Original Article

Experience of Functional MRI Protocol in King Chulalongkorn Memorial Hospital [KCMH] for Thai Language Lateralization

Phattharachuda Chosakun MD[1], Theerachai Chaitusaney MD[1], Yothin Rakvongthai PhD[2], Sukalaya Lerdlum MD[2]

[1] Department of Radiology, King Chulalongkorn Memorial Hospital, Thai Red Cross Society and Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

[2] Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Objective: To investigate the effects of statistical thresholding and to determine an optimal functional magnetic resonance imaging [fMRI] statistical threshold for Thai language lateralization.

Materials and Methods: The present study was prospective descriptive study of twenty Thai native speaker right-handed healthy volunteers performed Thai verb and word generation paradigms during 3T fMRI. Bihemispheric activation difference of language region of interests was calculated for laterality index [LI] through ranks of statistical threshold, from the threshold that generated an empty map to the minimal threshold with *p*-value less than 0.05.

Results: LI of both verb generation and word generation paradigms tended to rise in higher statistical thresholds. In two subjects, shifted of LI from co-dominant to left dominant were found as an effect of statistical thresholding on both paradigms. A threshold (t-value) of 7 in verb generation paradigm and a threshold (t-value) of 6 in word generation paradigm significantly increased mean LI (with *p*-value 0.004 and 0.003, respectively) and categorized 95% of the subjects as left hemispheric dominance.

Conclusion: LI varies across different statistical thresholds. Optimal thresholds (t-value) for language lateralization are 7 in Thai verb generation and 6 in Thai word generation paradigms.

Keywords: Functional MRI, fMRI, Statistics, Threshold, Language lateralization, LI, Dominant hemisphere, Right-handedness, Thai

J Med Assoc Thai 2018; 101 (11): 1501-7
Website: http://www.jmatonline.com

Functional imaging assists neurosurgeons with information in determining surgical candidacy for patients with brain tumor. It also allows function-preserving operations that reduce postoperative morbidity and maximize resection of pathology, thus, enhance patients' quality of life.

Language lateralization and localization are one of the most important considerations in surgical planning. Functional magnetic resonance imaging [fMRI] is a non-invasive imaging technique that has high concordance to Wada test (the gold standard) for language lateralization(1,2). In fMRI, brain function is assessed by measuring the hemodynamic responses to neuronal activity. During activation period, oxyhemoglobin-to-deoxy-hemoglobin ratio at cortical region changes from baseline. Different magnetic properties of the oxyhemoglobin and deoxyhemoglobin result in blood oxygen level dependent [BOLD] contrast and enable generation of a functional brain mapping.

Changes of BOLD signal during activation is low, being 3% to 5% in 1.5 Tesla MRI(3). Signal originated from activated brain regions must be differentiated from physiological and physical noise. Statistical thresholding is one of the essential post processing steps to determine the statistically significant signal changes (increase or decrease responses). Only the change whose absolute values were above a certain threshold is displayed. The activated brain volume is used to calculate the laterality index [LI] to determine the hemispheric language dominant for language. Several studies found that LI varies with the statistical threshold(4-7). Setting the threshold too low may cause spurious activation in bilateral cerebral hemispheres from false-positive correlations. On the contrary, setting threshold too high may fail to depict true activations. Therefore, an optimal statistical threshold is necessary for accurate language lateralization.

To the best of the authors knowledge, there has been no guideline or standard routine protocol

Correspondence to:

Chosakun P. Department of Radiology, King Chulalongkorn Memorial Hospital Thai Red Cross Society, Bangkok 10330, Thailand.
Phone: +66-2-2564413
Email: phattharachuda@gmail.com

How to cite this article: Chosakun P, Chaitusaney T, Rakvongthai Y, Lerdlum S. Experience of functional MRI protocol in King Chulalongkorn Memorial Hospital [KCMH] for Thai language lateralization. J Med Assoc Thai 2018;101:1501-7.

regarding fMRI threshold selection. The present study investigated the effects of thresholding on the LI, and to determine an optimal statistical threshold for language lateralization using Thai language paradigm. This might potentially lead to a reference threshold level for routine fMRI procedures.

Materials and Methods

Subjects

Between June 2015 and March 2016, healthy volunteers who were native and capable to read Thai language, age 20 to 60 years old with at least nine years education, right-handed as determined by Edinburgh Handedness Inventory[8] (Thai version questionnaire), and had no prior history of neurological disease or current usage of medication were enrolled in the present study. The volunteer who was pregnant, had contraindication to perform MRI, had metallic material that caused unacceptable susceptibility, unable to complete all designed paradigms, or had poor MR image quality due to unacceptable motion artifact were excluded. The required sample size for comparison of two dependent means that were statistical thresholds and lateral index was 17. However, the study needed 20 volunteers to account for potential dropouts (about 15%). The volunteer recruitment and human subject data collection were done under an approval of the Institutional Ethic Committee at King Chulalongkorn Memorial Hospital [KCMH].

Functional and morphologic MRI

Before the examination, all subjects were given instructions and followed training for each paradigm. Block design fMRI was started with resting for 30 seconds and then alternated to activation for 30 seconds for each cycle. Total of 5-cycles were obtained and total paradigm runtime was five minutes. Two Thai language paradigms were visually triggered silent verb and word generations (Figure 1) by binocular visual presentations. For silent verb generation, subjects were asked to generate as many related verbs for given Thai nouns (one trigger at a time and 10 triggers per activation period). Similarly for silent word generation, subjects were requested to generate as many meaningful words initiated with the triggers, which were Thai alphabets. Only the 30-most common Thai alphabets were used in random mode. One trigger was shown at a time and 10 triggers per activation period. During the rest period, a plus symbol was displayed on the screen and subjects were asked to discontinue language production and relax. Silent verb

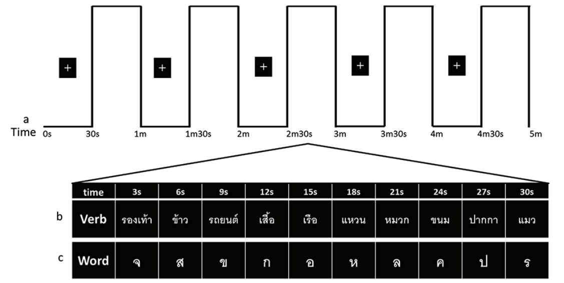

Figure 1. Example sets of Thai language paradigms: (a) Block design functional MR imaging was performed, 30 seconds for each rest and activated period. Totally 5 cycles and 5 minutes were done for a run. (b) Example set of Thai verb generation paradigm which triggered by a Thai noun. One trigger was presented for 3 seconds and total 10 triggers per an activation period. (c) Example set of Thai word generation paradigm which triggered by a Thai alphabet. One trigger was displayed for 3 seconds and total 10 thiriggers per an activation period. + represent rest period; s and m stand for second and minute, respectively.

generation was run initially and followed by silent word generation for all subjects.

All subjects underwent functional and morphological brain MRI by using GE Discovery MR 750 w 3.0 Tesla (General Electric Healthcare, Milwaukee, WI, USA) with 32-channel headcoil. Preformed foam cushions were used for biparietotemporal head fixation. The fMRI protocol included BOLD contrast, using 2D T2*-weighted single shot gradient-echo echo planar imaging sequence in axial plane, TR/TE (msec) 3,000/35, flip angle 90 degree, Field of View 220 mm, slice thickness 3.6 mm, no spacing, number of slice 42, matrix 64×64mm^2, voxel size 3.4×3.4×3.6 mm^3, and NEX 1.

Morphological images were acquired for overlay of activation map, using 3D FSPGR on axial plane, TR/TE (msec) 8.5/3.3, flip angle 12 degree, Field of View 240 mm, slice thickness 1.2 mm, no spacing, number of slice 140, matrix 256×256 mm^2, voxel size 0.93×0.93×1.2 mm^3, and NEX 1. FLAIR T2-weighted image with fat suppression were also performed for screening any brain pathology, acquisition on axial plane, TR/TE (msec) 8,025/95, flip angle 160 degree, ETL 16, TI (msec) 2,356, Field of View 240 mm, slice thickness 5 mm, space 1 mm, number of slice 24, matrix 320×224 mm^2, and NEX 1.

Real-time display of activation images, data quality and motion parameter were monitored during scan. If the subject was moving more than 5 mm, stopping the scan was considered. Repeated scan was done after resolving the problem.

Processing and analysis of functional and morphologic MRI

Two authors (Chosakun P with one year experience of neuroimaging and Chaitusaney T with four years expereince of neuroimaging) processed and analyzed all data, independently.

BrainWaveHW Lite software was used for synchronization of function and anatomical mapping, motion correction, spatial and temporal smoothing, and coregistration. Furthermore, Avotec software was used for paradigm display and voxelwise calculation of BOLD activations. Two authors (Chosakun P and Chaitusaney T) manually segmentated activated voxels in the presumed language areas which were inferior frontal gyrus, supramarginal gyrus, angular gyrus, and superior temporal gyrus of bilateral cerebral hemispheres. These gyri were anatomically define on the basic of T1-weighted morphological images and according to Naidich et al[9] This regions of interests [ROIs] were in concordance to prior studies[6,9-11]. The number of activated voxels in each ROIs in the left and right cerebral hemispheres were used to calculated language LI[12-14] as follows: Laterality index [LI] = sum(Activation in left hemis) - sum(Activation in right hemis) / sum(Activation in left hemis) + sum(Activation in right hemis).

LI was calculated at various statistical thresholds, ranging from the maximal threshold that did not display any signal on activation map (empty map) and decrement of 1 until the minimal threhold that still had true correlation with brain activation (*p*-value less than 0.05). For example, if the empty map was t-value 8, and the minimal threshold was t-value 5, LI were calculated at t-value 8, 7, 6, and 5.

LI ranges from +1.0 (fully left lateralized activity) to -1.0 (fully right lateralized activity). In corcordance to prior studies[5,12], LI greater than 0.2 represented left hemispheric dominant, -0.2 to 0.2 was co-dominant, and LI less than -0.2 represented right hemispheric dominant.

Optimal statistical thresholds for language lateralization were defined as a t-value that provided high LI (approached to +1.0) and left lateralized of right-handed subjects as many as possible. Optimal statistical threshold of each Thai language paradigm were determined separately.

Statistical analysis

Mean of LI of the rank of statistical threholds of each of Thai language paradigms, verb generation and word generation paradigms, were separately calculated. Repeated analysis of variance [ANOVA] with SPSS software version 22 was used to define the difference of the LI of the rank of statistical thresholds, where *p*-value less than 0.05 for this difference was considered statistically significant. LI of each individual subjects was assessed separately by two authors (Chosakun P and Chaitusaney T). Intraclass correlation coefficient [ICC] of these authors was evaluated; 0 to 0.2 indicates poor agreement; 0.3 to 0.4 indicates fair agreement; 0.5 to 0.6 indicates moderate agreement; 0.7 to 0.8 indicates strong agreement; and greater than 0.8 indicates almost perfect agreement.

Results

Twenty-two healthy volunteers were enrolled in the present study. Two volunteers were excluded due to unacceptable motion and incidentally found non-specific white matter change on FLAIR T2-weight sequence. Therefore, 20 healthy volunteers were studied (ten men and ten women, mean age: 30.7 (26 to 49) years). All of them were right-handed with Edinburgh Handedness's score, mean +96.5 (+80 to +100), where Edinburgh Handedness's score ranging from -100 (left handedness) to +100 (right handedness).

LI variably depended on statistical threshold as demonstrated by the LI curves of each Thai language paradigm (Figure 2, 3). LI of both verb and word generation paradigms tended to rise in higher statistical thresholds. For verb generation paradigm, two subjects (No. 7 and No. 17) showed co-dominant (LI = 0.11 and 0.06) at minimal statistical threshold (t-value 5), and then shifting to the left dominant (LI = 1) at the peak threshold (t-value 10 and 13), Figure 4. In the same way, for word generation paradigm, subject No. 15 and No. 17 were co-dominant (LI = 0.16 and 0.17) at the lowest threshold (t-value 5). The subject No. 18 failed to generate LI curve due to no activated voxel in the presumed language region of interest at all statistical thresholds. No right lateralization (LI less than -0.2) was seen throughout the ranking of statistical threshold of both verb and word generation paradigms for all of our subjects.

At higher statistical threshold of both verb and word generation paradigms, there was a trade-off between rising of mean LI and falling number of subjects that were categorized as left hemispheric dominant (LI greater than 0.2) in Figure 5. For verb generation paradigm, using t-value of 7 for calculating LI, nineteen subjects (95%) were categorized as left hemispheric dominant with mean LI 0.91. Repeated ANOVA demonstrated that changing t-value from

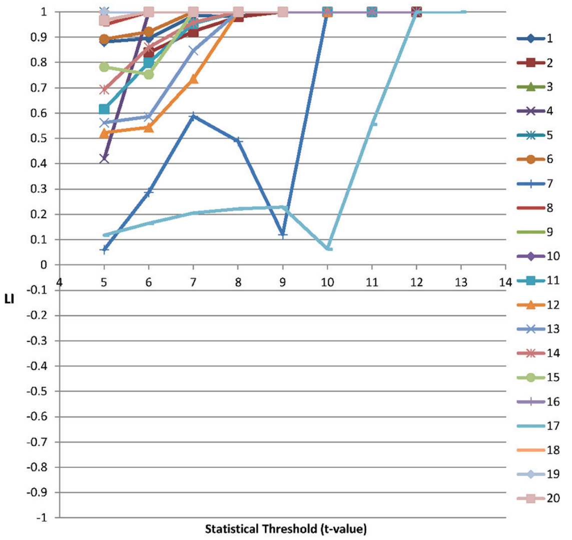

Figure 2. Laterality Index [LI] curve of verb generation paradigm tended to rise in higher statistical thresholds. At the minimal threshold (t-value 5, *p*-value <0.05) showed lower LI compare to the higher threshold. Two subjects (No. 7 and No. 17) showed co-dominant at initial threshold (LI = 0.11 and 0.06 at t-value 5), and then shifting to the left dominant at the peak threshold (LI = 1 at t-value 10 and 13). No right lateralization (LI <-0.2) was seen throughout the ranking of statistical threshold of verb generation paradigm.

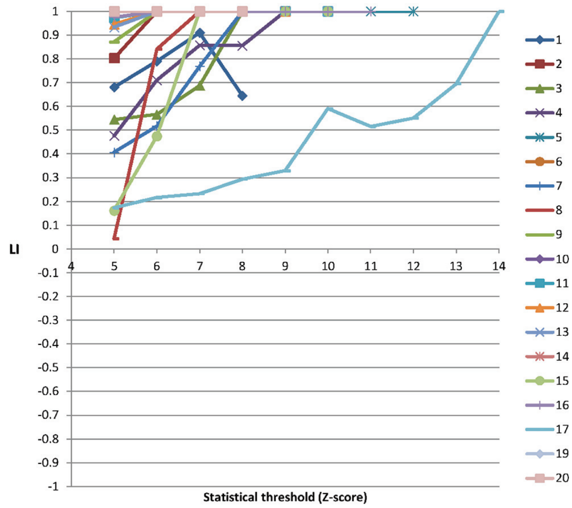

Figure 3. Laterality Index [LI] curve of word generation paradigm of most of subjects were rising when increasing statistical threshold, except the subject No. 1 which slightly falling of LI (LI = 0.64) at peak threshold (t-value 9). Subject No. 8, 15, and 17 were co-dominant at initial threshold (LI = 0.84, 0.16, and 0.17 at t-value 5, respectively). The subject No. 18 was failed to generate LI curve due to no activated voxel in language region of interest at all threshold. No right hemispheric dominant (LI <-0.2) was seen throughout the ranking of statistical threshold of word generation paradigm.

6 to 7 significantly increased mean LI with *p*-value 0.004. However, when using t-value of 7, one subject (Subject No. 18) could not be calculated LI due to an empty map. Similarly, for word generation paradigm, applying t-value of 6, nineteen subjects (95%) were defined as left hemispheric dominant with mean LI 0.85. Compared with t-value of 5, mean LI was significantly increased while changing to t-value of 6 (*p*-value 0.003). However, there was no significant difference of mean LI between t-value of 6 and 7 (*p*-value 0.056). Only one subject (No. 18) could not calculated LI of word generation paradigm due to no activated voxel on language regions of interest even if the lowest threshold as t-value of 5 was used.

Inter-rater reliability for LI of each subject at the certain thresholds of both language paradigms demonstrated almost perfect agreement. Intraclass correlation of two authors (Chosakun P and Chaitusaney T) was 0.93

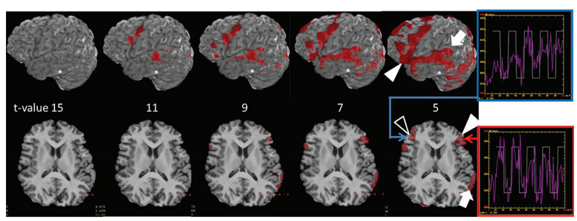

Figure 4. The fMRI images of subject No. 17 on silent verb generation paradigm. 3D volume rendering of left hemisphere (top row) showed the variable extent of activated area through the rank of statistical thresholds. Functional activation map overlaid on axial 3D FSPGR TR/TE (msec) 8.5/3.3 at level of Sylvian fissure (bottom row) demonstrated activation in right inferior frontal gyrus (black arrow head), left inferior frontal gyrus (white arrow head) and left superior temporal gyrus (white arrow) which were measured to calculate LI. After rising the t-value to 9, the activated voxels in right inferior frontal gyrus were not survived. Empty map was showed at t-value of 15 which no any activated signal was displayed. BOLD signal time course of activation at bilateral inferior frontal gyri were showed in the rightmost column.

Discussion

LI varies across different statistical thresholds. Optimal thresholds (t-value) for language lateralization are 7 in Thai verb generation and 6 in Thai word generation paradigms. Using these thresholds significantly increased mean LI of our subjects and widely defined our right-handed subjects as left lateralization.

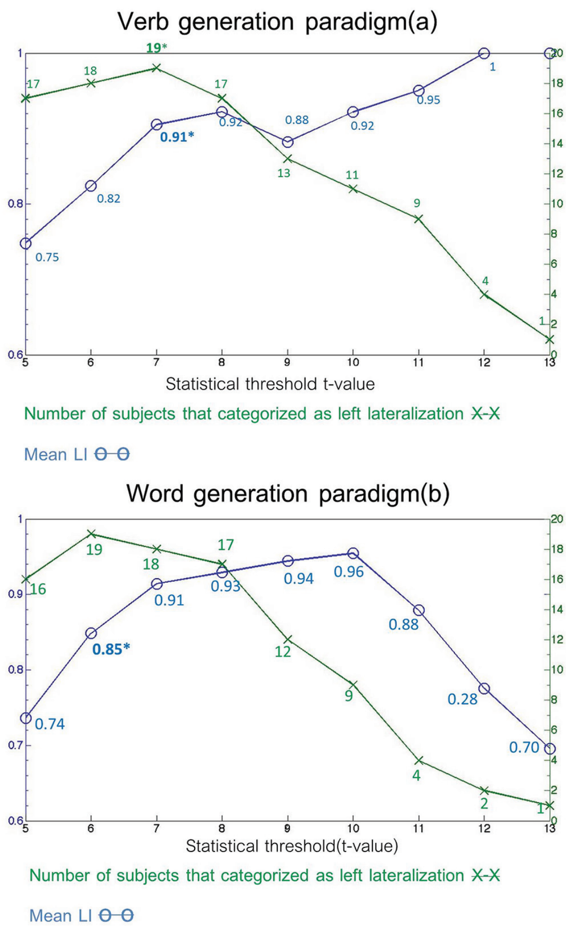

Figure 5. Graphs of the mean LI and number of left lateralized subjects through the rank of statistical thresholds of verb generation paradigm (a) and word generation paradigm (b). Mean LI of both language paradigms tended to increase against the number of subjects that define as left lateralization. (a) For verb generation paradigm, t-value of 7 significantly increased mean LI (p-value 0.004) while categorizing nineteen subjects (95%) as left hemispheric dominant. (b) For word generation paradigm, t-value of 6 significantly increased mean LI (p-value 0.003) and defined nineteen subjects (95%) as left lateralized

To enhance the impact of statistical threshold on LI and avoid too much heterogeneity in language lateralization, we included only right-handed healthy volunteers for assumption left lateralization[12,15-18].

The present study designed to use visual triggered language paradigm for prevention of false positive due to similar area of brain activation using auditory trigger, according to study of Chee et al[19].

Both silent verb and word generation paradigms which were used in the present study were categorized in word production task[20,21]. For language lateralization, word production task had more sensitivity and specificity than semantic task, according to meta-analysis which evaluated language lateralization of fMRI in comparison with Wada test[1].

Evaluation of language lateralization with multiple paradigms provides more accuracy[5,6,22], which also consistenly demonstrated in the present study. One of the study subjects whose LI was fail to calculate on word generation paradigm, but verb generation paradigm was able to determine language lateralization.

LI was used for quantitative assessment of hemispheric language dominance by measuring volume of voxels that survive on certain statistical thresholds[13]. This method is more accurate for language lateralization than the average magnitude method in comparison with Wada test[4,14,23].

The present study determined the language LI by calculating activated voxels in the language specific regions, including inferior frontal gyrus, supramarginal gyrus, angular gyrus, and superior temporal gyrus of bilateral hemispheres. These regions were defined by anatomical landmark according to the study of Naidich et al[9]. Stippich et al[6] used these regions and found high validity (98%) for language lateralization and localization in comparison with Wada test and electrocorticography. However, one recent meta-analysis study[1] demonstrated that determination of language dominance by whole brain LI gave higher LI value than by regional LI.

Statistical thresholding is a significant processing step for BOLD-contrast fMRI. Aim of statistical threshold is to define the true correlation of BOLD signal change and the hemodynamic response function of the activated brain region and to minimize effect of both physiological and physical noise fluctuation[24]. The neglect of this issue may result in incorrect interpretation of language hemispheric dominant and the spatial extent of a functional brain area[6,24,25].

The basis of t-value is the analysis of the difference of the means, which is related to the variability of data. In case of fMRI, it means a comparison of the two mean values during rest and activation by concerning the effect of noise fluctuations. The higher the t-value estimates, the less likely is the difference of the mean value, which is affected from the noise[24]. In contrast, a lower t-value is more likely to be affected by the mean value from the noise.

The present study clearly demonstrated the impact of statistical threshold on language lateralization. Some of our subjects demonstrated shifts from co-dominant to left dominance at higher threshold regardless to specific paradigm. All of them were strong right handedness (Edinburgh Handedness's score +100). There is likely more false positive voxel increment in bilateral hemispheres at lower threshold and concordance to the results of prior study[4-6,14]. In contrary, at peak threshold, most of the present study subjects failed to evaluate lateralization. The reasonable explanation is due to both true and false positive activated voxel that did not survived. To define the optimal statistical threshold that is not too low to include the false positive voxel, and not too high to miss the true positive voxel, is important for precise language lateralization. The authors demonstrated that optimal thresholds (t-value) for language lateralization are 7 in Thai verb generation and 6 in Thai word generation paradigms. The present results agree with the results of Adcock et al[3] that use 3T-fMRI and single English word generation paradigm in healthy controls and patients with temporal lobe epilepsy. They found that LI was threshold dependent and demonstrated a z-score of 5.3 compared to a z-score of 2.3, which significantly increased the LI in both controls and patients with right temporal lobe epilepsy. Slight difference of the optimal statistical threshold may be the result of different segmentation method.

One limitation of the present study is that the authors did not validate and confirm the results with gold standard (Wada test), which is a common limitation of the study done on healthy volunteers. Further application of the results in clinical controlled trial studies is needed to be established.

Conclusion

LI varies across different statistical thresholds. Optimal thresholds (t-value) for language lateralization are 7 in Thai verb generation and 6 in Thai word generation paradigms.

What is already known on this topic?

The impact of the statistical threshold on the language lateralization is known.

What this study adds?

This study is the first that defines the optimal statistical thresholds for Thai language lateralization. This might be useful in clinical controlled trial studies in Thai patient.

Acknowledgement

The present study was supported by the Ratchadapiseksompotch Fund, Faculty of Medicine, Chulalongkorn University.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Dym RJ, Burns J, Freeman K, Lipton ML. Is functional MR imaging assessment of hemispheric language dominance as good as the Wada test?: a meta-analysis. Radiology 2011;261:446-55.
2. Wongsripuemtet J, Wongfukiat O, Vichianin Y, Ngamsombat C, Witthiwej T, Sitthinamsuwan B, et al. Feasibility study of language lateralization using Thai version of language paradigm for functional MRI in clinical service. J Med Assoc Thai 2016;99:1344-54.
3. Conklin CJ, Faro SH, Mohamed FB. Technical considerations for functional magnetic resonance imaging analysis. Neuroimaging Clin N Am 2014; 24:695-704.
4. 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.
5. 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.
6. Stippich C, Rapps N, Dreyhaupt J, Durst A, Kress B, Nennig E, et al. Localizing and lateralizing language in patients with brain tumors: feasibility of routine preoperative functional MR imaging in 81 consecutive patients. Radiology 2007;243: 828-36.
7. 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.
8. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 1971;9:97-113.
9. Naidich TP, Valavanis AG, Kubik S. Anatomic relationships along the low-middle convexity: Part I--Normal specimens and magnetic resonance imaging. Neurosurgery 1995;36:517-32.
10. Bethmann A, Tempelmann C, De Bleser R,

Scheich H, Brechmann A. Determining language laterality by fMRI and dichotic listening. Brain Res 2007;1133:145-57.
11. Harrington GS, Buonocore MH, Farias ST. Intrasubject reproducibility of functional MR imaging activation in language tasks. AJNR Am J Neuroradiol 2006;27:938-44.
12. 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.
13. 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.
14. Seghier ML. Laterality index in functional MRI: methodological issues. Magn Reson Imaging 2008;26:594-601.
15. Knecht S, Deppe M, Drager B, Bobe L, Lohmann H, Ringelstein E, et al. Language lateralization in healthy right-handers. Brain 2000;123(Pt 1):74-81.
16. Knecht S, Drager B, Deppe M, Bobe L, Lohmann H, Floel A, et al. Handedness and hemispheric language dominance in healthy humans. Brain 2000;123 Pt 12:2512-8.
17. Frost JA, Binder JR, Springer JA, Hammeke TA, Bellgowan PS, Rao SM, et al. Language processing is strongly left lateralized in both sexes. Evidence from functional MRI. Brain 1999;122 (Pt 2):199-208.
18. Pujol J, Deus J, Losilla JM, Capdevila A. Cerebral lateralization of language in normal left-handed people studied by functional MRI. Neurology 1999;52:1038-43.
19. Chee MW, O'Craven KM, Bergida R, Rosen BR, Savoy RL. Auditory and visual word processing studied with fMRI. Hum Brain Mapp 1999;7: 15-28.
20. Engstrom M, Ragnehed M, Lundberg P, Soderfeldt B. Paradigm design of sensory-motor and language tests in clinical fMRI. Neurophysiol Clin 2004;34:267-77.
21. Price CJ. The functional anatomy of word comprehension and production. Trends Cogn Sci 1998;2:281-8.
22. 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.
23. Baciu MV, Watson JM, Maccotta L, McDermott KB, Buckner RL, Gilliam FG, et al. Evaluating functional MRI procedures for assessing hemispheric language dominance in neurosurgical patients. Neuroradiology 2005;47:835-44.
24. Stippich C, editor. Clinical functional MRI presurgical functional neuroimaging. 2nd ed. Berlin Heidelberg: Springer; 2015.
25. Wilke M, Schmithorst VJ. A combined bootstrap/histogram analysis approach for computing a lateralization index from neuroimaging data. Neuroimage 2006;33:522-30.