SHORT REPORT

Agraphia and acalculia after a left prefrontal (F1, F2) infarction

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Abstract
A patient presented with agraphia and acalculia associated with a left frontal (F1, F2) infarction. He made mainly phonological but also lexical errors in writing (syllabograms), but his ability to write kanji (morphograms) was relatively preserved. Although he could add and subtract numbers, he could neither multiply nor divide them because of a difficulty in retrieving the multiplication tables and calculation procedures. Positron emission tomography showed decreased cerebral blood flow and metabolism limited to the infarct site. These findings suggest that agraphia and acalculia may occur associated with a left prefrontal lesion, and that the retrieval of arithmetic processes is modality specific.

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Keywords: agraphia; acalculia; prefrontal cortex

Pure agraphia was first ascribed to lesions in the premotor cortex (Brodmann's area 6) by Exner in 1881, and this view was supported by early researchers.[1 2] Many later studies, however, reported agraphia associated with parietal lesions,[3-7] implicating the angular gyrus as a graphic centre,[8 9] or to interruption of the transfer of writing information between the parietal and frontal cortices.[10] More recently there have again been reports of some patients with pure agraphia due to frontal lesions.[11-14] An isolated acalculia (anarithmia) has been also ascribed to a parieto-occipital lesion in most cases,[15-17] but to a frontal lesion in one patient.[18] Some patients with agraphia or acalculia showed dissociations between different orthographic[14 19-21] or arithmetical operations,[16 22-24] suggesting domain specificity of individual processes in the writing and calculation system. We describe a patient with pure agraphia and acalculia associated with a left frontal lobe (F1, F2) infarction.

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Case report

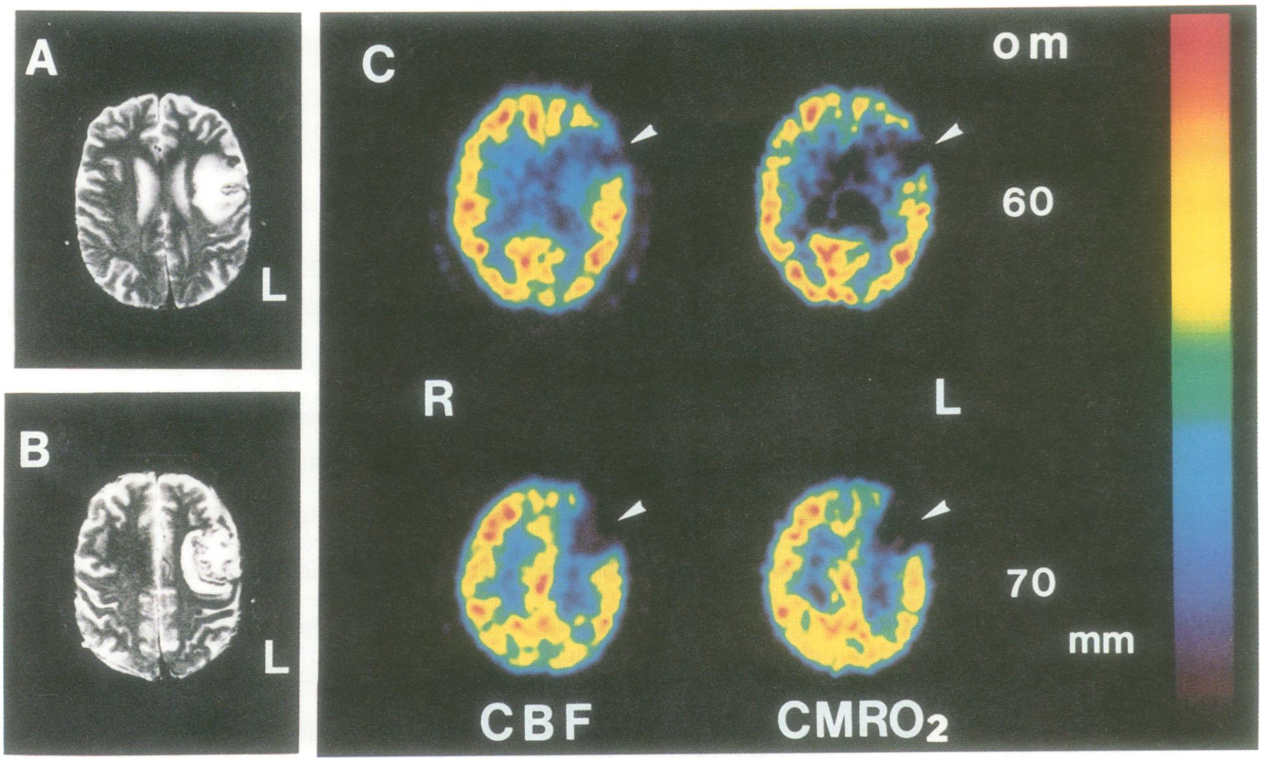
The patient, a 59 year old, right handed man had had 11 years of formal education and had been working in a construction company. His job was mainly to procure building materials. For six years before admission he had diabetes and hypertension, which were being treated but he had been in normal health. Two days before admission, when he was talking with a carpenter, he suddenly became unable to respond with even a single word.

On admission, he was alert and well oriented for both time and space. Neurologically, he had a mild right hemiparesis and a mild stocking type sensory disturbance due to diabetic neuropathy. Computed tomography and MRI showed a haemorrhagic infarction in the left frontal lobe; the high intensity area on T2 weighted MRI involved mainly the middle frontal gyrus, the upper part of the inferior frontal gyrus, and part of the precentral gyrus (figure, A, B). In other areas, only a few lacunes were found. Brain PET studies showed a severe (~ 70%) reduction in regional cerebral blood flow (CBF) and metabolic rate of oxygen ($CMRo_2$) in the left prefrontal area (figure, C). CBF and $CMRo_2$ were some 20% less than controls in the supramargical and angular gyri, and the reductions were symmetric (figure, C).

LANGUAGE

The Japanese writing system consists of kana and kanji. Kana are syllabograms representing vowels (a, i, u, e, o) or combinations of consonants (k, s, t, n, h, m, y, r, w) with vowels (ka, ki, etc) and most kana are orthographically regular. Kanji are morphograms, or ideographs, developed from Chinese characters, and are read using the original Chinese sound or the Japanese sound—for instance, a kanji meaning "east" is read as [tou] (original sound) or as [higashi] (Japanese sound) depending on the context. All Japanese sentences can be written with kana only, but are usually written with both kanji (for nouns and roots of verbs, adjectives, and adverbs) and kana (for inflexions, conjunctions, and propositions).

A week after onset, his auditory and reading comprehension of words and sentences were normal (28/30, 93% for each), but his ability to carry out oral and written commands (such as to place a coin and a fountainpen on a handkerchief) was severely impaired (3/19, 30% for each). He could correctly choose a kana that corresponded to a



(A) T2 weighted MRI of horizontal planes (TR = 2500, TE = 110) at level of corpus callosum; (B) at level of centrum semiovale; the infarct area includes mainly Brodmann's areas 6 and 8, and a posterior part of area 9, but spares area 44; (C) PET images of cerebral blood flow (CBF), and cerebral metabolic rate of oxygen ($CMRo_2$) in the horizontal planes 60 and 70 mm above and parallel to the orbitofrontal (om) line (8 weeks after onset using Headtome IV, Shimadzu, Japan, with the full width at half maximum of 4·5 mm). The CBF and $CMRo_2$ were determined using $C^{15}O_2$ inhalation methods and $^{15}O_2$ respectively. The right side of the head is on the left in all figures. The CBF and $CMRo_2$ are profoundly decreased in the left prefrontal areas (arrowheads). Quantitative data are as follows (ml/100 ml/min): prefrontal area, CBF 33·8 and $CMRo_2$ 2·42 on the right, and CBF 12·2 and $CMRo_2$ 0·79 on the left; supramarginal gyrus, CBF 33·6 and $CMRo_2$ 2·51 on the right, and CBF 32·8 and 2·42 on the left; angular gyrus, CBF 29·8 and $CMRo_2$ 2·45 on the right, and CBF 31·7 and $CMRo_2$ 2·58 on the left; and control values, CBF ~ 40 and $CMRo_2$ ~ 3·0.

phoneme pronounced by the examiner (20/20, 100%), could name objects (18/20, 90%), and could repeat words orally that were spoken by the examiner (10/10, 100%). He could describe what a person was doing on single action pictures (7/10, 70%), but could not narrate a story for composite pictures. He could read aloud and comprehend perfectly single kana words written in kanji and kana and sentences composed of both kana and kanji (25/25, 100% for each). If he was asked to say as many words as possible (word naming), he said only two words (control $\geqslant$ 12). His writing ability was severely impaired: the correct responses were far less frequent for spontaneous writing (1/25, 4%) than for dictation (7/25, 28%; $\chi^2 = 5{\cdot}4$, $p < 0{\cdot}025$).

His linguistic abilities gradually recovered after admission. Seven weeks after onset, he made almost no errors in speaking, listening, and reading, but made many errors in writing. His writing errors for kana (24/62 words, 39%) were significantly more frequent than for kanji (4/65 words, 6%) ($P < 0{\cdot}001$). His oral responses to 60 pictures of the Boston naming test (40–55 for the average Japanese) were correct for 45 pictures (75%), but his graphic responses were correct for 31 pictures (52%)—that is, he made errors in writing in 14 out of 45 words (31%) that he could express orally. His writing errors for kana included (table) (*a*) omission of phonetic marks (two dots on the right upper corner of a kana) to convert voiceless consonants to voiced ones (for example, h to b, k to g, s to z, and t to d), or of those to convert h to a voiceless bilabial sound p (a small circle on the right upper corner of a kana) (60%); (*b*) difficulty in writing kana that are used to denote double vowels, or to prolong the precedent kana's sound (kya, kyo, kyo, or hou, kou) (14%); (*c*) confusion with a graphically similar kana (4%); (*d*) confusion with phonetically similar kana (2%); (*e*) confusion with orthographically irregular kana (8%); and (*f*) failure to complete a word (12%). He also made similar errors in writing non-words. Although Japanese kana are in most cases orthographically regular, there are a few exceptions: the subject of a sentence is indicated by a kana postposition "ha" which is pronounced as [wa]; the object of a sentence is indicated by a postposition written by a kana used for "wo" in ancient times which in modern Japanese is pronounced simply as "o". He almost always wrote kana "wa" instead of "ha" as the postposition for the subject, and kana [o] instead of "wo" for the object, which was inconsistent with his 11 year educational history. He could correctly copy words both in kanji and kana. The kanji character is composed of a radical that is related to its meaning (semantic component)

Examples of writing errors of the patient for kana (footnote 1 to 6) and kanji (footnote 7 and 8)

Types of errors	*Correct Japanese word*	*Patient's writing*	*English meaning*
1	みず (mi/zu)	みす (mi/su)	Water
1+6	えんぴつ (e/n/pi/tsu)	えん_つ (e/n/-/tsu)	Pencil
2	ぼうし (bo/u/shi) [bo:shi]	ぼし (bo/shi)	Hat
2	さんきゃく (sa/n/ki/ya/ku) [sankyaku]	さんかく (sa/n/ka/ku)	Tripod
3	めん (me/n)	ぬん (nu/n)	Mask
4	びょうぶ (bi/yo/u/bu) [byo:bu]	ぶようぶ (bu/yo/u/bu)	Screen
4+6	やま (ya/ma)	ゆ (yu/-)	Hill
5	私は (watakushi wa)	私わ (watakushi wa)	I am
5	私を (watakushi o)	私お (watakushi o)	To me
2+3+6	ほうれんそう (ho/u/re/n/so/u) [ho:renso:]	ほねんう (ho/ne/n/-/u)	Spinach
1+2+6	じどうしゃ (ji/do/u/shi/ya) [jido:shya]	じと (ji/to/...)	Automobile
7	子供 (ko/do/mo)	子共	Child
8	机 (tsu/ku/e)	枅	Desk

Pronunciations for individual kana are shown in parentheses, and pronunciations for double vowels in square brackets.
1 = Omission of a mark (double dots at the right upper corner of a kana) to convert k to g, s to z, t to d, and h to b, or omission of a mark (a small circle at the right upper corner of a kana) to convert h to p, or omission of kana denoting pa, pi, pu, pe or po; 2 = difficulty in writing kana that are used to denote a double vowel, or to prolong a precedent kana's sound; 3 = confusion with a graphically similar kana; 4 = confusion with a kana representing similar sound; 5 = errors in orthographically irregular kana; 6 = failure to complete a word; 7 = errors in writing the radical (left half) of kanji; 8 = errors in writing the non-radical portion (right half) of kanji.

and a non-radical portion that may provide a clue as to its Chinese way of reading (phonetic component). The patient's errors in writing kanji were in either the radical or non-radical portions (table).

CALCULATION
A week after onset, he could only perform additions of one digit numbers not including carrying (for example, $3 + 2 = 5$), but could not add numbers requiring carrying processes (for example, $7 + 5 = 7$ instead of 12), or subtract one digit numbers. Multiplication and division were totally impossible because he could not remember the multiplication tables. He could, however, indicate which of the paired two numbers was greater, and write numbers corresponding to the numbers spoken, suggesting that he could read, understand, and write digits.

Seven weeks after onset, he became able to add and subtract up to three digit numbers with carrying and borrowing. He sometimes succeeded in multiplying or dividing one digit numbers, but still often made errors (for example, $4 \times 6 = 48$ instead of 24, or $9 \div 3 = 9$ instead of 3). He could not multiply or divide two digit numbers, because of difficulty in completely remembering the multiplication tables, and an inability to retrieve calculation procedures (for example, $18 \times 8 = 74$ instead of 144).

Eight weeks after the onset, his Wechsler adult intelligence score (WAIS) was 71 for the verbal tests and 89 for the performance tests.

Discussion

The main findings are the rare associations between pure agraphia and acalculia with a left frontal lesion and the patterns of orthographic and arithmetic errors.

The writing is generated by semantic or phonological inputs to orthography in the linguistic processes, and then is processed through an orthographic buffer, physical letter code, graphic motor pattern, and graphic code in the peripheral aspects.[21] Our patient's ability to select correct kana and kanji from a visual array indicates an intact physical letter code. His ability to write well formed kana and kanji, although with some confusions for morphologically or phonetically similar kana, suggests that his lexical and non-lexical phonology, orthography, and stroke motor programmes (graphic motor pattern) were relatively intact. The main feature of phonological agraphia as contrasted with lexical agraphia in Indo-European languages is the disproportionate failure in writing non-words, probably because each word (for example, water) is recognised as if it were an ideogram (whole word reading) rather than a simple combination (w-a-t-e-r) of alphabetical letters. This is not usually the case in Japanese because kanji are ideograms and because there are no spaces between words in kana writing (like writing "iamalondoner." instead of "I am a Londoner." in English). Although our patient showed no dissociation between the writings of real words and non-words, the relative preservation of writing kanji compared with kana and the most frequent errors in using phonetic marks to convert pronunciations of consonants suggest that impairments of phoneme-grapheme conversion may be the main cause of his agraphia. The failure to construct double vowels by combining kana that are originally pronounced differently (for example, kyou (today) from ki-yo-u) may apparently resemble those in surface dysgraphia in Indo-European languages in which patients write phonetically correct but lexically incorrect words because of an impairment of the lexical route.[19,20] This view, however, cannot be applied to the findings in our patient's errors in Japanese. In French, for example, one cannot, like in kanji writing, write "eau" (/o/; water) without knowing its meaning, and the sound /o/ is phonetically ambiguous because it may be written in several different ways (o, au, aux, etc). By contrast, the Japanese phoneme-grapheme system is not ambiguous because one can write "kyou" using kana "ki-yo-u" without knowing its meaning, and there is no alternative way of writing the same sound. By contrast, our patient's errors in writing orthographically irregular kana that are used as postpositions for subjects and objects of sentences indicate that the patient could not correctly write different kana for the sound /o/ and /wa/ depending on its syntactic significance. In addition, our patient's more severe impairments of spontaneous writing than of writing to dictation, similar to the discrepancy between impaired spontaneous speech and preserved repetition and comprehension in transcortical motor aphasia, suggest that his lexical and semantic routes may also be disturbed.

Agraphia associated with a left frontal

lesion is rare: one patient described by Gordnier[1] could not write or correctly form a single letter, and those described by Aimard *et al*[11] and Hodges[13] could write letters and words correctly but extremely slowly and laboriously. Agraphia in these patients may probably be due to kinaesthetic writing disorders. The patient reported by Rapcsak *et al*[14] could spell non-words and regular words better than irregular words, with most of his spelling errors being phonologically correct, and was diagnosed as having lexical agraphia. In our patient phonological impairment was greater than lexical impairment. The neuropsychiatric characteristics of frontal agraphias seem, therefore, to be different depending on the cortical areas involved.

The preserved ability to write numbers despite the disorders in writing words in our patient is similar to the findings in the patient (with a left premotor lesion) reported by Anderson *et al*,[12] indicating the domain specificity for cognitive representations. The patient's failures in the processes of carrying and borrowing and in remembering the multiplication tables in the early period despite his well preserved aspects of numbers is consistent with isolated acalculia, not with asymbolic (aphasic), or visuospatial acalculia.[2] In one of the current models of arithmetic processing,[25] the calculation system consists of (*a*) comprehension of operation signs or words, (*b*) retrieval of arithmetic facts, and (*c*) execution of calculation procedures, and the retrieval of arithmetic facts may involve modality specific processes.[24] The dissociation between addition and subtraction and multiplication and division and between relatively retained knowledge of the multiplication tables and the inability to use them seen in the later stage are similar to the findings in the patient reported by Benson and Weir.[15] In the patient with dyscalculia reported by Luchelli and Renzi after a left medial frontal lesion simple calculations with square roots and powers were preserved.[18]

Although acalculia is most often associated with aphasia, a few studies have linked isolated acalculia with a left parieto-occipital lesion.[15-17] A regional cerebral blood flow study in normal volunteers, however, showed that when the subject was attending to silent arithmetical mental activities there was a consistent activation of the anterior intermediate prefrontal cortex and the middle superior prefrontal cortex, in addition to the supramarginal and angular gyri of both hemispheres.[26] The results from our patient suggest that the domains of arithmetic knowledge and of graphemes may be located close together, but agraphia without acalculia may occur in rare instances as in the patient reported by Anderson *et al*.[12]

The present case illustrates that further careful studies on patients with frontal lesions may provide opportunities to reveal the function of the frontal lobe in writing and calculation.

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