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Case report

Pure alexia after damage to the right fusiform gyrus in a right-handed male

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ABSTRACT

Pure alexia refers to a rare acquired reading disorder commonly associated with damage to the posterior part of the left medial occipito-temporal (fusiform) gyrus, which is known as the visual word-form area (VWFA) and thought to be the neural basis for visual processing of letters and words. Right-sided lesions very rarely lead to pure alexia in right-handed individuals. We report a case of a 33-year-old right-handed man with isolated pure alexia resulting from a hemorrhagic lesion to the right fusiform gyrus. A limited recovery of reading skills was observed within six weeks post onset. During this period, the patient spontaneously developed a letter-by-letter reading strategy. Functional magnetic resonance imaging revealed right-hemisphere dominance for language as well as bilateral reading-related activity in the fusiform gyri. Our case indicates that pure alexia may arise as a consequence of damage to the right fusiform gyrus even in right-handed patients (who still may have right hemisphere dominance for language and reading skills), and may lead to a severe reading disorder, as in individuals with left-hemisphere dominance for language.

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1. Introduction

Pure alexia is an acquired reading disorder characterized by impaired visual identification of familiar words that cannot be explained by sensory impairments, aphasic symptoms, or generalized cognitive decline. Common visual errors during reading (e.g. problems discriminating visually similar letters), a letter-by-letter reading strategy, and relatively good writing and spelling skills suggest that there is a deficiency in visually processing letter strings [1–3]. Loss of the rapid and parallel identification of strings of several letters leads to a characteristic word-length effect [4], while healthy individuals typically exhibit constant reading latencies, irrespective of word length [5]. Alexic patients use modalities other than visual or have improved reading and letter identification when presented regular printed text [6].

Pure alexia may present as an isolated impairment; however, very often it is accompanied (especially in early stages, post stroke) by anomia (usually limited to colors),

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memory deficits, and homonymous hemianopia [7]. A brain disorder (usually posterior cerebral artery stroke) is commonly found in the inferior occipito-temporal region of the left hemisphere, including the fusiform and parahippocampal gyri. However, damage to the posterior part of the former region (Brodmann area 37) containing the visual word-form area (VWFA) and/or a disconnection from visual and language areas seem critical to this type of alexia [2,4,8,9].

Pure alexia from right-sided lesions occurs very rarely in right-handed individuals. To date, multiple case reports have described pure alexia after lesions in the right occipital lobe [10–17], but the patients were right-handed in only three cases [10,11,14]. Here, we present the case of a young patient who acquired pure alexia subsequent to a right posterior vascular incident.

2. Case report

AB is a right-handed, Polish-speaking male, who was 33 years old at the time of injury. He was admitted to the stroke unit in November 2011 because of severe pain on the right side of his head. Computed tomography (CT) and magnetic resonance imaging (MRI) revealed a long (5 cm $\times$ 1 cm) hemorrhage in the right occipito-temporal area encompassing the fusiform gyrus, as well as blood in the ventricular system (Fig. 1A). A routine neurological examination revealed only meningeal signs and a transient nystagmus. No signs of motor or sensory impairment were observed. Similarly, both visual acuity and the left visual field proved normal in the confrontation test. However, AB complained of persistent inability to read including severe difficulties in identifying single letters. Consequently, three days after admission, the patient underwent a neuropsychological assessment. He was reexamined six weeks post onset, and underwent functional neuroimaging to investigate his brain laterality for language functions and reading-related activity.

2.1. Neurobehavioral assessment

The neuropsychological assessment performed in the first week did not reveal any signs of aphasia (maximum scores in all subtests of the Boston Diagnostic Aphasia Examination, except the reading subtests), neglect syndrome (Behavioral Inattention Test score of 146), or other visual problems (including object and space perception assessed by the Cortical Vision Screening Test) that could cause central or peripheral alexia. AB was able to recognize familiar faces (i.e. family members, famous people, and hospital personnel) and to estimate the age of an unknown person from a photograph. The only cognitive disturbance found in the assessment was mild, visual or nonverbal memory impairment by the Rey Complex Figure Test (5th percentile); however, this did not interfere with daily activities. His Laterality Index [18] score was 90, indicating relatively strong right-handedness. AB was able to quickly and correctly write whole sentences, but his reading was very slow (14 words/min) and laborious with frequent errors that he tried to correct using contextual information. Reading of random single words was even more impaired. During the hospitalization, AB's reading speed significantly improved without any specific therapeutic intervention, but it remained well below normal range (30 words/min) at discharge. Six weeks post onset, his visual-nonverbal memory improved (88th percentile in an alternative version of the Complex Figure Test; (standard ten score of 5 on the California Verbal Learning Test). His attention (normal scores in Paced Auditory Serial Addition Test) and visual perception (normal or borderline scores in subtests of the Visual Object and Space Perception battery) were fairly intact. His reading speed increased to 53 words/min (still below the 3rd standard deviation) (Table 1).

The word-length effect was investigated six weeks post stroke using the High Speed Eye-tracker (SensoMotoric Instruments GmbH, Germany). A total of 80 lower-case familiar words (nouns, adjectives, and verbs; 4–7 letters in length) were presented to the patient on a computer screen while recording his right eye position. The total fixation time on a target was used to analyze the reading time of each word. This was then used to calculate the mean reading time for each word-length. The analysis revealed a clear word length effect with a slope ranging from 165 to 250 milliseconds (ms) per letter (Fig. 2). This suggested that AB had developed a strategy of letter-by-letter reading, which is typical for individuals with pure alexia [4,19].

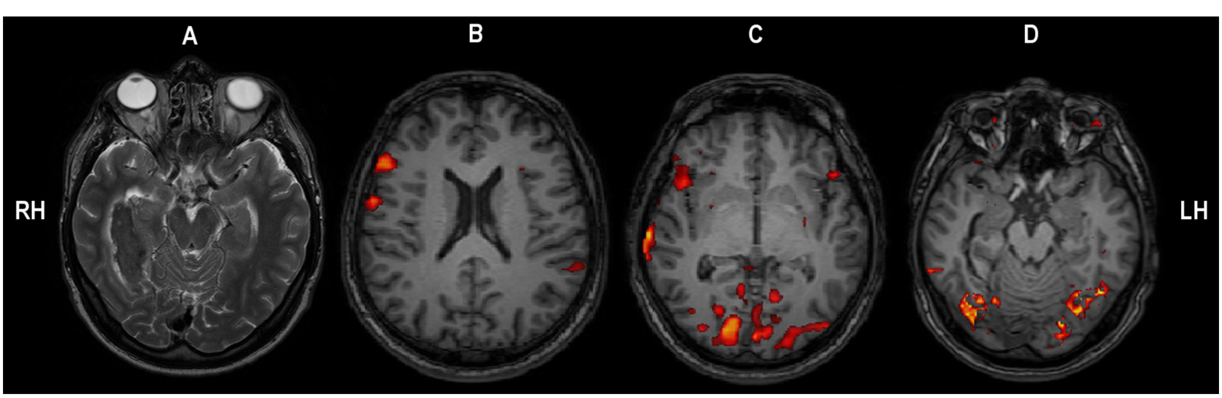

Fig. 1 – (A) T2-weighted MRI (performed at admission) of AB showing a hemorrhage in the right medial occipito-temporal (fusiform) gyrus. (B) and (C) Activation of the fronto-temporal language network in AB's brain in response to silent naming tasks versus fixation. (D) Activation of the fusiform gyri when reading words versus a string of crosses. Images are presented in radiological convention; RH, right hemisphere; LH, left hemisphere.

Table 1 – Test scores obtained in the neuropsychological assessment of AB.

Test/Measure	Raw score	Range
California verbal learning test (CVLT)	55	Average
Paced Auditory Serial Addition Test (PASAT)		
2.4 s interval	43	Average
2.0 s interval	39	Average
Rey's complex figure (alternative version)		
Copy	36	Average
Immediate Recall	29	Superior
Visual Object & Space Perception Battery (VOSP)		
Shape Detection Screening Test	20	Normal (cut-off 15)
Incomplete Letters	19	Normal (cut-off 17)
Silhouettes	16	Borderline (cut-off 16)
Object Decision	17	Normal (cut-off 15)
Dot Counting	8	Borderline (cut-off 8)
Position Discrimination	20	Normal (cut-off 18)
Number Location	9	Normal (cut-off 7)
Cube Analysis	10	Normal (cut-off 6)
Reading speed (words/min)	53	Severe deficit

Note: for VOSP subtests, 5% cut-off points were used; reading speed (number of words per min) was evaluated based on a 100-word text of moderate difficulty; results of 10 healthy controls (mean 122 words/min, standard deviation 20) were used to determine standard scores.

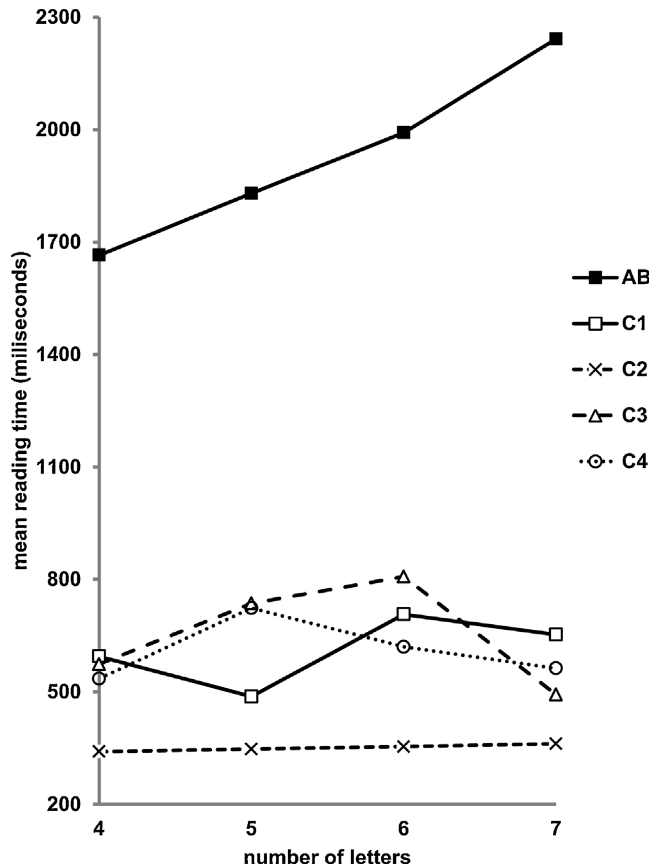

Fig. 2 – Plot of the mean total fixation times on words with 3–7 letters for AB and four age-matched controls (C1–4).

2.2. *Neuroimaging*

Functional MRI (fMRI) imaging was performed on a 3 T MR scanner (Achieva 3T TX, Quasar Dual gradients, Philips, Best) with a BOLD Specialist Package, using an 8-channel Sense Head Coil. A single-shot gradient echo, echo planar sequence was used for fMRI acquisition (FFE-EPI, TE = 30 [ms], TR = 3000 [ms], slice thickness = 3 [mm], gap = 0 [mm], matrix = 96 $\times$ 96, FOV = 192 [mm], voxel size = 2/2/3 [mm], number of slices = 42, SENSE factor 1.8, dynamics = 120]. For stimulus presentation, nordicActiva software was used, and the analysis was performed with nordicBrainEx (both provided by NordicNeuroLab, Bergen).

To identify the brain areas involved in language function, we examined AB during simple line drawings (the patient was asked to silently name each picture) and a letter fluency task (the patient was asked to generate, without articulation, as many nouns beginning with the presented letter as possible) and made comparisons relative to fixation. These paradigms are commonly used for preoperative diagnosis and research for verbal functions tests, and most authors conclude that functional imaging based on these paradigms are highly correlated with intraoperative cortical stimulation mapping and invasive methods such as the Wada Test [20]. In our case, the comparison revealed a strongly right-lateralized fronto-temporal network in which Broca's and Wernicke's areas could be easily distinguished (Fig. 1B and C).

To identify activations more specific to reading words, we showed real words (nouns, adjectives, and verbs) as well as a string of crosses covering the area on the screen, similar to the word presentation, and compared the results. Bilateral posterior occipito-temporal regions were specifically activated when reading words and the activation was more dispersed in the left hemisphere (Fig. 1D). Importantly, an increased BOLD signal was observed in posterior parts of both fusiform gyri.

3. Discussion

The presented case is a rare example of pure alexia associated with damage to the right fusiform gyrus. Although the patient was strongly right-handed and there was no history of left-handedness in his family, functional neuroimaging revealed right hemisphere lateralization for language, which can take place in roughly 4% of strong right-handers, as Knecht and colleagues [21] found in their study of a healthy population. The localization of the VWFA (which supports rapid recognition of letter strings preceding phonological and lexical decoding) in the right fusiform gyrus was most likely a consequence of this variant of functional organization of the brain. As the determination of laterality is one of the most important issues in clinical practice, these data emphasize the complexity of this problem.

It has been shown in children, after surgical deafferentation of the left VWFA, that the right fusiform gyrus may become the primary word-responsive area and serve as a basis for developing normal reading skills [22]. It is likely that in our case the improvement in reading ability, and more specifically the development of the letter-by-letter strategy, was associated with the recruitment of homologous areas in the left hemisphere, which served as a supplementary network for decoding written words. A similar pattern of activation was shown previously for the right VWFA in a patient with pure alexia after an infarct involving the left fusiform gyrus [23]. Pyun and colleagues [24] argued that a critical factor in the interhemispheric shift of reading function during recovery from brain damage was intact white matter connectivity between both cortical areas. In our patient, the lesion was relatively small and white matter tracts linking both hemispheres were spared. However, as Seghier et al. [25] suggested, an alternative pathway (including the superior temporal sulcus) for rapid word processing may exist that does not use the ventral occipito-temporal network in either hemisphere. Moreover, complete recovery of reading is not necessarily accompanied by a re-shift to the dominant hemisphere [26]. It is also likely that, after the brain injury, neural networks responsible for reading are shaped based on structural factors (the lesion site and volume) as well as dynamic aspects of the disease. Thus, some functional reorganization may be present, e.g. during the process of tumor growth, which may explain certain differences between the neural reorganization in diseases with gradual and sudden onsets. For example, Tsapkini [27] observed additional activation in anterior temporal areas bilaterally during reading in a patient after surgery for a tumor located in the left fusiform gyrus.

Two other hypotheses may explain the functional imaging results observed in our patient. First, it is possible that given the atypical functional organization of his cortex, both fusiform gyri were premorbidly engaged in reading with the right hemisphere having a dominant role. This pattern of bihemispheric activation was observed in healthy individuals [27]. Second, as overactivation of the intact hemisphere is a well-known compensatory mechanism early after unilateral stroke [28–30], the BOLD response in AB's occipito-temporal regions may have been caused by a disruption in the balance of interhemispheric inhibition with ambiguous functional meaning.

This case also supports other observations [31] that the word-length effect does not reflect only a limited visual span resulting from a visual field defect; rather, it is associated with a disturbed processing of letter strings within the VWFA. However, hemianopia is a common coexisting symptom in individuals with pure alexia. This overlap is probably due to the anatomy of the posterior cerebral artery and its branches, which supply this region of the brain and make it very unlikely that an isolated infarct would be limited to the posterior part of the fusiform gyrus [8]. Sheldon et al. [32] calculated that, in patients with reduced reading efficiency after posterior lesions, a word-length effect of up to 160 ms per letter can be explained by complete hemianopia (either right or left-sided) involving the central part of the visual field. As our patient's visual field was normal and the word-length effect was minimal or none in individuals with full field vision [32], we believe that the word-length effect observed in his reading (mean 192 ms per letter) can be attributed mainly to his alexia.

In conclusion, this case provides evidence that the VWFA may be situated in the right fusiform gyrus in individuals with right hemisphere dominance for language. Damage to this area may cause severe pure alexia, as observed in patients with left hemisphere language regulation. During recovery, homologous areas in the intact hemisphere can be recruited, most likely to compensate for impaired reading skills.

Conflict of interest

None declared.

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None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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