A Case of Pure Agraphia Due to Left Thalamic Hemorrhage

Minoru TOYOKURA[*1], Ryouko KOBAYASHI[*2] and Kouji AONO[*3]

[*1]*Department of Rehabilitation Medicine and* [*2]*Division of Rehabilitation, Tokai University Oiso Hospital*
[*3]*Department of Rehabilitation Medicine, Tokai University School of Medicine*

(Received May 12, 2010; Accepted June 11, 2010)

Pure agraphia is an isolated writing disturbance without intellectual impairment, aphasia, alexia, or apraxia. The authors report a case of pure agraphia following left thalamic hemorrhage. The patient showed impairment in the writing of both kanji and kana. The most frequent error in the writing of kanji was substitution (46%) followed by no reaction (23%) and partial omission or addition of characters (21%). The copying of kanji by hand was normal. Even when the patient was unable to write a kanji character, he understood the meaning and correctly recited the other readings. He complained that he could not recall the graphic image of the kanji. When we cued the patient by writing a part of a kanji he initially failed to recall, he correctly completed the character. The kanji and kana he was unable to write were inconsistent over time: in some cases he was unable to write words he had successfully written a week before, and vice versa. These findings suggested that the patient's pure agraphia resulted from combined impairments in recalling and selecting letters. While the thalamic lesion might have influenced the manifestation of pure agraphia, the dysfunction seemed to originate from the secondary negative effect of the lesion on the function of the left cerebral cortex.

Key words: pure agraphia; thalamus; Japanese language; rehabilitation

INTRODUCTION

Pure agraphia is an isolated writing disturbance without intellectual impairment, aphasia, alexia, or apraxia. The condition is considered a sole deficit of language organization, not a variation of aphasia or the residual of a more general linguistic dysfunction. Several lesions of the left frontal [1, 2], parietal [3, 4], and temporal lobes [5–7] have been reported in the patients with pure agraphia, but the precise lesions and neuropsychological mechanism responsible for pure agraphia are not fully understood.

Aside from the above lesions, involvement of the left thalamus might also produce pure agraphia [8–10]. Cases with thalamic lesions, however, have seldom been reported. The background pathomechanism of pure agraphia also remains unclear.

The authors report a case of pure agraphia due to left thalamic hemorrhage. The clinical characteristics and pathomechanism of this writing disorder are discussed.

A CASE REPORT

A 63-year-old, right-handed, male university graduate was admitted to an emergency hospital after experiencing a sudden onset of right hemiparesis on March 20, 2009. He had been living a normal life as a company executive without any difficulties. Neuroradiological examination revealed a fresh cerebral hemorrhage at the left thalamus. He was transferred to our hospital for rehabilitative intervention on April 6, 2009, after acute care.

On admission he was alert and fully oriented. Minimal dysarthria was noted, but verbal communication was otherwise normal.

Neurological examination revealed that the cranial nerves were almost intact, but the patient manifested moderate right-hemiparesis and used his left hand for both writing and eating. Superficial and deep sensations were mildly disturbed in the right upper and lower extremities. Tendon reflexes on the right side were slightly increased. No involuntary movements were observed. He was unable to walk and was dependent in most of his ADL. Urinary and bowel continence were well preserved. The Barthel Index was 37.

Neuropsychological examination showed no findings of apraxia, finger agnosia, right-left agnosia, or unilateral spatial neglect. The patient, however, complained of a disturbance in the writing of kanji and kana.

The Japanese language is written with two different writing systems, kanji and kana. A Kanji character is a structurally complex morphogram (or ideogram) with various meanings and different phonetic readings. A Kana letter is a graphically simpler phonogram (syllabogram) with one unambiguous phonetic value. Every kanji can be represented by kana. For example, "花" [hana], the kanji for "flower" is also represented by the two kana leters "はな [hana]". And the same kanji, "花" has the different reading [ka]. Kanji and kana are combined together in regular printed matter in Japan. All 46 kana letters and most of the structurally simple kanji characters are taught during the first year of elementary school.

Minoru TOYOKURA, Department of Rehabilitation Medicine, Tokai University Oiso Hospital, 21-1 Gakkyo, Oisomachi, Nakagun, Kanagawa 259-0198, Japan Tel: +81-463-72-3211 Fax: +81-463-72-2256 E-mail: toyokura@juno.dti.ne.jp

Table 1 Results of neuropsychological tests

Task	score/full score	mean*1	cut-off*1
Digit span (forward)	5/9	5.8	4
Digit span (backward)	3/9	4.3	3
Tapping span (forward)	6/9	5.6	4
Tapping span (backward)	5/9	4.8	4
Visual cancellation of a number (%)*2	100/100	99.1	not available
Visual cancellation of a letter (%)*2	96/100	96.1	not available
Paced auditory serial addition task (2s) (%)*2	40/100	63.1	38
Raven's Colored Progressive Matrices	30/36	29.2	24

*1, values for normal subjects in the same decade of life as the patient *2, percent of correct responses

Table 1 presents the results of several neuropsychological tests performed by the patient. The digit span is a standard task for attention and short-term memory. The maximum numbers of digits the patient could correctly answer for forward- and backward-recall order were 5 and 3, respectively. The tapping span task is a visuospatial counterpart to the verbal-memory span (digit span) task. Starting with a grouping of nine blocks irregularly arranged on a sheet of paper, the examiner points to a series of two to nine blocks, one by one. For each series, the patient is asked to point to the same blocks in the order of the presentation. The method to assess patient's performance in the digit span task was also applied to the forward- and backward-recall order task. The examiner records the maximum length of the block sequences the patient can correctly reproduce by pointing tracks. The task sheet for the visual cancellation task is a white paper with 6 rows and 52 columns of letters or numbers. The subject is instructed to cross out all targets (one letter or number) as quickly and accurately as possible. In the PASAT (paced auditory serial addition task), the subject is asked to serially add pairs of single-digits (1 to 9). Specifically, the subject attends to the auditory presentation of a series of numbers and tells the examiner the sum of the number just heard plus the number heard immediately before it. Sixty-one numbers are presented at an inter-stimulus interval of 2s, and the percentage of correct responses from among the 60 answers is calculated. Working memory and speedy information-processing are both required for PASAT. All of these tasks are subtests of CAT (Clinical Assessment for Attention) (Shinko Igaku Shuppann, Co., 2006), an assessment developed by the Japan Society for Higher Brain Dysfunction. CAT kit gives mean values for healthy subjects and cut-off values for subjects in their third to eighth decades of life (twenties to seventies) for each task (see Table 1). The final test listed in the table, RCPM (Raven's Colored Progressive Matrices) (NIHON BUNKA KAGAKUSYA, Co., 1993), is a visual task reflecting general intelligence. The subject is asked to identify the missing segment required to complete a larger pattern among six possible pieces pictured at the bottom of a page. The task consists of 36 different puzzles, and the number of correct answers (max, 36) is assessed.

Our patient performed almost within normal range in all of these tasks for the assessment of attention, memory, information processing, and visual cognition.

Neuroradiological findings

The T2-weighted MR image 8 weeks after onset showed an area of high signal intensity in the posterolateral portion of the left thalamus with slight involvement of a portion of the internal capsule (Fig. 1).

Language test

The results of the SLTA (Standard Language Test of Aphasia) (Shinko Igaku Shuppann Co., 2003) are shown in Table 2. The SLTA is the most widely used procedure in Japan for evaluating dysfunction in Japanese language. The test consists of various subtasks in four major language modalities: auditory comprehension, speaking, reading comprehension, and writing.

As shown in Table 2, the patient's function was well preserved in three of the language modalities and perfect in calculation. His function in the language modality of writing, however, was disturbed.

To evaluate the patient's agraphia in detail we conducted a dictation exercise with 210 kanji words learned in elementary school and the corresponding words in kana. He correctly transcribed only 72% of the words in kanji and 92% of the words in kana. Fig. 2 presents examples of his writing errors. His most frequent error in the writing of kanji was substitution (paragraphia) (46%) followed by no reaction (23%) and the partial omission or addition of characters (21%). Scrawling and neographism were seldom seen. Four different types of substitution can take place: morphologic, phonologic, semantic, and unrelated types. The first three types are substitutions with other kanji characters with similar forms, identical readings, or meanings related with the correct kanji, respectively. The phonologic type was the most frequent (59%) substitution error, followed by semantic (18%), unrelated (15%), and morphologic (8%) types. Most of the errors in kana-writing were also substitutions. The patient accurately copied the kanji and kana he failed to remember. When unable to write a kanji character, he complained that he had forgotten the graphical form. But when we wrote out a part of the forgotten kanji for him as a cue, he could correctly complete it. The kanji and kana he failed to write were inconsistent over

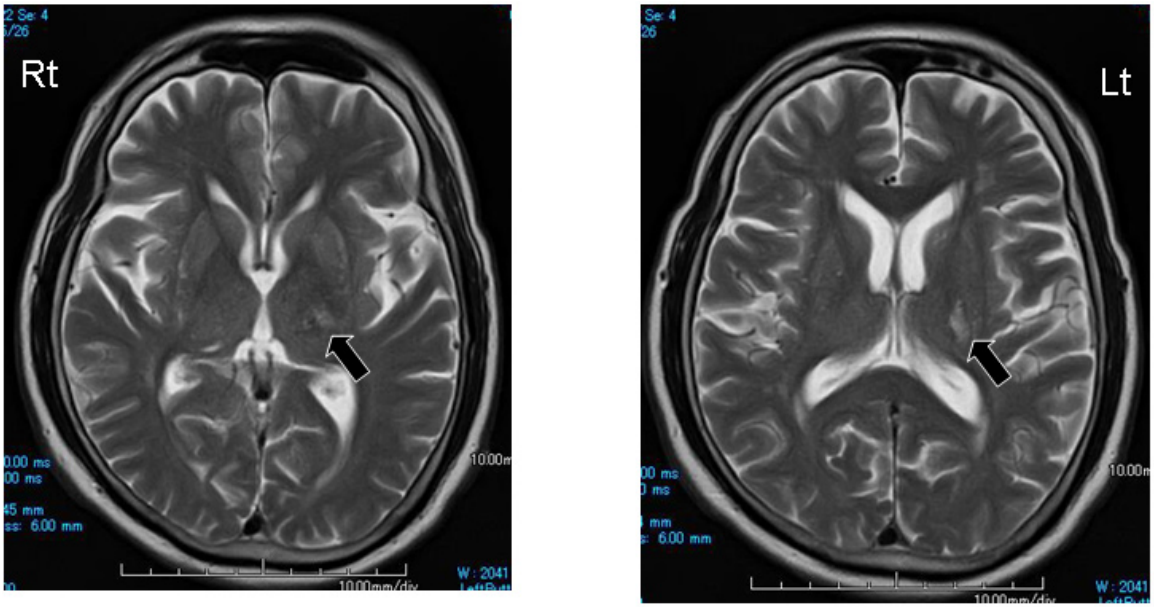

Fig. 1 MRI T2-weighted image (8 weeks after onset)
A low-signal-area mixed with high-signal-area is shown in the posterolateral portion of the left thalamus (an arrow). No enlargement of the ventricle is seen.

Table 2 Results of SLTA

Subtasks	correct response (%)
(1) Auditory comprehension	
single kana	100
word	100
sentence	100
obeying verbal commands	90
(2) Speaking	
naming of objects	100
repetition of word	100
repetition of sentence	100
explanation of comic strip	100
explanation of actions	100
reminding words (animals)	100
reading aloud (words written in kanji)	100
reading aloud (words written in kana)	100
reading aloud (letters written in kana)	100
reading aloud (short sentence)	100
(3) Reading comprehension	
words written in kanji	100
words written in kana	100
short sentence	100
obeying written commands	100
(4) Writing	
name of objects in kanji	80
name of objects in kana	80
explanation of comic strip	60
dictation of single kana	90
dictation of words in kanji	80
dictation of words in kana	100
dictation of short sentence	60
(5) Written calculation	
addition (one- to three-digit numbers)	100
subtraction (one- to three-digit numbers)	100
multiplication (one- to two-digit numbers)	100
division (one- to four-digit numbers)	100

SLTA, Standard Language Test for Aphasia

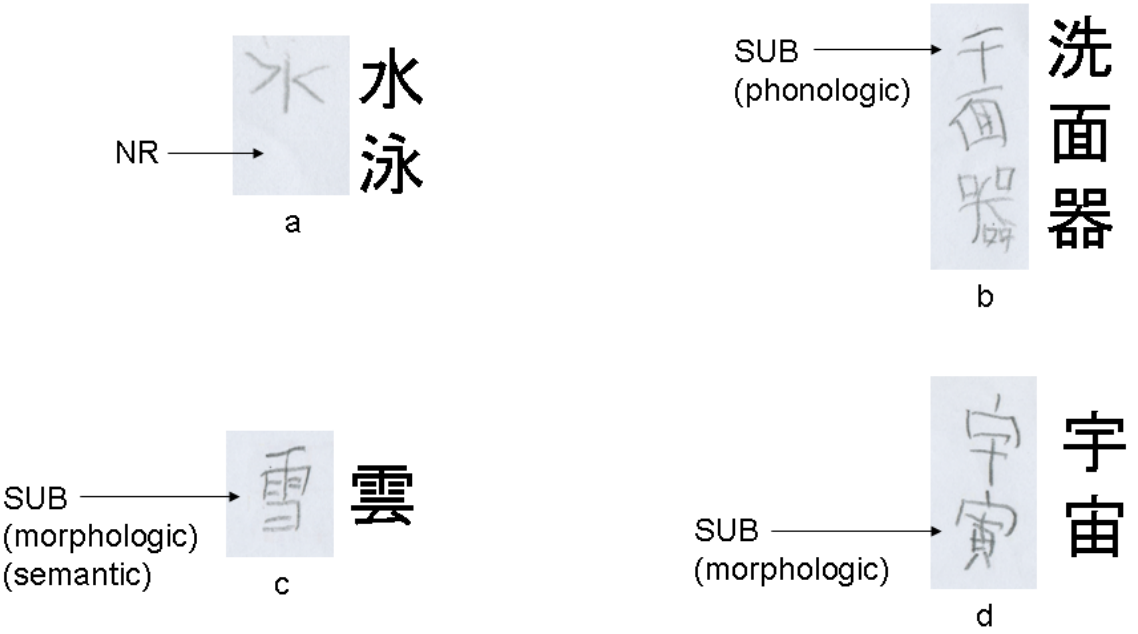

Fig. 2 Examples of kanji agraphia
NR, no response; SUB, substitution of other kanji
Four types of substitution take place: morphologic, phonologic, semantic, and unrelated. The morphologic type is a substitution by another kanji character graphically resembling the correct one. The phonologic type is a substitution by another kanji character with the same reading as the correct kanji. The semantic type is a substitution by another kanji with a meaning related to or semantically relevant to the correct answer. One substitution can sometimes be categorized as more than one type.
a, " 水泳 [suiei]" means "swimming". He correctly wrote " 水 " but showed no response for " 泳 ".
b, " 洗面器 [sen men ki]" means "a washbowl". He wrote " 千 ", the kanji for "a thousand", instead of " 洗 ", the kanji for "wash". Both have the same reading [sen] but completely different meanings and morphology.
c, " 雲 [kumo]" means "cloud". He wrote " 雪 [yuki]", a kanji morphologically similar to the correct answer. As " 雪 " means snow, it is also semantically relevant to the correct answer.
d, " 宇宙 [uchu:]" means "universe". The latter kanji " 宙 [chu:]" was replaced with " 寅 [tora]", the kanji for "tiger". These kanji are morphologically alike but have completely different meanings and readings.

time: in some cases he was unable to write words he had successfully written a week before, and vice versa. He understood the meanings of the kanji characters he was unable to write out. Thus, he correctly answered other readings for the kanji characters and mentioned other idioms with the kanji in combinations. Even when he failed to write " 海 [umi]", the kanji for "sea", for example, he could tell us the meaning of the kanji, recite another reading, [kai], and use " 海 " in "海岸 [kaigan]", an idiom for "beach". The corresponding kana representation of " 海 " is " うみ [umi]".

Clinical course

Exercises in dictation, spontaneous writing, and written naming for writing were continued throughout his hospital stay. Having succeeded in showing him parts of kanji as an effective visual cue for writing, we continued to cue the patient in the same manner to facilitate his writing performance. His agraphia gradually improved. Though his right hemiparesis almost recovered, prominent ataxia of the right upper extremity emerged and he continued to use his left hand for writing and eating. At discharge from our hospital in June he could walk with a T-cane and ankle-foot-orthosis. Most of his ADL became independent (Barthel Index, 85).

Eight months after onset his writing ability was restored to almost a normal level. He retired from his company but accomplished a full return to his social life.

DISCUSSION

Writing requires various and complex brain functions involving higher intellectual processes. General hypofunction of the brain or acute confusional state might therefore cause agraphia [11]. The present case, however, was fully oriented and retained almost full intellectual function. He manifested an isolated writing disturbance without any other language dysfunction or deficits such as apraxia, spatial neglect, or graphomotor disturbance. These clinical findings indicate that he had developed pure agraphia as a result of left thalamic hemorrhage.

His agraphia was characterized by a light impairment in the writing of kana and a somewhat heavier impairment in the writing of kanji. Most of his writing errors were no reaction, substitution (paragraphia), and the partial omission or addition of characters. Most of replaced kanji shared morphological, phonological, or semantic features in common with the correct kanji. Nearly 60% of substitutions were of the phonologic type. His performance in the copying of

kanji and kana was normal. During the writing tasks, he complained that he could not recall the forms of some kanji characters. When we cued him by showing him parts of the characters he was able to recall better. These characteristics of agraphia are thought to relate to amnestic agraphia, a failure to remember the structure of characters. Meanwhile, substitutions are associated with a disturbance in selecting kanji or kana. Yamadori has pointed that disturbances in both recalling and selecting letters arise from the same neuropsychological mechanism and commonly appear together [12]. He further reported that this type of agraphia, that is, combined impairment of recalling and selecting, seemed to be most common among patients with pure agraphia and possibly appears due to left thalamic lesion.

Aiba *et al*. reported two cases with pure agraphia due to left thalamic hemorrhage [10]. Both patients had the similar findings: agraphia to dictation and in spontaneous writing; difficulty of writing both kanji and kana; and an intact ability to copy both kanji and kana. One patient manifested neographism, scrawl, and paragraphia (most commonly unrelated substitution). The other patient mainly showed paragraphia and no response. Another case of pure agraphia resulting from left thalamic hemorrhage has been reported by Ikegami *et al*. [9]. Their case was similar to the cases reported by Aiba, manifesting disturbances in the writing of kanji and kana in dictation but normal copy writing. Most of the writing errors were no responses and morphologic substitutions, including partial omissions and additions of characters. Ikegami *et al*. suggested that the agraphia is caused by difficulties in graphemic figure-finding. Sugishita *et al*. have also presented a case of pure agraphia after left subthalamotomy [13]. The agraphic responses in their case were paragraphias (51%) and no response (30%). They suggested that the agraphia was mainly produced by a disorder in the selection (retrieval) of graphemes.

The findings of these cases are generally consistent with those of the present patient. Specifically, the disturbances seem to derive from a similar neuropsychological mechanism for agraphia, a combined impairment of recalling and selecting letters. The features of their paragraphia, however, were somewhat more variable. Phonologic substitution was the most common feature in our patient, whereas unrelated or morphologic substitutions were so in the other cases. The precise mechanism for this inconsistency is unknown, though it may derive from individual differences in the neuropsychological strategies to recall the forms of characters.

Pure agraphia commonly results from frontal or parietal lesions [1–3, 14]. Katanoda *et al*. [15] investigated the functional neuroanatomy of writing using functional MRI. Functional images were obtained during three different tasks: writing of the names of pictures with the right index finger; naming of pictures silently; and visually cued finger tapping. By analyzing subtracted functional images they identified two cerebral activations during the writing process: one in the anterior part of the left superior parietal lobule and one in the posterior part of the left superior and middle frontal gyri. These findings are consistent with those on a previously reported lesion for pure agraphia. In addition to the parietal and frontal lobes, the occipital and temporal lobes are also important for writing [5–7, 14], especially the writing of Japanese kanji. Iwata anticipates that the selection of correct kanji graphemes based on the meaning involves an important pathway from Wernicke's area to the occipital lobe by way of the posterior inferior temporal area [16].

Thalamic agraphia has been much less frequently reported than writing dysfunctions in cases with above lesions, and its pathogenesis remains unclear. Lesions within the thalamus are reportedly localized to the left posterolateral [9, 10] or ventral portion of posteromedial [8] areas. Studies of cerebral blood flow and tissue metabolism have indicated low perfusion and hypoactive metabolism of the left cerebral hemisphere [9, 10], left frontal region [17], and left fronto-temporal [10] region secondary to the remote effect of left thalamic lesion. The hypofunction of the left cerebral cortex is generally thought to be the cause of pure agraphia, whereas thalamic lesions might influence the manifestation of agraphia. No functional images are available on our patient, though the thalamic lesion seems identical to that of Aiba's cases. The lesion might thus have caused cortical hypofunction in the left hemisphere, where no definite lesion was detected in MR images.

Thalamic lesion has been reported to result in another type of pure agraphia. Ohno *et al*. described a case of pure apraxic agraphia following left thalamic infarction [17]. The patient showed difficulty in forming written letters in spite of normal praxis, but could orally describe the orientation of each stroke of a kanji character. Most of the errors were partial omissions or additions of characters, yet, unlike the cases of thalamic agraphia presented above, absent response or paragraphia were not seen. Ohno *et al*. proposed that this condition was produced by tissue hypoactivity of the left frontal cortex as a remote effect of the thalamic lesion. Araki *et al*. reported another type of agraphia accompanied by alexia following cerebral infarction of the left anterior portion of thalamus [18]. Positron emission tomography demonstrated a dysfunction of the left parietal and temporal lobes and left thalamus. Araki *et al*. pointed out that these secondary cortical lesions seemed to play a causal role in the development of agraphia and alexia in their case.

These findings indicate that a left thalamic lesion might produce various types of agraphia as a remote effect, depending on the location of the functionally damaged cortex. The specific relationship between the location of the thalamic lesion and cortical area with functional deficit remains unclear. Further studies will be needed to elucidate the neuropsychological mechanism of pure agraphia due to thalamic lesion.

Acknowledgments: none

REFERENCES

1) Sakurai Y, Matsumura K, Iwatsubo T, Momose T. Frontal pure agraphia for kanji or kana: dissociation between morphology and phonology. Neurology 1997; 49: 946–952.
2) Vernea JJ, Merory J. Frontal agraphia (including a case report). Proc Austral Ass Neurol 12; 1975: 93–99.
3) Toyokura M, Shigeno K, Murakami K. A case with agraphia due to left parietal hemorrhage (in Japanese). Shinkeishinrigaku 9;

1993: 129–138.
4) Maeshima S, Yamaga H, Masuo O, Kuwata T, Ozaki F, Moriwaki H. A case with agraphia due to cerebral infarction in the left parietal lobe (in Japanese). Nosinkeigeka 26; 1998: 431–437.
5) Yokota T, Ishiai S, Furukawa T, Tsukagoshi H. Pure agraphia of kanji due to thrombosis of the Labbe vein. J Neurol Neurosurg Psychiatry 1990; 53: 335–338.
6) Sakurai Y, Mimura I, Mannnen T. Agraphia for kanji resulting from a left posterior middle temporal gyrus lesion. Behav Neurol 19; 2008: 93–106.
7) Rosati G, De Bastini P. Pure agraphia: a discrete form of aphasia. J Neuorol Neurosurg Psychiatry 42; 1979: 266–269.
8) Sugishita M, Ishijima B, Hori T, Fukushima T, Iwata M. "Pure" agraphia after left CM-thalamotomy (in Japanese). Rinshoshinkei 13; 1973: 568–574.
9) Ikegami K, Kojima C, Maeda H, Hojo K, Fujishima I. A case of pure agraphia improved by writing training with a word-processor. Japanese Journal of Speech, Language, and Hearing Research 3; 2006: 116–124.
10) Aiba E, Souma Y, Aiba T, Kurita I, Kishida K. Two cases of pure agraphia developed after lt. thalamic hemorrhage (in Japanese). No To Shinkei 43; 1991: 275–281.
11) Chedru F, Geschwind N. Writing disturbance in acute confusional states. Neuropsychologia 10; 1972: 343–353.
12) Yamadori S. Agraphia (in Japanese). In: Shimazono Y, Hozaki H, Torii H, eds. SEISHINKA Mook No29. Tokyo: KANEHARA & Co., 1993: 96–105.
13) Sugishita M, Narabayashi H. "Pure" agraphia after the left subthalamotomy. No To Shinkei 26; 1974: 568–574.
14) Kawamura M, Kezuka M. The neural mechanism of writing (in Japanese). Shinkei Kenkyu No Shimpo 47; 2003: 755–762.
15) Katanoda K, Yoshikawa K, Sugishita M. A functional MRI study on the neural substrates for writing. Hum Brain Mapping 13; 2001: 34–42.
16) Iwata M. Kanji versus Kana: Neuropsychological correlates of the Japanese writing system. Trends Neurosci 7; 1984: 290–293.
17) Ohno T, Bando M, Nagata H, Ishii K, Yamanouchi H. Apraxic agraphia due to thalamic infarction. Neurology 2000; 54: 2336–2339.
18) Araki S, Kawamura M, Isono O, Honda H, Shiota J, Hirayama K. Reading and writing deficit in cases with localized infarction of the left anterior thalamus (in Japanese). No To Shinkei 42; 1009: 65–72.