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Dorsal type letter-by-letter reading accompanying alexia with agraphia due to a lesion of the lateral occipital gyri

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ABSTRACT

We report a patient with alexia with agraphia accompanied by letter-by-letter reading after hemorrhage in the left middle and inferior occipital gyri that spared the angular gyrus and the fusiform gyrus. Kanji (Japanese morphograms) and kana (Japanese phonetic writing) reading and writing tests revealed that alexia with agraphia was characterized by kana-predominant alexia and kanji-predominant agraphia. This type of “dorsal” letter-by-letter reading is discernable from conventional *ventral type* letter-by-letter reading that is observed in pure alexia in that (1) kinesthetic reading is less effective, (2) kana or literal agraphia coexists, and (3) fundamental visual discrimination is nearly normal.

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Introduction

Letter-by-letter reading has been thought to be characteristic of pure alexia (Coslett, 2011); however, some neuropsychological studies have indicated that letter-by-letter reading is also observed in alexia with agraphia due to a lesion of the left posterior inferior temporal cortex (Rapcsak & Beeson, 2004; Sakurai, Takeuchi et al., 2000b).

We begin with introducing the Japanese writing system. Two writing characters, kanji (morphograms of Chinese origin) and kana (Japanese phonetic syllabic writing simplified from Chinese characters) are used. Kanji are graphically complicated and have meaning and multiple pronunciations, whereas kana are graphically simple and have one pronunciation and usually no intrinsic meaning. Therefore, single-character kanji are words as well as letters, whereas single-character kana are usually letters, such as European alphabet. Both kanji and kana words consist of two or more kanji or kana characters and usually have one pronunciation. Thus, a kana reading impairment implies disturbance of letter/syllable identification or grapheme–phoneme conversion, whereas a kanji reading impairment implies disturbance of whole-word reading. Likewise, a kana writing impairment implies disturbance of letter/syllable recall or phoneme–grapheme conversion, whereas a kanji writing impairment implies disturbance of whole-word recall or spelling stroke (or letter) sequences. Kana are further divided into hiragana (a cursive form of kana that is normally used for grammatical morphemes, e.g., 走る [hashiru] meaning “run” is composed of 走 (kanji) and る (hiragana suffix denoting present tense), and katakana (a square form of kana used primarily for representing loan words, e.g., カメラ [kamera], camera). The kana described in this paper denotes hiragana. Hiragana and katakana are allographic with each other having the same phonetic value but are

orthographically different (Sakurai et al., 2010), and have a mutual priming effect irrespective of the orthographic similarity, e.g., か [ka], hiragana, and カ [ka], katakana (Kinoshita et al., 2019).

We have previously reported two anatomically different types of pure alexia: fusiform type and posterior occipital type (Sakurai et al., 2006). Fusiform type pure alexia is characterized by kanji-predominant alexia that can be generalized to designate alexia for words, whereas posterior occipital type pure alexia is characterized by kana-specific alexia that can be generalized to designate alexia for letters. Letter-by-letter reading and the resulting word-length effect are observed in both types of pure alexia, although letter-by-letter reading is less pronounced in the posterior occipital type (Sakurai et al., 2008, 2006). Our previous positron emission tomography study indicated that the precise lesion location for fusiform type pure alexia was in the left mid-fusiform gyrus (Brodmann area (BA) 37) medial to the activated site (mid-fusiform/posterior inferior temporal gyri) in kanji word reading (Sakurai, Momose et al., 2000a). A later study indicated that the lesion location for posterior occipital type pure alexia was in the posterior fusiform/inferior occipital gyri (BA 18/19) (Sakurai et al., 2008), which was activated in covert reading of kana words (Sakurai, Momose et al., 2001b).

In addition, we also found letter-by-letter reading in a patient with alexia with agraphia due to a lesion of the angular gyrus and the adjacent lateral occipital gyri (Sakurai et al., 2010). This lesion was clearly superior to those for pure alexia. That is, letter-by-letter reading in pure alexia is attributable to damage to the left ventral temporal (anterior fusiform/inferior temporal gyri) (Binder & Mohr, 1992), or lateral and ventral occipital gyri, including the occipitotemporal junction (Leff et al., 2001). We designate letter-by-letter reading in pure alexia as *ventral type* letter-by-letter reading, whereas letter-by-

letter reading due to a more superior lesion including the lateral occipital gyri is designated as *dorsal* type letter-by-letter reading. Little is known about this *dorsal* type of letter-by-letter reading. Herein, we report about a patient with letter-

by-letter reading due to a lesion of middle and inferior occipital gyri that did not involve the angular gyrus and discuss the difference between this *dorsal* type of letter-by-letter reading and the conventional *ventral* type.

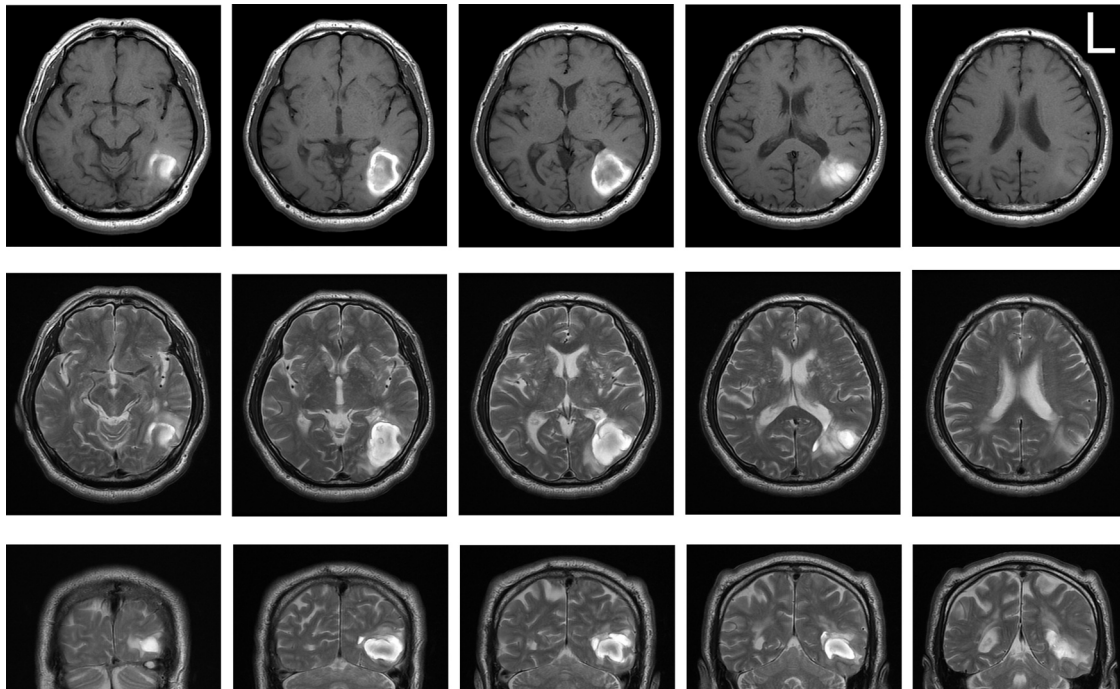


Figure 1. MR images 14 days after onset. T1- and T2-weighted axial (upper and middle) and T2-weighted coronal (lower) images indicated a subcortical high-intensity area in the left middle and inferior occipital gyri that extended to the posterior horn of the lateral ventricle. The fusiform and angular gyri were spared.

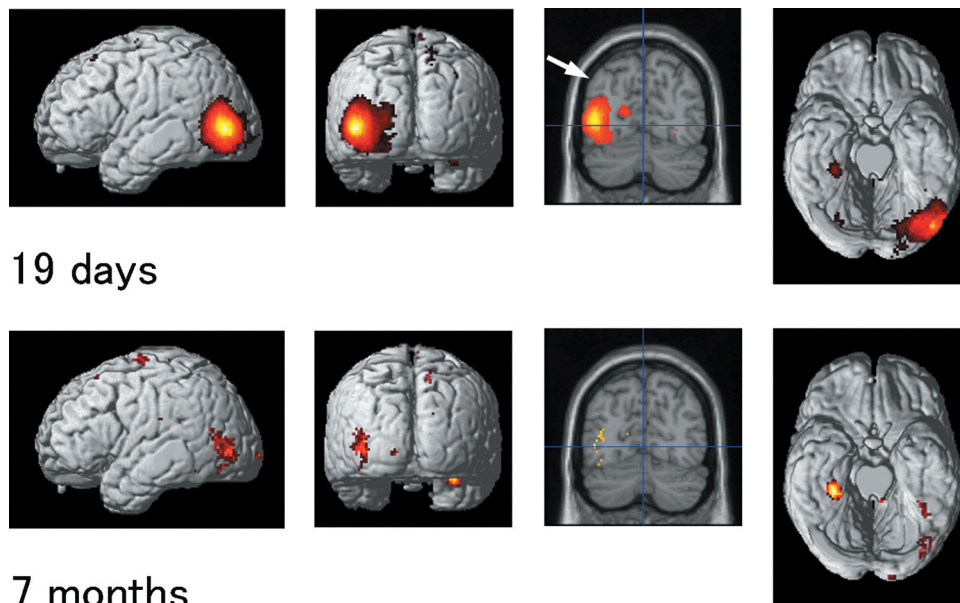


Figure 2. ^{99m}Tc -ECD-SPECT images at 19 days (upper panel) and 7 months (lower panel) after onset. Regional hypoperfusion is depicted in color. The red-to-bright yellow color gradient reflects increasing Z-scores. A focal reduction of the cerebral blood flow in the left lateral occipital gyri was noted at onset; the area with local maximum reduction was in the inferior occipital gyrus (Brodmann area (BA) 19, Montreal Neurological Institute (MNI) coordinates $(-40, -76, 2)$). The area with hypoperfusion did not involve the angular gyrus (arrow), but the posterior fusiform gyrus was affected. Over the course of 7 months, the hypoperfusion of the left lateral occipital gyri was limited to a small area: the local maximum reduction was in BA 19 (MNI coordinates $(-36, -78, 2)$). The imaging data were first normalized, smoothed, and adjusted to compare between laboratories with the easy Z-score Imaging System (eZIS version 3.4) (Matsuda et al., 2004), and constructed using a two-sample t test: patient vs. healthy men aged 60–69 years ($n=18$) (uncorrected $P < 0.001$) using Statistical Parametric Mapping (Friston et al., 1995) version 2 (SPM2) software. Areas with significant hypoperfusion were displayed on the standard surface brain images and the coronal section through the angular gyrus ($y = -70$ mm on the MNI coordinate). The vertical line denotes the z-axis ($x = 0$), and the horizontal line denotes the x-axis ($z = 0$) in the MNI space.

Case report

A right-handed, 61-year-old man presented with headache, inability to read tickers on the television, and inability to operate an electronic calculator. He was a self-employed baker and had a graduate-level education. His medical history was notable for hypertension; however, he was not being treated with medication. After being referred to our hospital, he was admitted with a diagnosis of cerebral hemorrhage that was detected through computed tomography (CT) imaging. Neurological examination indicated 1) alexia and agraphia, 2) acalculia, and 3) visual extinction on the right. Magnetic resonance imaging (MRI) 14 days after symptom onset indicated an area of hyperintensity in the left posterior middle and inferior occipital gyri, which extended to the posterior horn of the lateral ventricle (Figure 1). The fusiform gyrus and the angular gyrus were spared. Single photon emission computed tomography with a ^{99m}Tc -ethylcysteinate dimer (^{99m}Tc -ECD-SPECT) performed 19 days after symptom onset indicated a focal reduction of the cerebral blood flow in the left lateral occipital gyri (Figure 2). The local peak reduction was in the inferior occipital gyrus (BA 19; Montreal Neurological Institute (MNI) coordinates: $-40, -76, 2$). The area with hypoperfusion did not involve the angular gyrus, but the posterior fusiform gyrus was affected.

The patient underwent standard and special cognitive tests as detailed below at hospital admission and from 6 to 32 months later. The testing protocol was approved by the research ethics committee of our hospital, and written informed consent was obtained from the patient.

Standard cognitive tests (Table 1)

In the Wechsler Adult Intelligence Scale-III (WAIS-III) administered 2 weeks after admission, performance IQ was relatively lower than verbal IQ, and the processing speed was clearly low. Aphasia was not noted in the Western Aphasia Battery (WAB, Japanese edition) 7 days after onset, but reading was severely and writing was mildly impaired. The patient was unable to read words and sentences he had written. He could read kanji words but had difficulty reading kana characters. By contrast, he had difficulty writing kanji words, but he wrote kana words relatively easily; he was able to write 22 out of the 46 characters in the kana syllabary. He was able to read and write digits with ease. In all, kana-predominant alexia and kanji-predominant agraphia were noted. In the lexical decision task (to detect whether the stimulus character sequence is a real word or not) of the Test of Lexical Processing in Aphasia (TLPA) (I. Fujita et al., 2000), he achieved 72% (115/160) correct for the two-character kanji words and nonwords, suggesting that whole-word orthography of kanji words was relatively preserved. There was no frequency or imageability effect by Fisher's exact method.

Special cognitive tests (Tables 2 and 4)

Reading and writing test of 100 single-character kanji and kana transcriptions (Table 2, I) (Sakurai, Takeuchi et al., 2000b)

Lists of 100 character kanji and the transcribed kana words were displayed on a separate A4 sheet. All of the kanji

Table 1. Scores for standard neuropsychological tests at disease onset.

<i>WAIS-III</i>	
Verbal IQ	102
Digit span forward (raw score)	5
Performance IQ	82
Working memory	81
Processing speed	63
<i>WAB</i>	
Spontaneous speech	
Information content (/10)	10
Fluency (/10)	10
Naming total (/10)	9.1
Object naming (/60)	60
Repetition (/10)	10
Comprehension total (/10)	9.4
Reading total (/10)	2.49
Kanji reading (/6)	6
Kana reading (/6)	3
Writing total (/10)	7.95
Kanji writing (/6)	1
Kana writing (/6)	5
Calculation (/24)	20
Praxis (/10)	rt. 10, lt. 10
<i>TLPA</i>	
Lexical decision of two-character kanji	
High-freq., high-image. words (/20)	16
High-freq., low-image. words (/20)	15
Low-freq., high-image. words (/20)	16
Low-freq., low-image. words (/20)	11
Nonwords (/80)	57
Lexical decision of three-character kana	
Words (/60)	24
Nonwords (/60)	19

WAIS-III, Wechsler Adult Intelligence Scale-III; WAB, Western Aphasia Battery; TLPA, Test of Lexical Processing in Aphasia; freq., frequency; image., imageable; rt., right; lt., left.

characters are taught in the first 3 years of primary school in Japan. The patient was asked to write kanji, kana, then to read kanji, and kana in this order. Correct responses and time for reading were counted. Reading was more impaired in kana ($P < 0.0001$ by Fisher's exact method), whereas writing was more impaired in kanji ($P < 0.0001$ by Fisher's exact method). Errors were as follows: no response in kanji reading (10 out of 13 errors), phonological errors (phonemic paralexia; 52%), and no response (39%) in kana reading (Table 3A), no response in kanji writing, (94%) and phonological errors (phonemic paragraphia) in kana writing (65%; Table 3B). Kinesthetic reading was effective only in some kanji characters (footnote (b) of Table 2).

Reading test of kana single characters, two-character kanji words, three-character kana words and nonwords, five-character kana words and nonwords, and kanji transcriptions (Table 2, II, III) (Sakurai et al., 2010)

Single-character kana were 46 letters of kana syllabary that were randomly listed on a sheet. High-familiarity three- (mean 5.98 on a seven-point rating scale) and five-character kana words were selected from research reports (Amano & Kondo, 2000; T. Fujita et al., 1991), and three- and five-character nonwords were made by changing the sequential order of kana characters, e.g., あした ([ashita], tomorrow) → たしあ ([tashia], nonword). Low-familiarity kana words (mean 4.20 on a seven-point rating scale) (Amano & Kondo, 2000), two-character kanji words transcribed from the high-familiarity

Table 2. Scores for the special neuropsychological tests: reading and writing.

	Onset	6–30 months	Controls ^a	
			Mean score (SD)	Mean time (SD)
I. Reading and writing (100 single-character kanji and kana transcription), raw score and time (percentile) (follow-up 6 months after onset)				
Kanji reading (/100)	87 (<1) ^b	100 (>9)	99.6 (1.2)	1 min 32 s (32 s)
	7 min 1 s (>99)	2 min 31 s (96)		
Kana reading (/100)	12 (<1) ^b	95 (35)	99.6 (0.5)	1 min 13 s (24 s)
	16 min 1 s (>99)	6 min 8 s (>99)		
Kanji writing (/100)	32 (<1)	57 (<1)	95.9 (3.0)	10 min 11 s (136 s)
	11 min 16 s (61)	12 min 37 s (91)		
Kana writing (/100)	80 (<1)	97 (<1)	99.3 (0.9)	8 min 7 s (107 s)
	9 min 57 s (87)	8 min 17 s (60)		
II. Reading (100 two-character kanji words, three-character kana words and three-character kana nonwords), correct responses and time (follow-up 7–8 months after onset)				
Two-character kanji words (/100)	30 (<1)	98 (<11)	99.3 (0.8)	1 min 20 s (14 s)
	8 min 50 s (>99)	2 min 23 s (>99)		
Three-character kana words (hf) (/100)	54 (<1)	91 (<1)	98.3 (1.6)	2 min 1 s (37 s)
	13 min 41 s (>99) ^c	4 min 11 s (>99)		
Three-character kana words (lf) (/100)	2 (<1)	86 (<1)	96.6 (2.0)	2 min 28 s (41 s)
	16 min 22 s (>99)	not recorded		
Three-character kana nonwords (/100)	8 (<1)	84 (<1)	97.8 (1.3)	2 min 1 s (37 s)
	16 min 30 s (>99)	5 min 31 s (>99)		
III. Reading (46 single-character kana, 50 five-character kana words and five-character kana nonwords), correct responses and time (follow-up 7–8 months after onset)				
Single-character kana (/46)	24 (<1)	41 (<1)	45.7 (0.6)	24 s (4 s)
	4 min 14 s (>99) ^c	47 s (>99)		
Five-character kana words (/50)	0 (<1)	48 (<1)	49.5 (0.5)	1 min 24 s (32 s)
	12 min 25 s (>99) ^c	3 min 3 s (>99)		
Kanji transcription (/50)	12 (<1)	49 (10–50)	49.4 (0.6)	54 s (15 s)
	8 min 23 s (>99)	59 s (73)		
Five-character kana nonwords (/50)	0 (<1)	32 (<1)	47.0 (2.1)	2 min 16 s (33 s)
	13 min 47 s (>99)	5 min 24 s (>99)		
IV. Writing (50 three- and five-character kana words and nonwords), raw score and time (percentile) (follow-up 32 months after onset)				
Three-character kana words (/50)	47 (<1) ^d	47 (<1)	49.7 (0.9)	3 min 50 s (66 s)
	3 min 50 s (51)	3 min 38 s (48)		
Three-character kana nonwords (/50)	42 (<1) ^d	47 (5)	48.9 (1.3)	4 min 6 s (76 s)
	4 min 12 s (49)	3 min 59 s (48)		
Five-character kana words (/50)	36 (<1) ^d	47 (<1)	49.5 (0.7)	6 min 4 s (89 s)
	5 min 45 s (71)	5 min 25 s (60)		
Five-character kana nonwords (/50)	19 (<1) ^d	32 (11)	36.2 (5.3)	7 min 49 s (117 s)
	8 min 6 s	8 min 59 s		

^aHealthy controls: Reading and writing (100 words), $n = 11$ (mean, 68 years old) (Sakurai, Takeuchi, et al., 2000b); Reading (II, III), $n = 11$ (mean, 73 years old) (Sakurai et al., 2006); Writing (IV, three-character words), $n = 11$ (mean, 73 years old) (Sakurai et al., 2010); Writing (IV, five-character words), $n = 10$ (mean, 74 years old) (Sakurai et al., 2018); all with 9 or more years of education and no past history of neurologic illness.

^bKinesthetic reading was successful in 14/22 trials for kanji and 2/29 trials for kana.

^cMean time for reading kana in the patient (and the healthy controls) was as follows: single-character, 5.52 (0.53) s/character; three-character words, 8.21 (1.22) s/word; and five-character words, 14.90 (1.70) s/word.

^dWriting errors consisted of 1 phonological, 2 phonological/visual, for the three-character words; 7 phonological, 1 phonological/visual, for the three-character nonwords; 6 phonological, 5 phonological/visual, 3 allographic, for the five-character words; and 24 phonological, 1 phonological/visual, 3 transposition (changing the sequence of two consecutive characters), 3 partial, for the five-character nonwords. For the explanation of other errors, see the footnote of Table 3B.

hf, high familiarity; lf, low familiarity.

kana words, e.g., あした → 明日 ([ashita], tomorrow), and various kanji–kana compound words partially transcribed from the five-character kana words (kanji words with kana suffixes), e.g., なつやすみ → 夏休み [natsuyasumi], summer vacation, were also provided on a separate sheet. The patient was asked to read the stimulus characters successively from the beginning. Reading was impaired even at the level of single-character kana. Letter-by-letter reading was observed in three- and five-character kana words and nonwords. A word-length effect was observed: time for reading elevated from 5.52 s/character for the single-character to 14.90 s/word for the five-character words (footnote (c) of Table 2). Word-by-word reading (reading one word at a time with much reading pause) was also observed in three-character kana words. Reading of two-character kanji and kanji transcription of five-character kana words were also disturbed. The patient complained that he could not read kanji words because he did not understand the meaning or remember the reading even if he understood the meaning. Low-familiarity three-character kana words were read as poorly as three-character kana nonwords, suggesting that lexicality had little effect on the reading of low-familiarity words. Neither five-character kana words nor five-character kana nonwords were read, suggesting that sequential letter recognition was not available in five-character kana words and nonwords. Errors consisted of no response in two-character kanji (91%) and phonological errors (phonemic paralexia) in three-character kana words (83%) and nonwords (75%) (Table 3C).

Writing test of three-character kana words and nonwords and five-character kana words and nonwords (Table 2, IV) (Sakurai et al., 2018)

Test items were the anterior half of the 100 three-character word and nonword reading tests and all the 50 five-character word and nonword reading tests (Table 2, II, III). The patient wrote from dictation these words and nonwords separately on a sheet. Writing was more impaired for five-character words and nonwords than for three-character words and nonwords (word-length effect), and in nonwords than words for both three and five characters (lexicality effect). Phonological and phonological/visual (one kana character was changed to another visually similar character) errors accounted for most errors (100% in three-character words and nonwords, 79% in five-character

Table 3A. Types of reading errors in 100 single-character kanji and kana transcriptions test (Test I in Table 2).

	Onset	6 months
Kanji		
No response	10	0
Visual	2	0
Unrelated	1	0
Kana		
No response	35	0
Phonological	46	3
Phonological/visual	3	1
Partial	3	0
Unrelated	1	0

Visual: changing the kanji reading to the reading of another kanji with a visual resemblance to the correct answer, e.g., 休 (lyasumu), rest → read as 体 ([karada], body); unrelated: changing to the reading of another word that has no phonological or orthographical similarity; phonological: one or more characters of a kana word were substituted for other kana (phonemic paralexia), e.g., あめ ([ame], rain) → あお ([ao], blue); phonological/visual: one kana character was pronounced incorrectly for a visually similar character, e.g., いわ ([iwa], rock) → いつ ([itsu], when); partial response: one or more characters of a kana word were not read.

Table 3B. Types of writing errors in 100 single-character kanji and kana transcriptions test (Test I in Table 2).

	Onset	6 months
Kanji		
No response	64	41
Visual	1	0
Constructional	1	1
Unrelated	2	0
Neographism	0	1
Kana		
No response	1	0
Partial	1	0
Phonological	13	1
Phonological/visual	4	2
Allographic	1	0

Visual: substitution of another kanji visually similar to the target character, e.g., 指 ([yubi], finger) → 脂 ([abura], fat); constructional: omission or addition of a component of a kanji, e.g., 左 ([hidari], left) → 左 (nonword); unrelated: substitution of another kanji that has no visual, semantic, or phonological similarity to the correct answer; partial: one or more characters of a kana word were not written; phonological: one or more characters of a kana word were substituted for other kana (phonemic paraphasia), e.g., いぬ ([inu], dog) → いむ ([imu], detest); phonological/visual: changing one character to another visually similar character, e.g., くろい ([kuroi], black) → くるい ([kurui], aberration); allographic: one or more kana (more precisely hiragana, a cursive form of kana that is normally used for grammatical morphemes) characters were substituted for katakana (a square form of kana that is used primarily for representing loan words) characters, e.g., くる ([kuru], come) → くる ([kuru], hiragana-katakana).

words, and 81% in five-character nonwords). Three allographic errors (changing one kana character into another form of kana [katakana], see footnote of Table 3B) were observed in five-character words, and three transposition errors (changing the sequence of two consecutive characters) were observed in five-character nonwords (footnote (d) of Table 2).

Modality-specific digit span and letter/character span (Table 4) (Sakurai et al., 2018)

Digit or letter sequences were presented auditorily (usual digit or letter span forward, one digit or letter/s) and visually using a laptop with a presentation duration of 500 ms and an interval of 500 ms. To investigate the effect of spatial working memory, we also administered visual memory span of the Wechsler

Table 3C. Types of reading errors in two-character kanji word, three-character kana word (high familiarity), and three-character kana nonword tests (Tests II and III in Table 2).

	Onset	6 months
Two-character kanji word		
No response	64	0
Partial	4	0
Lexical	0	2
Unrelated	2	0
Three-character kana word (hf)		
Phonological	38	8
No response	7	0
Lexical	0	1
Unrelated	1	0
Three-character kana nonword		
Phonological	69	14
Phonological/visual	3	1
No response	13	0
Partial	7	0
Lexical	0	1

Partial: only one character was read correctly; lexical: changing to another word that contains the same kanji or kana characters of the correct word, e.g., 範囲 ([haini], extent) → read as 模範 ([mohan], model); うてん ([uten], rain) → read as うんてん ([unten], driving); unrelated: changing to the reading of another word that has no phonological or orthographical similarity; phonological/visual: one character is read as a visually similar character, and another character is pronounced incorrectly, e.g., うくつ ([ukutsu], nonword) → うかう ([ukau], nonword); for other errors, see the footnote of Table 3A.

hf, high familiarity.

Table 4. Scores for the special neuropsychological tests: digit span, calculation, and visual discrimination.

	Onset	9–12 months	Controls ^a Mean score (SD)
Digit span forward (percentile) (follow-up 12 months after onset) ^b			
Auditory digit span	5.0 (45)	4.8 (33)	5.28 (1.15)
Auditory letter span	4.2 (7)	3.8 (<1)	4.9 (0.74)
Visual digit span	5.0 (45)	4.4 (11)	5.38 (1.34)
Visual letter span	< 2.0 (<1)	4.2 (6)	5.2 (1.07)
Visual memory span (WMS-R)	5.0 (56)	7.0 (98)	5 (56%ile) ^c
Calculation, raw score (percentile) (follow-up 9 months after onset)			
Mental arithmetic (/40)	23 (<1)	32 (1)	36.25 (2.73)
Dictated calculation (/40)	27 (<1)	37 (1)	39.25 (0.96)
Scientific calculator (/40)	40 (>18)	40 (>18)	39.83 (0.97)
Visual discrimination test (follow-up 12 months after onset)			
Line length (/12)	11 (<28)	12 (>36)	11.67 (0.49)
Circle size (/12)	12 (1–100)	12 (1–100)	12.00 (0.00)
Parallel line (/12)	12 (1–100)	12 (1–100)	12.00 (0.00)
Circle-oval (/12)	10 (<10)	11 (19–54)	11.25 (0.75)
Square-rectangle (/12)	12 (>81)	12 (>81)	10.75 (1.06)
Vertical point location (/12)	12 (>18)	12 (>18)	11.83 (0.39)
Horizontal point location (/12)	12 (>18)	12 (>18)	11.67 (0.89)
Distortion of a square (/12)	12 (>27)	12 (>27)	11.67 (0.65)
Angle (/12)	12 (>18)	12 (>18)	11.75 (0.62)

^aHealthy controls: digit span, $n = 10$ (mean, 58 years old) (Sakurai et al., 2018); calculation, $n = 12$ (mean, 67 years old) (Sakurai et al., 2018); visual discrimination, $n = 12$ (mean, 74 years old) (Sakurai et al., 2016); all had 9 or more years of education and no past history of neurologic illness.

^bIn the visual or auditory digit span test, five sets of stimuli were given for each digit sequence, and 0.2 points were given for a correct response. In the visual memory span test, two sets of stimuli were supplied for each dot sequence, and 0.5 points were given for a correct response.

^cBased on the Manual for the Wechsler Memory Scale-Revised (WMS-R, Japanese edition), $n = 50$ (age range, 55–64 years).

WMS-R: Wechsler Memory Scale-Revised.

Memory Scale-Revised. The digit span forward score, either auditory or visual, was approximately 5, within normal range. Letter/character span forward score was slightly lower, ≤ 4 . The visual memory span score was 5, average level.

Calculation test (Table 4) (Sakurai et al., 2018)

A total of 40 calculations, consisting of an equal number of addition, subtraction, multiplication, and division tasks, were performed. The examiner first read a calculation task, and then the patient conducted mental arithmetic, dictated calculation, and calculation with a scientific calculator. Mental arithmetic and dictated calculation were both impaired. Since dictated writing was complete, incorrect answers in dictated calculation suggested anarithmetia (impairment of the calculation process per se). In addition, the difference between mental arithmetic and dictated calculation scores reflected the involvement of reduced working memory.

Visual discrimination test (Table 4) (Sakurai et al., 2016; Sakurai, Ichikawa et al., 2001a)

Two sets of line-drawings with slightly different lengths, sizes, shapes, spatial locations, etc. were provided. The patient was asked whether the two drawings on a card were the same or different and, if different, to explain the difference (For examples of the stimulus figures, see Sakurai et al., 2016). Results suggested that fundamental visual discrimination, such as line length, shape size, shape difference, horizontal distance, and slope, was nearly normal.

Recovery of function over time

Alexia of kanji and kana recovered within six months after hospital admission, although the patient still read kanji and kana characters slowly. Agraphia of kana recovered substantially, but the patient wrote 20 out of the 46 kana syllabary even at three and a half years after onset. On the other hand, kanji writing recovered slightly. Digit and letter span scores had not changed by 1 year after admission, except for visual letter span, whereas the visual memory span score improved from 5 to 7. Mental arithmetic and dictated calculation recovered, but not to within normal range by 9 months after admission. Because digit span had rarely changed, this recovery was not due to the improvement of verbal short-term memory but that of the arithmetic skill itself and spatial working memory (to maintain the alignment of digits), as demonstrated by the increase of visual memory span. He returned to work five months after discharge. Of note is that he found it difficult to knead the bread well and divide it into two halves accurately, which he had done almost automatically before the disease onset. As a result, he had to weigh the divided part on a saucer scale. This disorder lasted for six months. On ^{99m}Tc -ECD-SPECT performed 7 months after onset, hypoperfusion of the left lateral occipital gyri was limited to a small area (Figure 2).

Discussion

The patient in this case report presented with alexia with agraphia, more precisely kana-predominant alexia with letter-by-letter reading, lexical agraphia of kanji, and literal and allo-graphic agraphia (Rapcsak & Beeson, 2002) of kana, accompanied by acalculia and working memory impairment. Single-character kana reading was impaired, and a word-length effect was evident. Although single-character kanji reading was

relatively preserved, whole-word reading of two-character kanji was severely impaired. This is either because orthography of a two-character word was disrupted or orthography did not connect with the phonological lexicon. The latter is more concerned because the patient achieved 72% correct in the lexical decision task for kanji (Table 1). Fundamental visual discrimination was preserved. The alexia with agraphia resolved to lexical agraphia for kanji and phonological agraphia (selective impairment of nonword spelling) for kana over the course of 32 months.

Alexia with agraphia due to an angular gyrus lesion has been previously described (Benson, 1985). Angular alexia with agraphia typically presents with lexical agraphia (selective impairment of irregular word writing), corresponding to Japanese kanji agraphia. In addition, in Japanese cases of angular alexia with agraphia, alexia of kana also occurs (Kawamura, 1990; Miyake & Tanaka, 1992). However, limited damage to the angular gyrus does not cause alexia, but rather isolated kanji agraphia (Sakurai, Takeuchi et al., 2000b). Thus, it was assumed that the alexia in angular alexia with agraphia was the result of lesion extension into the adjacent lateral occipital gyri. A subsequent case report indicated that kana-predominant alexia with agraphia became evident only after a new infarction that involved the lateral occipital gyri after an old infarction in the angular gyrus (Kuriyama et al., 2006).

The patient presented here directly demonstrates that alexia arises from a lesion of the middle and inferior occipital gyri and manifests as letter-by-letter reading. The lesion location is similar to that of posterior type of pure alexia for kana (Oishi et al., 2018; Sakurai, Ichikawa et al., 2001a; Sakurai et al., 2008); however, the posterior fusiform gyrus was not structurally involved in the present patient (although it may have been functionally affected in the acute phase ECD-SPECT). It should be noted that the MNI coordinates in the inferior occipital gyrus for local maximum blood flow reduction were (-40, -76, 2) in the present patient, 14 mm above the peak reduction site (-38, -80, -12) observed in the posterior fusiform/inferior occipital gyri (Sakurai et al., 2008) for the ventral posterior occipital type of letter-by-letter reading. This anatomical difference influenced semiology, as described below.

Characterization of dorsal type of letter-by-letter reading as compared with ventral type (Table 5)

Letter-by-letter reading in the present patient did not differ from conventional ventral letter-by-letter reading in its characteristic features; that is, a word-length effect and impaired letter identification were noted (Sakurai et al., 2006). However, there were some differences between dorsal and ventral letter-by-letter reading. One is that kinesthetic facilitation was less functional in our patient. This is probably because the hematoma was extensive enough to interrupt kinesthetic information traveling from the parietal somatosensory cortex to the ventral occipitotemporal area. In this regard, previous studies have reported that a subregion of the lateral occipital complex (LOC) is activated in tactile naming and object naming (Amedi, Jacobson, Hendler, Malach & Zohary, 2002; Amedi et al., 2001); it is possible to assume that damage to the left LOC interfered with kinesthetic reading. The fact that the

Table 5. Comparison of two types of letter-by-letter reading.

	Ventral type	Dorsal type
Letter-by-letter reading	present	present
Word-length effect	present	present
Single-letter identification	impaired	impaired
Kinesthetic reading	effective	less effective
Reading impairment	Kanji > < Kana ^a	Kana > Kanji ^b
	Words > < Letters	Letters > Words
Writing impairment	Kanji	Kanji > Kana ^c
	Words	Words > Letters
Visual discrimination	sl. impaired (post O type)	normal
Lesion location	mid-Fu (fusiform type)	mid and inf O
	post Fu/inf O (post O type)	

^aKanji (or word) reading is more impaired than kana (or letter) reading (fusiform type) or kana (or letter) reading is more impaired than kanji (or word) reading (posterior occipital type).

^bKana (or letter) reading is more impaired than kanji (or word) reading.

^cKanji (or words) writing is more impaired than kana (or letter) writing.

sl., slightly; post O, posterior occipital; mid-Fu, mid-fusiform gyrus; mid and inf O, middle and inferior occipital gyri; post Fu, posterior fusiform gyrus.

patient had difficulty kneading the bread and dividing it into two halves suggests evidence of tactile–visual disconnection.

The second difference is that our patient had difficulty writing kana characters, which is not observed in ventral pure alexia (Sakurai et al., 2006). However, kana writing is slightly impaired in alexia with agraphia from a posterior inferior temporal cortex (BA 37, more precisely mid-fusiform/posterior inferior temporal gyri) lesion (Kawamura, 1990; Sakurai, Takeuchi et al., 2000b; Soma et al., 1989), the location of which is lateral to that of fusiform type pure alexia (Sakurai et al., 2006). We thought that visual images of kana or letters are widely distributed in the ventral occipitotemporal area and the lateral occipital gyri and are used for both phonology (grapheme–phoneme conversion) and orthography (whole-word recognition) (Sakurai, 2004). In writing from dictation, visual images of kana are sent to the parietal graphemic area to output visuokinesthetic pattern of the kana character to the frontal motor hand area (Sakurai et al., 2007). The existence of kana agraphia or literal agraphia in general implicates interruption of kana (or letter) visual images traveling from the ventral occipitotemporal area or lateral occipital gyri to the parietal and frontal lobes. Damage to the lateral occipital gyri (demonstrated by MRI) in the patient presented here may have contributed to his kana agraphia. Because the mid-fusiform/posterior inferior temporal gyri (BA 37) were spared damage both on the MRI and ECD-SPECT images, it is less probable that this area was involved in the kana agraphia.

The third difference is that fundamental visual discrimination was preserved in our patient, whereas it was slightly impaired in the ventral posterior occipital type letter-by-letter reading patients (Sakurai et al., 2008). It is possible that deficits of fundamental visual discrimination affect kana character identification in the ventral posterior occipital type letter-by-letter reading whereas grapheme–phoneme conversion is more concerned in the dorsal type letter-by-letter reading.

In summary, coexisting agraphia and normal visual discrimination distinguish the dorsal type of letter-by-letter reading from the ventral type. The distinction between dorsal and ventral letter-by-letter reading is clinically important because the dorsal type implies the involvement of the dorsal part of the lateral occipital gyri and requires rehabilitation not only for alexia but also for agraphia. As the lateral occipital gyri are

rarely damaged in cerebrovascular disease, further study is needed to elucidate the functional role of this area.

Disclosure statement

No potential conflict of interest was reported by the authors.

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