: There was good lateralization using the created Thai paradigm. Regional calculation from frontal lobe gave the best result. The result supported possibility of using it as an alternative tool to identify the dominant hemisphere in Thai patients.

Keywords: Functional MRI, Thai, language

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INTRODUCTION

With the development of functional MRI (fMRI), we can now see brain function on the images.[1] The underlying of fMRI is for identifying areas with hemodynamic response during neuronal activation compared with the resting stage.[2] Change of oxy- and deoxy-hemoglobin concentration in the supplying blood leads to signal change on the images. The effect of this physiologic change is used in blood-oxygen-level dependent (BOLD) fMRI experiments.[3]

The signal change during activation was very small compared with resting stage, 2-3% difference.[3] The most important factor for variable

Correspondence to: Yudthaphon Vichianin
E-mail: yudthaphon.vic@mahidol.ac.th
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results of fMRI was the paradigm design.[4] Accuracy of identifying sensorimotor cortex by fMRI was between 83-92% compared with intracranial stimulation,[5,6] whereas accuracy of language area was 75% compared with Wada test.[7] However, many studies reported high correlation of fMRI and Wada test in lateralization of language dominant hemisphere.[8,9] Due to its non-invasive technique, fMRI, screening for lateralization of dominant hemisphere, has increasingly been used for preoperative planning in many epilepsy centers.

Most of the language fMRI reported in the literature were using English paradigm. A few studies in non-English, such as Chinese[10] and Persian,[11] reported a similar pattern of language areas with robust lateralization. Different activation in non-native speakers with English stimuli was reported.[12] The paradigm with native or mother-tongue language is very important. Thus, the purpose of this study was to create a Thai language paradigm to identify hemispheric dominance of language function in Thai people in order to use for patients who are native Thai speakers.

MATERIALS AND METHODS

Paradigm creation

An expert speech language pathologist (S.M.) developed the first test as a research tool which was based on Thai language. Validity of this first test had been done as follows:

1. Three speech language pathologist experts with at least 2 years of clinical experiences investigated the test. The suggestions were taken as baseline information for developing the second test.

2. Content validity of the second test was performed by 35 normal Thai subjects. The result was used for creating the third test "Siriraj Thai Paradigm 1" (SiTP1).

The SiTP1 was composed of 4 tasks. Task 1, word generation (WG) from 20 selected letters shown. Task 2, verb generation (VG) from the 30 selected words. Task 3, naming picture (NP). Task 4, sentence completion (SC).

Healthy volunteers

The volunteers were native Thai speakers, age 20-40 years old, able to read and speak Thai, with at least 6 years education, right handedness, no history of neurological or psychological diseases and no problems in hearing or seeing, not pregnant, and no contraindication to undergo MRI study.

A group of left-handedness adults was initially identified using the handedness questionnaire[13] and rapidly confirmed by the Vase-Face Test. After ruling out ones who had a visual problem, the rest were screened for hearing with Whispered Voice Test[14] then administered a battery of speech-language screening tests. The tests were the Aphasia Language Performance Screening Test (Thai version)[15] and the Communication Checklist.[16] Ten subjects comprised 5 males and 5 females with ages ranging from 22 to 37 years old. Eight of these 10 were post-graduate students, whilst one was a residential training fellow and the other one was a student at the grade 12 level.

Functional MRI and imaging technique

The subjects were prepared (one day before) by avoiding antihistamine-containing drug and having enough rest the night before. The subjects were told to look and follow the command shown on the screen attached to the head coil during the scanning. Every subject was briefly informed about the procedure and the study, followed by a short training session. Consequently, subjects were introduced to the paradigm one by one.

Each fMRI experiment was preceded by the display of an instruction slide for 3 seconds that specified the category. Subjects performed non-vocalized (silent) language generation tasks. The tasks were implemented as blocked designs consisting of 5 pairs of alternating active and control blocks with 30 second-block duration. Each stimulus (letter, word, picture or sentence) was introduced for 3 seconds with 10 different stimuli in each active block. During a rest block, sharp sign (#) was presented on the screen. All stimuli for both tasks were in white over a black background, presented visually through a task presentation system for fMRI (Esys, Invivo).

Images were acquired on a 3.0 Tesla MR scanner (Achieva, Philips Medical systems, Best, NL) using SENSE-8 head coils. A single shot gradient-echo echo-planar imaging (EPI) was used to acquire BOLD functional image (voxel size= 3.75x3.75x5mm, repetition time (TR)= 3000 msec, echo time (TE)= 35 msec, flip angle = 90^o, field of view= 240x240 mm, slice thickness = 5 mm, NSA =1, dynamic time = 3 sec, Total number of dynamics = 100). Total scan time was 5 min 9 sec for each task (including a 9 sec pre-stimulus period excluded from analysis to allow stabilization of the BOLD signal). Whole brain T1-weighted axial 3D Turbo fast field echo (3D TFE) MR structural images were also acquired in the same image session (voxel size= 1x1x1 mm, repetition time (TR) = 7.7 msec, echo time (TE) = 3.6 msec, flip angles = 8^o, TFE factor = 144, FOV = 230x290 mm, matrix = 232x288, slice thickness =1 mm, NSA =1). Diffusion weighted imaging and FLAIR were also performed for screening any possible pathology in the brain.

Imaging processing and LI analysis

Statistical Parametric Mapping (SPM8) (www.fil.ion.ucl.ac.uk/spm/software/spm8) running under MATLAB (www.mathworks.com) on a LINUX system was used for image processing.

The functional images of each participant were realigned to reduce movement-related artifacts, then co-registered with the T1-weighted structural images, and normalized to the standard Montreal Neurological Institute (MNI) space using the ICBM152 template.[17] 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 and group analysis 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 brain's hemispheric activity was grounded upon the lateralization index (LI) shown in equation (1):

$$LI = \frac{\sum(Activation\ left) - \sum(Activation\ right)}{\sum(Activation\ left) + \sum(Activation\ right)} \quad (1)$$

This results in values between -1 (purely right) and 1 (purely left). A set of tools namely "LI-tool" was selected as an automated tool for calculating the LI in this study.[18]

The image analysis of both individual and group data shares the similar workflow as suggested by the SPM manual.[19] The LI-tool generates all results in separate windows. The LI-tool is available and can be downloaded freely from a website at http://www.fil.ion.ucl.ac.uk/spm/ext/#LI.

Example of the SPM result and LI analysis curve have beenshown in Figs 1 and 2.

The statistical analysis for significant difference between each weighted mean LI was performed by paired sample t-test (SPSS 18). The predetermined significance was p<0.05.

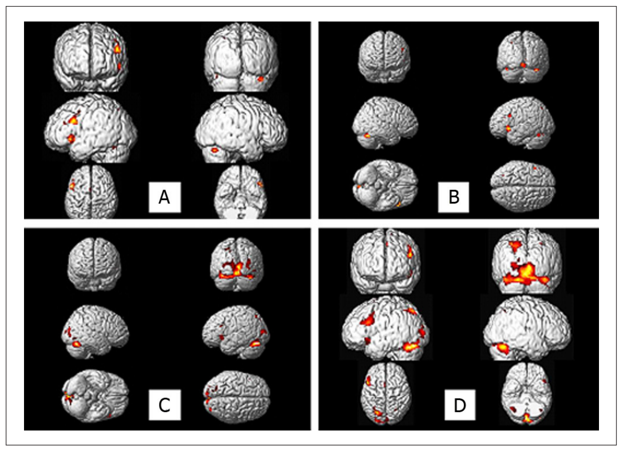

Fig 1. Activated areas on SPM from group analysis of word generation (A), verb generation (B), naming picture (C) and sentence completion (D) paradigms fMRI.

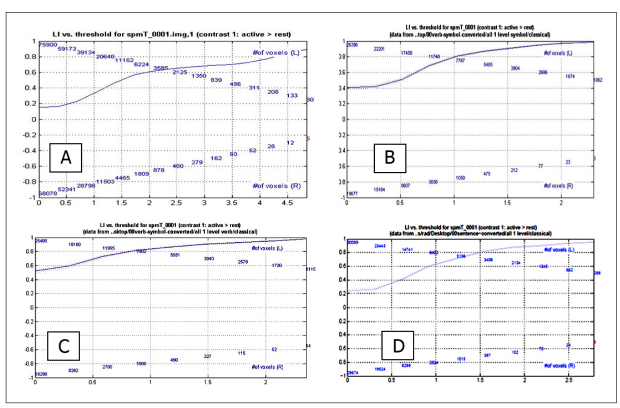

Fig 2. LI curve of group analysis from word generation (A), verb generation (B), naming picture (C) and sentence completion (D) paradigms fMRI.

RESULTS

The demographic data of each subject has been shown in Table 1. The Edinburgh's score 13 with 10 standard handedness questionnaires from all subjects ranged from +80 to +100% (right handed score) with 5^{th} to 10^{th} percentile.

In group analysis from whole brain calculation, the weighted mean LI from word generation paradigm was left lateralized (weighted mean LI = 0.7). The verb generation from word and complete sentence paradigm gave an ambiguous result (weighted mean LI = 0.13 and -0.11, respectively), whereas the naming picture paradigm gave weakly right lateralization (weighted mean LI = -0.26) as shown in Table 2.

TABLE 1. Demographic data and Edinburgh's handedness score by lateralization index (LI).

No.	Sex	Age	LI (Edinburgh's score)
1	F	37	+100
2	F	23	+100
3	M	23	+100
4	F	22	+100
5	F	22	+80
6	M	25	+100
7	M	26	+100
8	M	24	+100
9	M	29	+80
10	F	29	+100

When using frontal or parietal lobe as regional calculation in group analysis, all paradigms gave strong left LI as shown in Table 2. Comparison of weighted mean LI between frontal lobe and parietal, temporal or whole brain from each paradigm were significantly different ($p<0.05$) as shown in Table 3.

When analysis of activation was done in frontal lobe only, no significant difference was found between each paradigm, except between verb generation and naming picture ($p=0.016$) as shown in Table 4.

DISCUSSION

This study was a pilot study in normal native Thai speakers who were assumed to be right-handed by clinical test.[13] The study was conducted to compare the result of fMRI based on the assumption of a left dominant hemisphere in all subjects.

TABLE 4. Comparing weighted mean LI between the four paradigms in frontal lobe analysis (p value).

Analysis	p value
Word generation vs. verb generation	0.106
Word generation vs. naming picture	0.631
Word generation vs. complete sentence	0.526
Verb generation vs. naming picture	0.016*
Verb generation vs. complete sentence	0.084
Naming picture vs. complete sentence	0.594

TABLE 2. Group analysis of LI (weighted mean) of each paradigm calculated from whole brain, frontal, parietal and temporal lobe activation.

Paradigm	Whole brain	Frontal lobe	Parietal lobe	Temporal lobe
Word generation	0.7	0.85	0.67	0.33
Verb generation	0.13	0.9	0.81	0.14
Naming picture	-0.26	0.89	0.59	-0.13
Complete sentence	-0.11	0.83	0.64	0.064

TABLE 3. Comparing weighted mean LI between frontal lobe and parietal, temporal or whole brain analysis (p value).

Analysis	Word generation	Verb generation	Naming picture	Complete sentence
Frontal vs. parietal	0.023	0.033	0.007	0.001
Frontal vs. temporal	0.006	0.002	<0.0001	0.011
Frontal vs. whole brain	0.009	0.028	<0.0001	0.010

When calculating LI from the whole brain, only a simple task like word generation gave good left lateralization. This may due to the difference in difficulty of the paradigms. Except for the tonal feature of Thai language, the other features are quite similar to English. A single word comes from a combination of letters (consonants) and vowels. In Thai, vowels and tones have different characters and setting positions from consonants. The vowels can be positioned above or below the consonants, whereas the tones appear only on the top of the consonants. Also, in some Thai words, the vowels and tones may be not shown but pronounced out. The nature of the tonal feature of Thai language may occupy more cortical brain functions, especially in the non-dominant hemisphere (i.e. music task).[20] When doing more complicated tasks, other cortical areas, as well as the right hemispheric, are activated. Therefore, the calculated LI from whole brain may not represent the exact basic cortical function of Thai language.

The educational and environmental factors are also crucial. The subjects were in an education environment (9 of them are in universities) and might use '*modern*' language in their daily life. The '*modern*' Thai language has been influenced from foreign languages (such as English, Korean) as well as '*internet*' language. These may lead to unfamiliarity with the classic language, such as poems, employed in the sentence completing tasks.[21] Further studies in various age groups and educational levels should be performed. However, the result from this study confirmed findings of the others about the appropriate or robust paradigm of the word generation task for language lateralization.[22]

Calculation of LI from the regional brain has been proposed in many studies.[23,24] In this study, the frontal lobe calculation gave clear left lateralization in every paradigm and statistically significant differences from LI calculated from other lobes. When comparing LI of different paradigms from frontal lobe, no significant differences were found except for between verb generation and naming picture paradigm. The similarity of frontal lobe LI from the 4 paradigms might emphasize the reliability of the SiTP1 for clinical use.

Although there was broad agreement between the results and a reasonably inter-subject variability, the SiTP1still needs to be improved for more validity and reliability. The SiTP1 was studied in only a limited number of normal Thai volunteers. There was no accuracy and validity confirmed from any standardized test (e.g., Wada test). The training of paradigm and orientation to the fMRI process were performed in all subjects. These may have some learning effects on responding to the test. Consequently, these normal subjects were familiar with the MR environment and had no problem with task focusing. As a result, further controlled trial studies using the SiTP1in a larger subject group based on standardization fMRI need to be conducted.

In conclusion, good lateralization of the signal from fMRI when using the created Thai paradigm was observed. This study has provided an alternative tool to identify dominant hemisphere in Thai patients. Further study should be done in preoperative patients planning for intraoperative awake surgery in order to test the diagnostic performance and efficiency in real clinical situations.

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