Neural substrates of aphasia in acute left hemispheric stroke using voxel based lesion-symptom brain mapping

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ABSTRACT

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Background: An acquired communication disorders, characterized by an impairment of language modalities, are most often caused by sequelae of stroke. The theory about brain lesions related to aphasia has well reported. However, it is unclear how these brain lesions fit into the language processing in acute stroke. In this study, we aimed to investigate neuroanatomical lesion related to language processing in acute post-stroke patients with left hemispheric lesion using voxel-based lesion-symptom mapping.

Methods: This retrospective study included 73 patients with acute first-ever stroke from January 2011 to April 2016. Magnetic resonance images (MRIs) of the brain and evaluation of aphasia using Korean version of the Western Aphasia Battery (K-WAB) were conducted within 1 month after stroke onset. Regions of interests (ROIs) were aligned manually at each affected slice of T1 weighted image with monitoring corresponding FLAIR and diffusion images to confirm plausibility of infarction. Normalization of ROIs and voxel-based statistical analysis have been done using Statistical Parametric Mapping 12 running under Matlab. The K-WAB assessment was included aphasia quotient (AQ), scores of four subtests. Each voxel, lesioned or non-lesioned, was compared with AQ and subtest scores as dependent variable.

Results: In our consecutive 73 subjects, 58 patients (79.5%) were verified to be

less than 92.8 in AQ. In subgroup analysis, aphasia group showed significantly much more involvement of extra-nuclear area, insula, inferior frontal gyrus and superior temporal gyrus compared to non-aphasia group ($p < 0.01$). Voxel-based lesion symptom mapping of significant association between brain lesions and the score of spontaneous speech domain was shown in inferior parietal lobule, inferior and middle frontal gyrus and insula. The lesion of insular cortex, inferior parietal lobule, inferior frontal gyrus, middle frontal gyrus and superior temporal gyrus were correlated with score of comprehension subtest. The lesion on inferior parietal lobule, insula, precentral gyrus, inferior frontal gyrus, BA 41 and 22 were correlated with score of repetition subtest. The lesion on inferior parietal lobule, insula and inferior frontal gyrus were correlated with score of naming ($p < 0.001$, false recovery data corrected).

Conclusion: In this study, it is possible to localize the brain lesion related to language processing using voxel-based lesion-symptom analysis from early MRI imaging study in acute stroke. It may be useful to understand the language process and brain lesion after stroke.

Key words : stroke, hemiplegia, aphasia, language and speech disorders, brain mapping

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I. INTRODUCTION

Aphasia, acquired communication disorders caused by injury in central nervous system, is most common as a result of stroke and has been reported to occur in 15 to 38% of ischemic stroke patients[1-3]. Aphasia is distinct from cognitive impairments or speech disorders which refer to the motor mechanism dysfunction involved in spoken words. It is well known that communication disorders could severely impact loss of social function and the quality of life of patients and their families as well as morbidity and mortality.

The factors affecting the recovery of aphasia are related to the age, education level, and ability to perform independent activities of daily living. In particular, the location and size of brain lesions determine the type and severity of aphasia and moreover prognosis.

Aphasia is conventionally classified into sensory and motor, or fluent and non-fluent, dichotomy by evaluating speech, comprehension, repetition, naming and furthermore reading and writing. A cortical regions of the left cerebral hemisphere was traditionally known to cause aphasia such as Wernicke's area, Broca's area, lateral frontal lobule, superior temporal gyrus, angular and supramarginal gyrus[4]. Several studies reported the relationship of subcortical structures, such as thalamus or putamen, and aphasia; however, there were no generally accepted classification system for the subcortical aphasia[4,5]. In recent

years, it has been argued that more complex processes will affect language formation.

The voxel-based lesion-symptomatic brain mapping(VLSM) study, which was first reported by Bates et al. in 2003[6], is a useful method of offering the statistical significant brain lesions related to certain performance ability. Also, VLSM analyses allow whether a certain performance could be predicted by the spatial location of brain lesions[7]. Although there are some studies on the relationship between language impairment and lesion site in stroke patients[8-13], studies limited to acute phase patients are rare. Also, there has been paucity of studies about type and severity of aphasia and brain lesion using VLSM.

The aim of this study was to investigate the correlation between brain lesion location and aphasia using voxel-based lesion-symptom mapping in acute stroke patients. We evaluated not only the presence of aphasia, also type and classification of aphasia using the Korean version of the Western Aphasia Test (K-WAB) in order to help establish the plan for early rehabilitation treatment.

II. MATERIALS AND METHODS

1. Enrollment

This retrospective study was conducted at the single tertiary medical center. From January 2011 to April 2016, 433 adult patients with stroke were included. Those who met all of the following criteria were included into this study: 1) first-ever stroke restricted to the left supratentorial hemisphere, either ischemic or hemorrhagic, confirmed by magnetic resonance imaging (MRI), 2) age 18 years or older, 3) elapsed time of 1 month or less after stroke onset, 4) no history of neurological or psychiatric disorders, 5) no history of communication disorder including hearing difficulty, 6) right handedness, 6) accomplishment of language assessment using K-WAB within 1 month after onset of stroke.

Seventy-three patients, consisting of forty men and thirty-three women,

in acute period following a first-ever isolated left supratentorial stroke were enrolled in this study. Patient characteristics, such as age, sex, type of stroke, date of evaluation and results were collected from medical chart reviews.

2. Language evaluation

All of the subjects were administered the validated language test using K-WAB[14]. The K-WAB assessment is well established evaluation tool for aphasia consisted of four language subtests including spontaneous speech, comprehension, repetition, and naming. Aphasia quotient (AQ) was evaluated to quantify the severity of aphasia by summating the score of above four domains. Subjects were classified into two groups by AQ scores; less than 92.8 as aphasia group and the rest as non-aphasia group based on previous study[15-17].

3. Acquisition of Brain MRI

All subjects underwent a brain imaging study with the same protocol in a single medical center. Brain MRI was performed using 3.0-Tesla scanners (Philips Gyroscan Intera, Netherlands). MRI images including 3-dimensional T1-weighted (axial plane, repetition time = 9.9ms, echo time = 4.6ms, field of review = 220mm, 160 slices), T2-weighted (axial plane, repetition time = 4553ms, echo time = 80ms, field of review = 230mm, 48 slices) and a fluid attenuation inversion recovery (FLAIR) scan (axial plane, repetition time: 11.000ms, echo time: 125ms, field of view: 230mm, 20 slices) were obtained.

4. Statistical analysis of clinical data

Descriptive statistics were used to characterize patients using SPSS Statistics software, Version 20.0 (IBM, USA). Statistical significance was set at a p-value of <0.05.

5. Lesion mapping and analysis

With brain MR images, regions of interest (ROI) were aligned manually at each affected slice on T1-weighted magnetic resonance images using MRIcron software (University of South Carolina, USA). Each slice was inspected with comparing corresponding FLAIR image to ensure the spatial location of lesion delineation and plausibility of ROI. And then, data was normalized to a standard brain template in order to examine the neural correlates of aphasia using voxel-based lesion-symptom mapping analysis. Normalization was performed using Statistical Parametic Mapping 12 software (Wellcome Department of Cognitive Neurology, UK) running under MATLAB (MathWorks, USA).

Using normalized lesion images, overlay map was created of all and each group of subjects. Also, voxel-by-voxel chi square analysis of each voxel was done for group comparison with statistical significance as $p < 0.01$.

A VLSM analysis was executed to ascertain correlations between brain lesions and the severity and each score of four domains of aphasia. For statistical analysis, only voxels which were lesion at least 20% of the patients were included. This test provides a Z score map which higher, the greater impact on lower score. Significant statistical value was defined as $p < 0.001$, corrected for multiple comparisons using the false discovery rate (FDR).

III. RESULTS

1. Characteristics of the Subjects

Seventy-three subjects, consisting of forty men and thirty-three women, meeting the inclusion criteria were enrolled. Clinical characteristics of the subjects are shown in Table 1. In our consecutive subjects, fifty-eight patients (79.5%) were verified to be less than 92.8 in AQ. Those who below 20 in AQ were 33 patients (45.2%). In aphasia group, the frequencies of the types of

aphasia were: global 31(53.4%), Broca's 6(10.3%), transcortical motor 1(1.7%), Wernicke's 8(13.8%), transcortical sensory 2(3.4%), conduction 1(1.7%) and anomic 9(15.5%). There are no significant differences in demographic and clinical characteristics except AQ score between groups. The age of patients ranged from 23 to 86 years (mean 63.32; standard deviation [SD] 16.20 years). Elapsed time after onset of the stroke was 18.07days (SD, 5.73 days) on average. Majority of subjects (94.5%) were ischemic stroke.

Table 1. Characteristics of the subjects (n=73)

Characteristics	Aphasia (n=58)	Non-aphasia (n=15)	*P* value
Age at the time of stroke onset (years)	64.59±16.74	58.40±13.25	0.286
Gender (male : female)	32:26	8:7	0.126
Type of stroke			0.659
Ischemia	55	14	
Hemorrhage	3	1	
Onset duration, days	18.97±5.76	14.60±4.24	0.063
AQ score	29.41±30.72	95.43±2.33	<0.001*

All values are presented as mean ± standard deviation

AQ, Aphasia quotient

2. Group comparison analysis

Fig. 1 presents the distribution of brain lesions in each group through an overlay map. Statistically significant difference in lesions between aphasia

and non-aphasia group was shown in Fig. 2. Peak intensity was showed in extra-nuclear area ($\chi^2 = 20.3$, peak MNI coordinate: -28, 14, 14, $p < 0.01$). Also high-powered regions were presented in insular cortex ($\chi 2 = 17.4$, peak MNI coordinate: -32,8,14), claustrum ($\chi 2 = 15.7$, peak MNI coordinate: -32,8,4), inferior frontal gyrus ($\chi 2 = 12.7$, peak MNI coordinate: -38, 4, 34) and superior temporal gyrus ($\chi 2 = 9.5$, peak MNI coordinate: -50, 2, 4) compared to non-aphasia group ($p < 0.01$). Subjects with below 20 in AQ were showed highest coordinate region in inferior parietal lobule ($\chi 2 = 31.0$, peak MNI coordinate: -42, -24, 30) and insular cortex/BA13 ($\chi 2 = 25.2$, peak MNI coordinate: -38,-16,18) ($p < 0.01$).

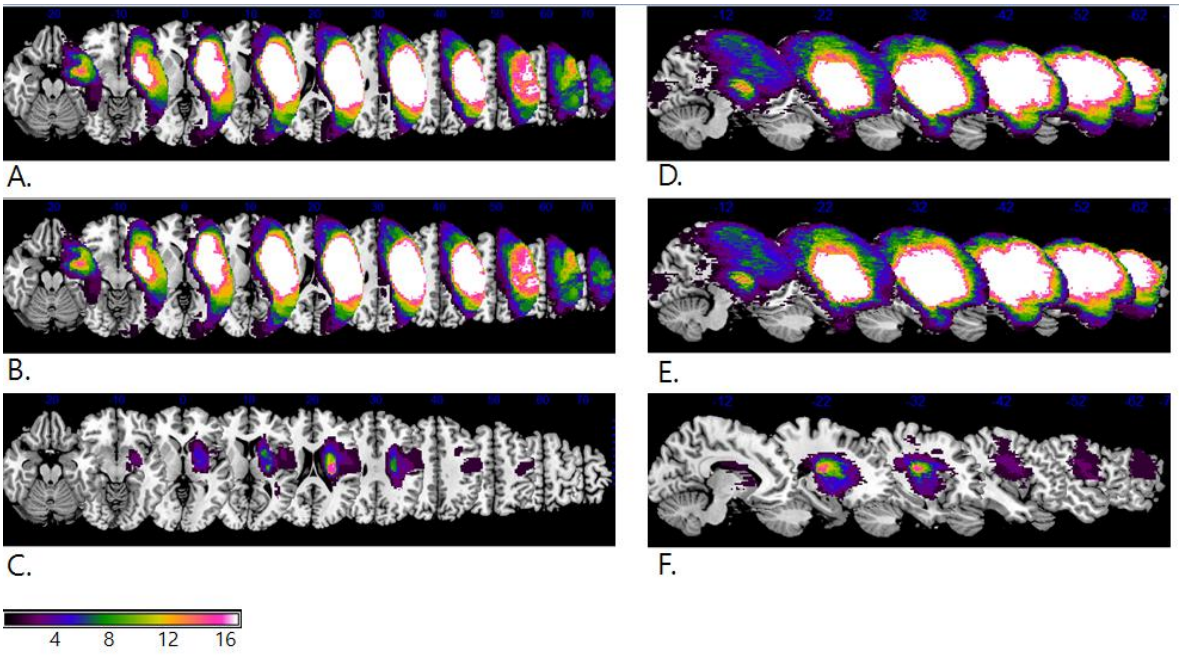


Fig. 1. Overlay map of subjects. (A,D) 73 patients included in this study, (B,E) 58 patients classified as aphasia group, (C,F) 15 patients as non-aphasia group. The higher score in color range indicates a larger number were lesioned.

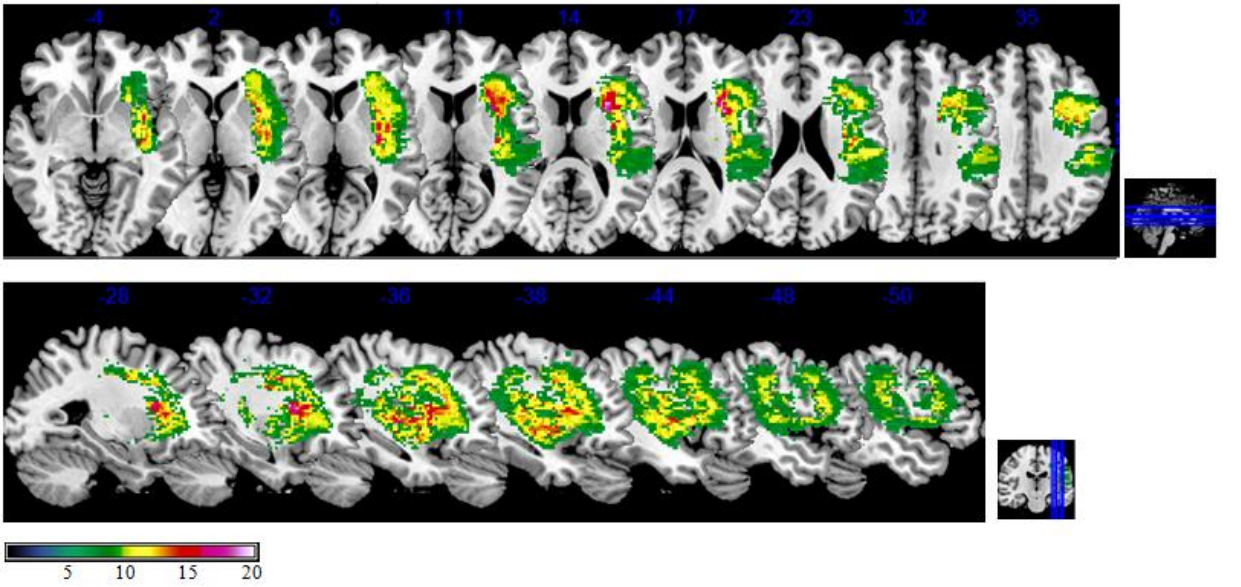


Fig. 2. Group comparison analysis between aphasia and non aphasia group. The color bar indicates chi square (χ^2) by $p < 0.01$. Higher χ^2 indicates anatomical regions related to aphasia group.

3. Relating lesion and language performance in acute stage

Voxel-based lesion symptom maps were showing the correlation between brain lesions and performance of K-WAB test. The scores of AQ and four subtests were used for analysis as dependent variables. Significant anatomical regions correlated with AQ of K-WAB were presented in Figure 3 and Table 2. Regions of peak intensity associated with AQ was left inferior parietal lobule (z = 7.2, peak MNI coordinate: -42, -24, 24, p <0.001). Figure 4 and table 3 presented the results of correlation analysis of K-WAB four subtests and brain lesions. Most highly powered regions as highest Z score related to spontaneous speech subtest were left inferior frontal gyrus (z = 6.7, peak MNI coordinate: -38, 4, 34, p <0.001) and inferior parietal lobule (z = 6.7, peak MNI coordinate: -42, -24, 24, p <0.001). Left insula/brodmann area 13 was

determined to most highly lesioned area in auditory comprehension (z = 6.7, peak MNI coordinate: -40, -12, 2, p <0.001) and naming (z = 7.2, peak MNI coordinate: -38, -8, 18, p <0.001) subtests. Repetition subtest was highest relationship with left inferior parietal lobule (z = 8.1, peak MNI coordinate: -42, -24, 24, p <0.001). The significant regions denoted as Montreal Neurological Institute (MNI) coordinates were listed in table 3 in order to Z score.

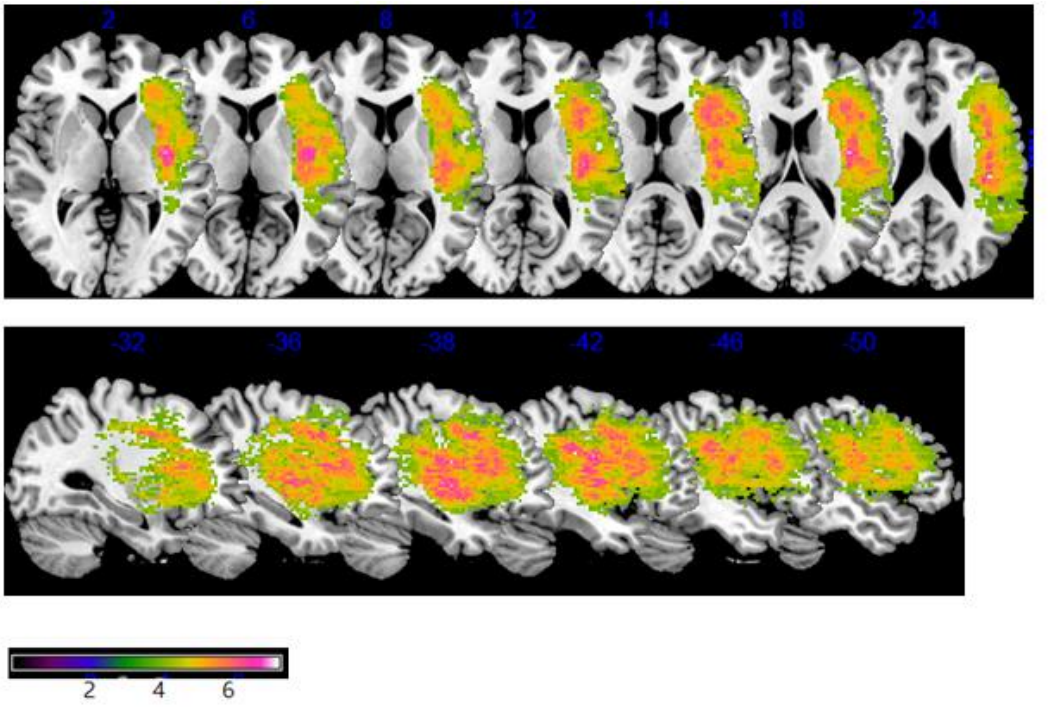


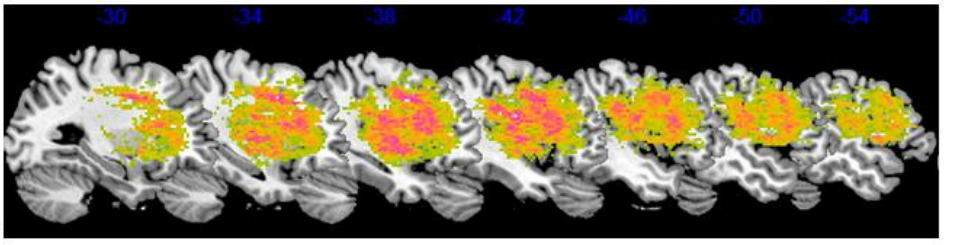
Fig. 3. Voxel-based lesion symptom maps of significant correlation between lesion and AQ (p < 0.001 with corrected false discovery rate). Anatomical correlation was shown as axial and sagittal view. The color range indicates Z score.

Table 2. Anatomic coordinates of AQ (p value <0.001, false discovery rate corrected)

Region	MNI coordinate	Z score
Lt inferior parietal lobule	-42, -24, 24	7.2
Lt insula/BA 13	-38, -8, 2; -36,-20,12	6.9
Lt middle frontal gyrus	-38, 10, 34	6.0
Lt precentral gyrus	-38, -4, 38	5.6
Lt inferior frontal gyrus	-38, 26, 12	5.4
Lt superior temporal gyrus	-46, -28, 7	4.9

Lt, Left; BA, brodmann area

A.



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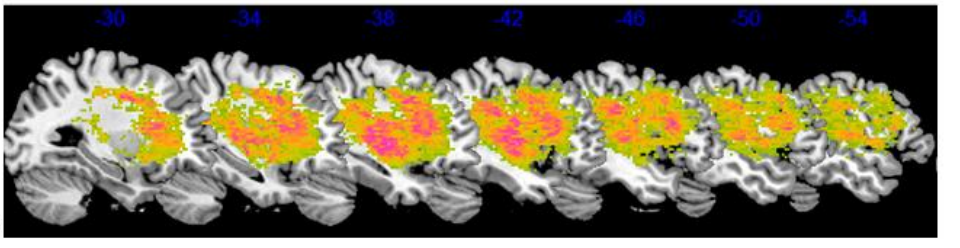

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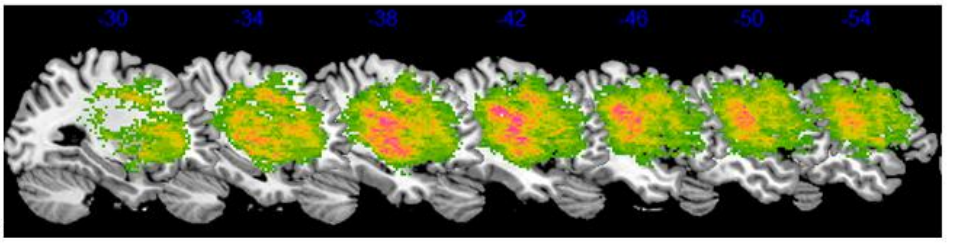

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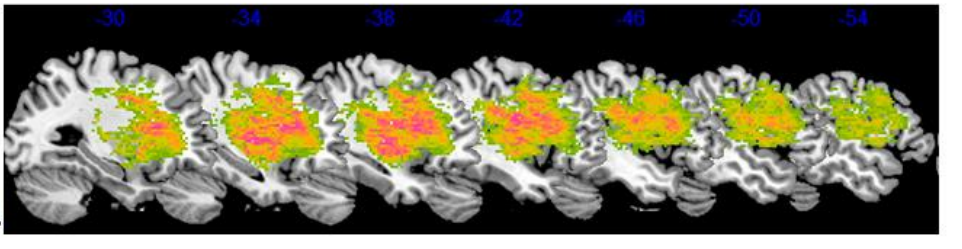

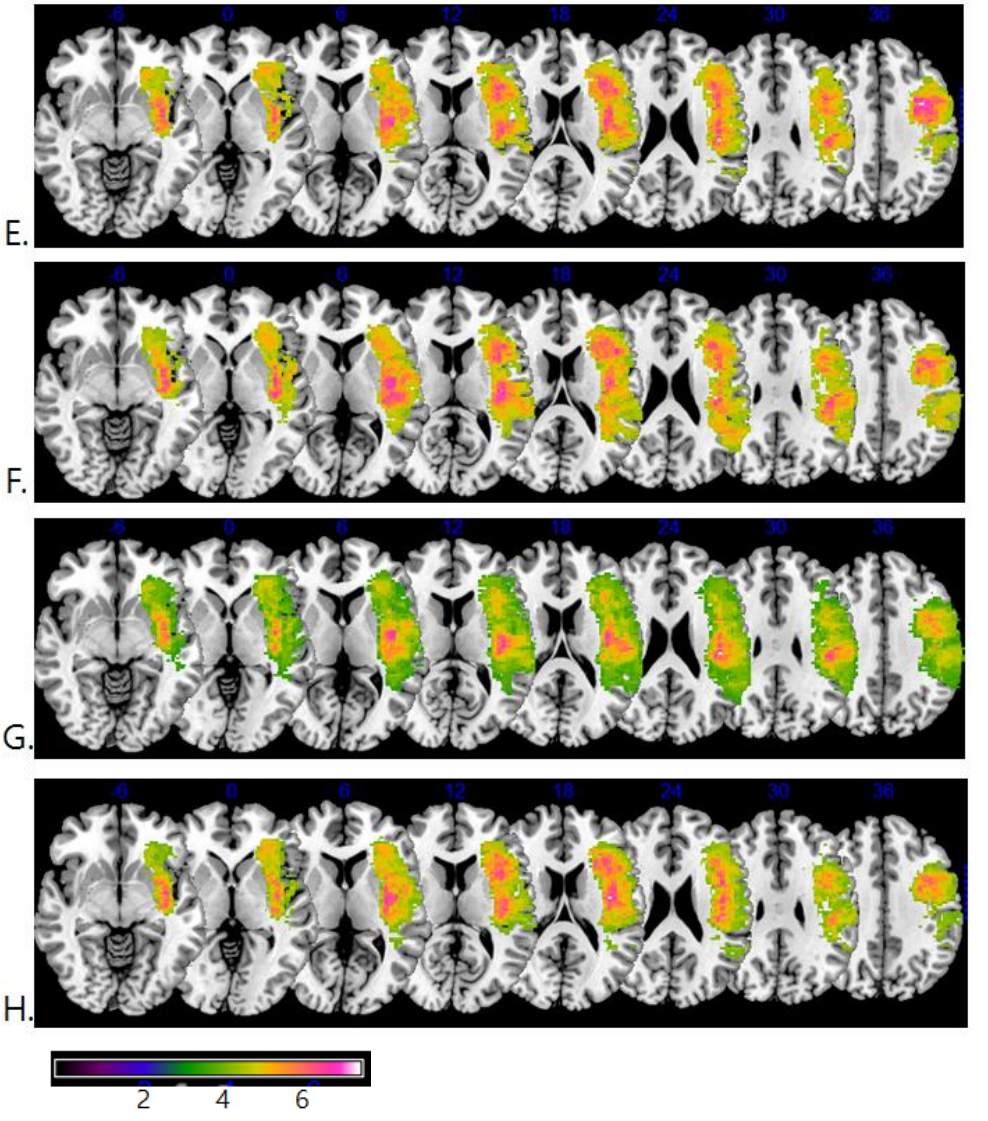

Fig. 4. Anatomical correlation between brain lesions and four subtests of K-WAB shown as axial and sagittal view. (A,E) spontaneous speech, (B,F) auditory comprehension, (C,G) repetition, (D,H) naming. The color range indicates Z score by statistical significance p value < 0.001, false discovery rate corrected. Higher Z score indicates areas associated with lower score of K-WAB subtests.

Table 3. Anatomic coordinates of four subtests of K-WAB ($p < 0.001$, false discovery rate corrected)

Spontaneous speech			Auditory comprehension			Repetition			Naming		
Region	MNI coordinate	Z score	Region	MNI coordinate	Z score	Region	MNI coordinate	Z score	Region	MNI coordinate	Z score
IFG /BA45	-38, 4, 34; -30, 23, 6	6.7	Insula /BA13	-40. -12, 2; -38,-8,2	6.7	IPL	-42, -24, 24	8.1	Insula	-38, -8, 18;	7.2
IPL	-42, -24, 24	6.7	IFG /BA45	-38, 4, 34; -30, 23, 6	6.1	Insula /BA13	-38, -8, 18; -40.-12,2	7.5	IPL	-42, -24, 24	6.9
Insula /BA13	-38, -8, 2; -38,-8,18	6.3	IPL	-42, -24, 24	6.0	IFG /BA45	-38, 4, 34; -30, 23, 6	6.9	IFG /BA45	-38, 4, 34; -30, 23, 6	6.3
MFG /BA9	-40, 8, 38	6.3	MFG BA9	-40, 8, 38	5.8	PCG /BA6	-38, -4, 42	6.2	MFG /BA9	-40, 8, 38; -38,10,34	6.0
PCG /BA6	-38, -4, 42;	5.5	TTG /BA41	-48, -20, 12; -44,-26,10	5.3	MFG /BA9	-40, 8, 38; -38, 10, 34	5.9	PCG/ BA6	-38, -4, 42; -38,-4,38	5.7
STG /BA22	-50, 2, 4; -50, -4, 4	5.0	STG /BA22	-48, -20, 8; -50, -4, 4	5.2	TTG /BA41	-48, -20, 12; -44,-26,10	5.7	TTG /BA41	-48, -20, 12; -44,-26,10	4.9
TTG	-44,-26,10	4.2	PCG /BA6	-38, -4, 38; -40, 8, 38	5.0	STG /BA22	-50, -4, 4; -50, 2, 4	5.3	STG /BA22	-50, 2, 4; -50, -4, 4	4.8

IFG, inferior frontal gyrus; IPL, inferior parietal lobule; MFG, middle frontal gyrus; PCG, precentral gyrus; STG, superior temporal gyrus; TTG, transverse temporal gyrus. All brain regions in left hemisphere.

IV. DISCUSSION

This study investigated a comprehensive assessment of how the structural damage in left hemisphere interferes the language performance in acute stroke patients using voxel-based lesion-symptom mapping. The outcome of language function was predicted by initial aphasia severity[18]; thus, this has significance because previous studies have been conducted with chronic stroke patients or without limitation of onset period and mostly focused on single characteristics of the language. Our main findings provide lesion-symptom mapping by linking severity and deficit in language domains, such as spontaneous speech, auditory comprehension, repetition and naming, to lesion location.

The cortical areas such as Broca's area and Wernicke's area of brain were traditionally regarded as critical regions of aphasia[4,14], however, more recently, more complex processes have been reported to be involved in language formation. We found that inferior parietal lobule and insula were most strongly associated with severity of aphasia and also subtests of K-WAB. These results make sense with previous work focused on speech and insular lesion. Insula, deep folded cerebral cortex, was known to most common region affected by middle cerebral artery territory infarction and greatest overlap among large strokes reflecting vulnerability to ischemia[19]. Also, complex process of speech probably depends on a network of brain regions including anterior insula[20]. Inferior parietal lobule, part of arcuate fasciculus, was known to important neural tract in language function. Neural connectivity and preservation of arcuate fasciculus was related to better aphasia outcome in previous study[21]. In this context, neural correlates of language functions in acute phase of stroke may extended and overlapped in spatial regions and then this will happen highest powered lesion correlation in insula and inferior parietal lobule such as arcuate fasciculus.

Correlation analysis of four main language domains to brain lesion site is considerably corresponding to previous functional neuroimaging studies about

aphasia. Although lobule or gyrus is anatomically large areas, we presented information of peak intensity regions via MNI coordinates. Brain areas were including well known brodmann area(BA) connected with aphasia; inferior frontal gyrus including BA 45, middle frontal gyrus including BA 9, superior temporal gyrus including BA 22 and transverse temporal gyrus including BA 41. There is substantial evidence of the association between verbal fluency and left inferior frontal gyrus, especially Broca's area known as BA 44/45 and left premotor and precentral gyrus known as motor area[22,23]. Some neuroimaging studies revealed damage in anterior insula had shown predictive role in speech production[24,25]. Auditory word comprehension engaged in left posterior superior temporal cortices and Heschl's gyri known as primary auditory cortex. Also, left inferior parietal lobe such as angular gyrus and inferior frontal and mid frontal cortex, which were associated with perisylvian cortex, were reported as brain regions involved in language comprehension[26,27]. Previous studies investigating the processing of syntactic information reported activation of left inferior frontal lobe in functional imaging study[28]. Another study reported similar results of inferior frontal gyrus which had role in selection and integration of semantic information for comprehension[29]. Language repetition test, especially auditory word repetition, has been known to activation of auditory-motor pathway. Arcuate fasciculus, connecting white matter tracts, damage and also left posterior temporal cortex, angular gyrus and inferior frontal gyrus were associated to repetition[24] corresponding to current study. The ability of naming is considered to multi-stages of complex processing, such as recognition of item, representation and articulation[8]. Left middle and superior temporal gyrus, inferior parietal cortex and inferior frontal cortex were revealed to relationship with naming in previous study[8,30].

The current study shows partially inconsistent correlation with previous studies. The previous studies revealed the role of left middle and inferior temporal gyrus as word production or naming[8,11,31], and no correlation was

observed in this study. Although relative large patient was enrolled in this study, this study included unilateral left supratentorial hemisphere patients predominantly middle cerebral artery lesions (75.3%) and significant voxels in this study were considerably concentrated to left perisylvian cortex. This could have resulted in failure to reflect sufficient lesions. The previous reported association of apraxia of speech and left precentral gyrus[32] were not fully evaluated in this study. The mean MMSE of enrolled patients with non fluent aphasia enrolled in study was 6.53, which was considerably lower than the overall mean of 13.82.

There are several limitations of this study. First, selection bias may affect on results. The number of subjects in the non-aphasia group was relatively small and did not include a sufficient range of brain lesions. The statistical significance of comparing the differences between aphasia and non-aphasia group, resulted in somewhat damped. And, in this study, the number of global aphasia was thirty-one patients (53.4% of aphasia group). Comparing previous study, selected patients were showed more severe types of aphasia and lower mean AQ[18]. These patients had relatively low tendency to other functions including cognitive function. Second, measurement bias nay have been present. However, for lesion mapping, measurements were conducted by a skilled clinician who was blinded to all clinical information. Also same equipment and protocol were used to produce the constant results. For language test, cut-off value of AQ was based on previous study, other reflective of age and education factors were nevertheless not considered. Also, medication effect may one of the confounding factors of the relationship between aphasic function and lesion location, but the duration of medications was between 3 days and 5 days and so it was not considered as a variable. Third, integrity of right hemisphere was not considered in this study. In previous study, right precentral gyrus and temporoparietal grey matter was positive correlation with spontaneous speech, naming and repetition scores after left hemispheric stroke[33]. Forth, more

advanced language features including reading and writing were not evaluated because majority of patients were severe aphasia. Fifth limitation is changes over time and recovery was not possible to address.

V. CONCLUSION

This study presents that it is possible to localize the brain lesion related to language processing using voxel-based lesion-symptom analysis from early MRI imaging study in acute stroke. It may be useful to understand the language process and brain lesion after stroke. Further prospective studies are required to verify these findings.

REFERENCES

1. Inatomi Y, Yonehara T, Omiya S, Hashimoto Y, Hirano T, Uchino M. Aphasia during the acute phase in ischemic stroke. Cerebrovasc Dis 2008;25:316-23.
2. Berthier ML. Poststroke aphasia : epidemiology, pathophysiology and treatment. Drugs Aging 2005;22:163-82.
3. Ellis C, Simpson AN, Bonilha H, Mauldin PD, Simpson KN. The one-year attributable cost of poststroke aphasia. Stroke 2012;43:1429-31.
4. Albert ML, Helm-Estabrooks N. Diagnosis and treatment of aphasia. Part I. JAMA 1988;259:1043-7.
5. Alexander MP, Naeser MA, Palumbo CL. Correlations of subcortical CT lesion sites and aphasia profiles. Brain 1987;110 (Pt 4):961-91.
6. Bates E, Wilson SM, Saygin AP, Dick F, Sereno MI, Knight RT, et al. Voxel-based lesion–symptom mapping. Nature neuroscience 2003;6:448-50.
7. Rorden C, Karnath HO, Bonilha L. Improving lesion-symptom mapping. J Cogn Neurosci 2007;19:1081-8.
8. Baldo JV, Arevalo A, Patterson JP, Dronkers NF. Grey and white matter correlates of picture naming: evidence from a voxel-based lesion analysis of the Boston Naming Test. Cortex 2013;49:658-67.
9. Baldo JV, Schwartz S, Wilkins D, Dronkers NF. Role of frontal versus temporal cortex in verbal fluency as revealed by voxel-based lesion symptom mapping. Journal of the International Neuropsychological Society 2006;12:896-900.
10. Butler RA, Lambon Ralph MA, Woollams AM. Capturing multidimensionality in stroke aphasia: mapping principal behavioural components to neural structures. Brain 2014;137:3248-66.
11. Schwartz MF, Kimberg DY, Walker GM, Faseyitan O, Brecher A, Dell

GS, et al. Anterior temporal involvement in semantic word retrieval: voxel-based lesion-symptom mapping evidence from aphasia. Brain 2009:awp284.

12. Geva S, Jones PS, Crinion JT, Price CJ, Baron JC, Warburton EA. The neural correlates of inner speech defined by voxel-based lesion-symptom mapping. Brain 2011;134:3071-82.
13. Pillay SB, Binder JR, Humphries C, Gross WL, Book DS. Lesion localization of speech comprehension deficits in chronic aphasia. Neurology 2017;88:970-5.
14. Albert ML, Helm-Estabrooks N. Diagnosis and treatment of aphasia. Part II. JAMA 1988;259:1205-10.
15. Kim H, Na DL. Normative data on the Korean version of the Western Aphasia Battery. J Clin Exp Neuropsychol 2004;26:1011-20.
16. Choi JY, Lee KH, Na DL, Byun HS, Lee SJ, Kim H, et al. Subcortical aphasia after striatocapsular infarction: quantitative analysis of brain perfusion SPECT using statistical parametric mapping and a statistical probabilistic anatomic map. J Nucl Med 2007;48:194-200.
17. Tak HJ, Jang SH. Relation between aphasia and arcuate fasciculus in chronic stroke patients. BMC neurology 2014;14:46.
18. Pedersen PM, Vinter K, Olsen TS. Aphasia after stroke: type, severity and prognosis. The Copenhagen aphasia study. Cerebrovasc Dis 2004;17:35-43.
19. Dronkers NF. A new brain region for coordinating speech articulation. Nature 1996;384:159-61.
20. Hillis AE, Work M, Barker PB, Jacobs MA, Breese EL, Maurer K. Re-examining the brain regions crucial for orchestrating speech articulation. Brain 2004;127:1479-87.
21. Kim SH, Jang SH. Prediction of aphasia outcome using diffusion tensor tractography for arcuate fasciculus in stroke. AJNR Am J Neuroradiol

2013;34:785-90.

22. Costafreda SG, Fu CH, Lee L, Everitt B, Brammer MJ, David AS. A systematic review and quantitative appraisal of fMRI studies of verbal fluency: role of the left inferior frontal gyrus. Hum Brain Mapp 2006;27:799-810.
23. 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.
24. Price CJ. The anatomy of language: contributions from functional neuroimaging. J Anat 2000;197 Pt 3:335-59.
25. Borovsky A, Saygin AP, Bates E, Dronkers N. Lesion correlates of conversational speech production deficits. Neuropsychologia 2007;45:2525-33.
26. Dronkers NF, Wilkins DP, Van Valin RD, Jr., Redfern BB, Jaeger JJ. Lesion analysis of the brain areas involved in language comprehension. Cognition 2004;92:145-77.
27. Caplan D, Hildebrandt N, Makris N. Location of lesions in stroke patients with deficits in syntactic processing in sentence comprehension. Brain 1996;119 (Pt 3):933-49.
28. Friederici AD, Ruschemeyer SA, Hahne A, Fiebach CJ. The role of left inferior frontal and superior temporal cortex in sentence comprehension: localizing syntactic and semantic processes. Cereb Cortex 2003;13:170-7.
29. Homae F, Hashimoto R, Nakajima K, Miyashita Y, Sakai KL. From perception to sentence comprehension: the convergence of auditory and visual information of language in the left inferior frontal cortex. Neuroimage 2002;16:883-900.
30. Walker GM, Schwartz MF, Kimberg DY, Faseyitan O, Brecher A, Dell GS, et al. Support for anterior temporal involvement in semantic error

production in aphasia: new evidence from VLSM. Brain Lang 2011;117:110-22.

31. Pihlajamaki M, Tanila H, Hanninen T, Kononen M, Laakso M, Partanen K, et al. Verbal fluency activates the left medial temporal lobe: a functional magnetic resonance imaging study. Ann Neurol 2000;47:470-6.

32. Itabashi R, Nishio Y, Kataoka Y, Yazawa Y, Furui E, Matsuda M, et al. Damage to the Left Precentral Gyrus Is Associated With Apraxia of Speech in Acute Stroke. Stroke 2016;47:31-6.

33. Xing S, Lacey EH, Skipper-Kallal LM, Jiang X, Harris-Love ML, Zeng J, et al. Right hemisphere grey matter structure and language outcomes in chronic left hemisphere stroke. Brain 2016;139:227-41.

ABSTRACT(IN KOREAN)

좌측 대뇌 반구 뇌졸중 후 실어증과 연관된 화소 기반 병변 증상 뇌 지도 연구

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박은지

목적: 실어증은 중추신경계의 손상으로 인해 후천적으로 발생한 언어장애로 뇌졸중의 후유증으로 발생하는 것이 가장 흔하다. 뇌졸중 후 실어증은 환자의 사회적 기능 소실 및 환자와 가족의 삶의 질을 저해할 뿐 아니라 질병이환율 및 사망률을 높이고, 이의 회복은 대부분 첫 6개월 이내에 이루어지므로 조기에 평가하고 위험요인을 분석하는 것이 재활치료에 중요한 부분이라고 할 수 있겠다. 실어증과 관련된 뇌 부위에 대한 이론들은 많이 알려져 있지만, 실제로 급성기 뇌졸중 환자들의 의사소통 및 언어기능에 관여하는 뇌신경해부학적인 연관성에 대해서는 뚜렷하지 않은 부분이 많다. 따라서 본 연구는 급성기의 좌측 대뇌 반구 뇌졸중 환자를 대상으로 화소 기반 병변-증상 뇌 지도 연구를 통해 뇌의 병변과 언어 수행 능력의 연관성을 살펴보고자 하였다.

방법: 73명의 대상자는 모두 발병 1개월 이내에 뇌 자기공명영상과 한국형 웨스턴 실어증 검사를 통한 평가를 실행하였다. 뇌 자기공명영상은 모든 환자에게서 동일한 방법으로 시행되었다. T1 강조 영상에 그려진 ROI (regions of interest)는 연구자에 의하여 직접 평가되고 그려졌으며, 표준화 및 통계적 분석은 Matlab 프로그램의 Statistical Parametric Mapping 8 (SPM8)으로 시행되었다. 언어평가는 환자의 실어증 유무 및 심각성 뿐 아니라, 스스로 말하기, 알아듣기, 따라말하기, 이름대기의 4가지 하부 항목의 점수도 각각

평가하였다.
결과: 73명의 대상자 중 실어지수(AQ) 92.8점 미만의 실어증 군으로 분류된 환자는 58명 (79.5%) 이었고, 이들 중 20점 미만의 심각한 실어증은 33명이었다. 두 군간의 비교분석에서 외핵(extra-nuclear area)이 실어증의 유무와 가장 의미있게 나타났으며, 섬엽(insula)과 하전두회(inferior frontal gyrus), 상측두회(superior temporal gyrus)가 높은 상관관계를 보였다. 화소 기반 병변-증상 뇌 지도 분석을 통하여 평가한 결과 스스로 말하기는 하전두회(inferior frontal gyrus) 및 하 두정 소엽(inferior parietal lobule)과 가장 높은 상관관계를 보였다. 알아듣기 영역은 섬엽(insula)이 가장 높은 연관성을 보였고, 상측두회(superior temporal gyrus)가 알아듣기 및 따라말하기에서 보다 높은 연관성을 보이는 것으로 관찰되었다. 따라말하기와 이름대기는 하 두정 소엽(inferior parietal lobule)과 섬엽(insula)이 높은 연관성을 보이는 것으로 관찰되었다.
결론: 본 연구에서는 급성기 뇌졸중 환자를 대상으로 초기 뇌병변 영상과 언어평가의 연관성에 대해 분석하였다. 본 연구를 통해 임상적으로 뇌졸중 환자들의 실어증 기전에 대한 이해에 도움이 될 것으로 기대한다.

핵심되는 말 : 실어증, 화소 기반 병변 증상 뇌 지도, 뇌졸중, 한국판-웨스턴 실어증 검사