Characteristics and the recovery process in children with acquired aphasia

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〔博士論文概要〕

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（小児失語症の特徴ならびに改善経過に関する研究）

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1. Introduction

Aphasia is a loss or impairment of language functioning caused by brain damage (Benson, 1979), and is an acquired language impairment affecting all modalities of language including listening, speaking, reading, and writing. Although aphasia in adulthood develops after the completion of linguistic development, acquired childhood aphasia arises during normal linguistic development.

There are some problems in studies of acquired childhood aphasia that are caused by its characteristics and the methodology used. First, acquired childhood aphasia is a rare language disorder (Robinson, 1991); the number of children with acquired aphasia is smaller than that of adults with aphasia. Most of the previous studies on childhood acquired aphasia were case studies, not group studies (Loonen *et al.*, 1990; Van Dongen *et al.*, 1994; Uno *et al.*, 2004). The knowledge gained from these case studies may not be generalizable to groups of children with acquired aphasia. Moreover, only a limited number of studies have been performed examining the relationship between language symptoms and cerebral lesion areas, because it is difficult to control for the lesion areas as most of them are caused by head injury and are difficult to localize compared with those in adult aphasia, most of which are caused by cerebrovascular diseases (Van Hout, 1994; Chilosi, Cipriani, Pecini, Brizzolara, Biagi, Montanaro, Tosetti, & Cioni, 2008).

The second methodological problem for childhood aphasia research is that there is no language instrument developed specifically for patients with acquired childhood aphasia. There is only one screening test for children with acquired aphasia, that is, the Children's Acquired Aphasia Screening Test devised by Whurr & Evans (1998).

This screening test evaluates linguistic and non-linguistic function in brain-damaged children aged between 3 and 7 years, thus it is difficult to evaluate language symptoms of children aged over 7 years old. The Standard Language Test of Aphasia (SLTA) for Japanese speakers (Hasegawa *et al.*, 1985), is a tool that can be used to evaluate language faculty, and not learning achievement, except for unlearned Kanji characters in children with acquired aphasia (Uno *et al.*, 2002).

The third methodological limitation of acquired childhood aphasia research relates to brain examinations. Methods to evaluate morphological changes, that is, methods to identify lesions and quantify their pathology, had not been established until recently. One of the cutting-edge methods for the analysis of morphological changes is voxel-based lesion-symptom mapping (VLSM), which was developed by Bates et al. (2003). VLSM provides statistical significance about the relationships between cerebral lesions at the spatial resolution of magnetic resonance imaging (MRI) and behavioral data at the voxel-level. Many studies of aphasia in adults have been performed using VLSM (Dronkers, Wilkins, Van Valin Jr., Redfern, & Jaeger, 2004; Baldo, Schwartz, Wilkins & Dronkers, 2006), but none have been applied to children, to the best of our knowledge.

One of the methodological limitations in childhood aphasia research using cerebral blood flow Single Photon Emission Computer Tomography (SPECT) is that relationships between language symptoms and areas of low regional cerebral blood flow (rCBF) have not been investigated fully, because cerebral blood flow and blood distribution change over time as a child's brain develops (Ogawa *et al.,* 1987, Chiron *et al.*, 1992). However, Ohnishi *et al.* (2000) and Fukushima *et al.* (2005) established a normal database (NDB) of cerebral blood flow, this database enabled the use of the

Easy Z-score Imaging System, which was developed by Matsuda (2002), and has contributed to an increase in statistical analysis of imaging data derived from cerebral blood flow SPECT examinations of children.

Therefore, upon improving the methodological limitations described above, the current study investigated the characteristics of childhood aphasia comparing with those in previous studies on adult aphasia.

2. Purposes

The aim of Study 1 was to investigate the relationships among language symptoms, cerebral lesions, and functional lesions in childhood aphasia.

The aim of Study 2 was to examine the relationship between the change of language symptoms and the change of rCBF while controlling for age-related changes in the recovery process of two children with acquired aphasia.

Through Studies 1 and 2, we aimed to determine whether the characteristics of childhood aphasia were similar or different from those in previous studies on adult aphasia.

3. Methods

Study 1 was a group study of 10 children with acquired aphasia and focal lesions due to cerebrovascular events. That was investigating associations between lesion location and language functioning. Furthermore, using 7 children with acquired aphasia who underwent SPECT examinations as part of their clinical care, the

relationships between language symptoms and regions of focal hypoperfusion, which can be interpreted as regions of reduced functioning, were examined.

Study 2 was a case study of 2 children with acquired aphasia who had a similar age at onset, underlying illness, and lesion location. The age at onset was 8 years and both underwent multiple SPECT examinations as part of their clinical evaluation. With regard to their language symptoms, the scores of the SLTA, which was administered approximately at the same time as the cerebral blood flow SPECT examinations, were transformed into z-scores by comparing their scores against those of healthy children of the same age group. With regard to rCBF, z-scores were computed that represent a comparison against data from the corresponding age group in the NDB.

4. Results

4.1 Results of Study 1

Nine of the participants in the first study exhibited language fluency. The results of these 9 fluently speaking participants indicated lesions in the area from the left temporal lobe to the parietal lobe. Conversely, the non-fluent participant exhibited lesions in the pars opercularis of the left frontal lobe, precentral gyrus, postcentral gyrus, supramarginal gyrus, Roland pars opercularis, insular, Heschl transverse gyrus, superior temporal gyrus, middle temporal gyrus, and temporal pole.

All 7 of the participants in rCBF study exhibited fluent language. The regions in which the participants' blood flow was significantly lower than in healthy children included the left posterior parts of the inferior, middle, and superior temporal gyrus to

the inferior parietal lobe, including the supramarginal gyrus and angular gyrus.

The lesion and rCBF results both showed overlapping relevance to 4 of the SLTA subtest results: “Oral commands,” “Picture naming,” “Explanation of activities in a picture,” and “Repetition of sentences.” In both analyses, the “Oral commands” result was associated with the left posterior parts of the superior and middle temporal gyri to the inferior parietal lobe (angular gyrus and supramarginal gyrus). The “Picture naming” result was associated with the left superior and middle temporal gyri and the temporal pole. The “Explanation of activities in a picture” result was associated with the left temporal pole. In addition, the “Repetition of sentences” result was associated with the left posterior parts of the superior and middle temporal gyri to the inferior parietal lobe.

4.2 Results of Study 2

For Case A, a statistically significant difference among the time points was found only for rCBF reduction in the left hemisphere ($\chi^2 = 12.771$, df = 3, $p < 0.01$). The reduction z-score in the left hemisphere was significantly smaller at the first time point compared to all other time points ($Z = -2.521$, $p = 0.012$) and no other statistically significant difference was observed. In Case B, a statistically significant difference among the assessment time points was detected only in the right hemisphere increase z-scores ($\chi^2 = 19.286$, df = 3, $p < 0.01$). The right-hemisphere increase z-score was significantly greater at the first time point relative to the other time points, and the z-score at the 4th time point was significantly smaller ($Z = -2.366$, $p = 0.018$).

In both cases, strong correlations were seen between some language regions in the

left hemisphere and their homologous regions in the right hemisphere. Conversely, there were differences between the two cases in the time course of rCBF changes during their recovery process. In Case A, strong correlations were seen within left hemisphere between adjacent regions or regions that are connected by neuronal fibers. However, in Case B, significant correlations were not seen between rCBF changes within left hemisphere.

About the change of the z-score on the SLTA subtests, Case A showed a significant difference among the time points (χ^2=11.743, df = 3, $p < 0.01$), with the performance at the first time point being significantly lower than at the second time points (Z = -2.521, p = 0.018). Case B showed a significant difference in SLTA performance among the time points (χ^2 =14.440, df = 3, $p < 0.01$), with the performance at the first time point being significantly lower than at the other time points (Z = -2.521, p = 0.012).

On the analysis of change in language performance and change in rCBF z-score in the language regions at the 4 time points, in Case A, strong correlations were found between performance changes in the SLTA subtest “Oral commands” and rCBF changes in the left 7 language regions, and right BA21, BA22 and BA45, and between performance changes on SLTA subtest “Picture naming” and rCBF changes in the left 7 language regions, and right BA21, BA22, and BA45, and between performance changes on SLTA subtest “Enumeration of animal names” and rCBF changes in the left BA20, and BA21. In Case B, strong correlations were found between SLTA subtest performance changes “Oral commands”, “Explanations of activities in picture” and “Explanation of a comic strip” and rCBF changes in the right BA39. However, no statistically significant correlations were found between language symptoms changes and rCBF changes in the language regions in the left hemisphere.

5. Discussion

5.1. Discussion of Study 1

In Study 1, as the children with acquired aphasia demonstrated fluent verbal output while also showing impaired auditory comprehension and repetition, it was considered that they examined had a type of aphasia analogous to Wernicke's aphasia in adults. The regions identified both as a structural lesion and an area of reduced functioning were the posterior part of the superior and middle temporal gyri and the inferior parietal lobe (supramarginal and angular gyri) including Wernicke's area. Therefore, our results suggest that the relationship between an aphasia subtype and the location of structural and functional damage observed in our patients with child-onset aphasia was similar to that in adult aphasia cases.

In addition, associations of SLTA subtest performance with structurally and functionally impaired regions reported in previous studies on adult aphasia were also observed in our patients with acquired childhood aphasia, namely, associations between auditory phonological processing and the posterior left superior temporal gyrus, between sentence repetition and the posterior left superior and middle temporal gyrus and inferior parietal lobe, and between naming and the left superior and middle temporal gyrus and temporal pole. Conversely, associations between syntax comprehension and Brodmann area 44/45, and between attention during a sentence repetition task and the performance of verb generation and the frontal lobe were not observed in the current study.

Language function is still under development in children's brains, and different

brain regions mature at different rates. Therefore, we suggest that the associations of language performance with structurally and functionally impaired regions were similar between child-onset cases and adult-onset cases for language function that had already localized in the brains in children, while those associations were different from adult cases for language function for which the processing neural network is still under construction in developing brains.

5.2. Discussion of Study 2

In Study 2, we followed the prognoses of 2 patients with acquired childhood aphasia while controlling for age-related changes. The changes in rCBF over time within the 7 regions related to language functions in the left hemisphere and their corresponding regions in the right hemisphere were highly correlated among the areas surrounding the lesion, or between the areas connected by nerve fibers within each hemisphere in case A, and within right hemisphere in Case B. Between the right and left hemispheres, strong correlations were observed regarding some of the corresponding regions in both cases. Consistent with previous reports on adult aphasia, the current study suggested that both hemispheres were involved in the long-term process of recovery from aphasia symptoms. Conversely, rCBF changes during the recovery process, as well as the relationship between the changes in language symptoms and changes in rCBF, were different between both cases. We suggest that the status of the brain prior to the onset of aphasia, and the timing and side of the revascularization operation contributed to the differences observed in both cases. However, due to the strong correlations between changes in rCBF and changes in

language symptoms, rCBF measurement has the potential to serve as a biomarker for capturing the changes of language symptoms. Although both cases showed an improvement in language symptoms, there were some residual symptoms at 5 years after onset, which suggests that compensatory abilities were limited despite the high plasticity of children's brains.

5.3 General Discussion

Through Studies 1 and 2, many findings were obtained from children with acquired aphasia that are consistent with those of previous studies on patients with adult aphasia, including the relationships between language symptoms and lesion location, between language symptoms and areas of functional reduction, and recovery process from aphasia. Conversely, the present study provided several findings that were inconsistent with previous studies on adult aphasia, for example, the results on language function, for which the neural network still be under development in children's brains, were only partially consistent with the results reported for adult cases.

The limitations of study 1 were that the number of participants was small, that was a bias for the fluent type of aphasia, and the time period from onset to testing was not controlled precisely among the patients. In addition, the present study did not acquire direct evidence showing that the neural networks for language processing were still under development in the children's brains. Additional studies, especially ones using diffusion tensor imaging, need to be performed to examine the development of language processing networks.