

The pathophysiology of letter-by-letter reading

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Abstract

Pure alexia is a frequent and incapacitating consequence of left occipitotemporal lesions. It is thought to result from the disruption or the disconnection of the visual word form area (VWFA), a region reproducibly located within the left occipito-temporal sulcus, and encoding the abstract identity of strings of visual letters. Alexic patients often retain effective single letter recognition abilities, and develop an effortful letter-by-letter reading strategy which is the basis of most rehabilitation techniques. We study a patient who developed letter-by-letter reading following the surgical removal of left occipito-temporal regions. Using anatomical and functional MRI in the patient and in normal controls, we show that alexia resulted from the deafferentation of left fusiform cortex, and we analyze the network of brain regions subtending letter-by-letter reading. We propose that during letter-by-letter reading (1) letters are identified in the intact right-hemispheric visual system, with a central role for the region symmetrical to the VWFA; (2) letters are serially transferred to the left hemisphere through the intact segment of the corpus callosum; (3) word identity is eventually recovered in the left hemisphere through verbal working memory processes involving inferior frontal and supramarginal cortex.

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1. Introduction

Pure alexia is a frequent and incapacitating consequence of left occipito-temporal lesions (Binder & Mohr, 1992; Damasio & Damasio, 1983). Affected patients suddenly lose expert reading abilities that they have acquired through years of academic training. At the same time, speech comprehension and production, as well as word spelling, are preserved. The essence of this lost perceptual skill is (1) letter identification invariant for position, size, font, and case; and (2) the fast and parallel identification of arrays of several letters (Dehaene et al., 2001; McCandliss, Cohen, & Dehaene, 2003). It is not before the age of 10 that children show the adult reading pattern (Aghababian & Nazir, 2000), i.e. short word reading latencies that are independent of word length, at least within a range of about three to seven letters and in optimal display conditions (Lavidor, Ellis, Shillcock, & Bland, 2001; Weekes, 1997). In severe cases, known as global alexia, patients cannot access abstract letter identity

(Miozzo & Caramazza, 1998), and are unable to name even single letters (Dejerine, 1892). More often, alexic patients keep effective letter recognition abilities and develop an effortful letter-by-letter reading strategy, which is the basis of most rehabilitation techniques (Greenwald & Gonzalez Rothi, 1998). Eventually, this procedure may become quite effective, although it remains easily detectable in the excessive effect of word length on reading latencies (Behrmann, Black, & Bub, 1990).

A variety of questions and hypotheses have been put forward concerning letter-by-letter reading (for selected references see Montant & Behrmann, 2000). Does it reflect the partial preservation of normal premorbid processes (Behrmann, Plaut, & Nelson, 1998), or is it based on novel strategies (Speedie, Rothi, Heilman, 1982)? Is it based on residual left-hemispheric (LH) or on compensatory right-hemispheric (RH) mechanisms (Coslett & Saffran, 1998)? Does it reveal a general impairment in processing simultaneous visual objects (Farah & Wallace, 1991) or complex displays (Montant & Behrmann, 2000), or is it specific to reading? Such issues may be clarified by referring to a simple model of the visual stages of reading (McCandliss et al., 2003). Letters displayed in one hemifield are first an-

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alyzed through a cascade of contralateral retinotopic areas, which compute increasingly abstract representations. Eventually, a representation of letter identities is created in the visual word form area (VWFA), reproducibly located within the left occipito-temporal sulcus, at about TC -42 , -63 , -15 (Cohen et al., 2003). This representation is invariant for parameters such as size, position, case, font. The transfer of visual information from lower-order retinotopic cortices to the VWFA takes place within the left hemisphere for stimuli displayed in the right visual field (RVF). For left visual field (LVF) stimuli, information is conveyed through inter-hemispheric fiber tracts that course in the splenium of the corpus callosum and over the posterior horns of the lateral ventricles (Binder & Mohr, 1992; Molko et al., 2002). The VWFA then projects to structures involved in phonological or lexico-semantic processing.

In this framework, pure alexia is thought to result either from the disruption of the VWFA itself, or from impaired projections to or from this system. We recently showed that the critical lesion for pure alexia overlaps accurately with the VWFA, as identified by its activation during normal reading (Cohen et al., 2003). In this study, functional imaging data were obtained in a patient with typical letter-by-letter reading (patient F.). We observed that the intact right-hemispheric cortex symmetrical to the VWFA, which we labeled the R-VWFA, showed a pattern of activation normally specific to the VWFA itself, i.e. stronger activation for alphabetic strings than for chequeboards. Moreover, there were abnormally strong activations in a left frontoparietal network related to verbal working memory. This pattern supported the idea that in letter-by-letter reading, (1) alphabetic symbols are identified in the R-VWFA, (2) they are serially transferred to the left hemisphere, and (3) word identity is recovered by the left hemisphere through an effortful verbal working memory process. Note that this construal is in line with a classical account of letter-by-letter reading (e.g. Binder & Mohr, 1992; Speedie et al., 1982).

Patient F.'s lesion spared the dorsal bank of the calcarine sulcus, and accordingly the lower right visual quadrant was intact. As we found some residual activations at coordinates close to those of the VWFA, it could not be excluded that a partially spared left-hemispheric pathway leading from V1 to the VWFA could contribute, or even be essential, to letter-by-letter reading. Here we study a young patient (C.Z.) who presented letter-by-letter reading following the surgical resection of left occipito-temporal structures, sparing the VWFA but including the entire primary visual cortex and all fiber tracts leading to the VWFA from both the right and the left visual fields.

Our aims were to assess the account of letter-by-letter reading summarized before, and to fully document a case of pure alexia due to deafferentation of an intact VWFA. Finally, the complete surgical removal of left posterior regions, as opposed to patchy lesions following infarcts, may help to delimit the role of residual left hemispheric structures in letter-by-letter reading.

2. Medical history and lesion description

Patient C.Z. was a 19-year-old student, 100% right-handed according to the Edinburgh inventory (Oldfield, 1971). She was operated twice for the complete resection of a left occipital neuroectodermal tumor, revealed by intracranial hypertension and right hemianopia. Surgery was followed by radiotherapy and chemotherapy. The present study was carried out between 6 and 12 months after the surgery. There was no indication of relapse on close clinical and radiological follow-up. Following the intervention, the patient complained of being unable to read, while she could write normally. Her family also reported substantial memory difficulties.

The anatomical MRI showed that the left occipital lobe had been removed, including the entire striate cortex and the left half of the splenium of the corpus callosum (Fig. 1). The most anterior part of the lateral occipital cortex was spared. The excision extended to the ventral and mesial temporal lobe, as well as to the underlying white matter, reaching TC $y = -40$ anteriorly. In the temporal lobe, the lesion affected the hippocampal and parahippocampal gyri, and stopped at the mesial edge of the fusiform gyrus.

3. Behavioural assessment

3.1. General data

Goldmann perimetry showed complete right hemianopia without sparing of the macula. There was a marked memory impairment, in the verbal more than in the visual domain: with the Wechsler Memory Scale Revised, she scored 9/50 (-2.4σ) and 0/50 on the immediate and delayed verbal memory tests; and 36/41 ($+0.5 \sigma$) and 23/41 (-1σ) on the immediate and delayed visual memory tests. Tests for color naming and object-color matching, as well as Benton's face matching test were performed flawlessly. Oral language production, comprehension, and repetition were normal. There were minimal word-finding difficulties (91/100 correct on the DENO 100 picture-naming test). C.Z. was asked to write to dictation a list of 36 frequent words (three to nine letters and one to four syllables in length), and to identify another set of 36 similar words orally spelled-out by the examiner. She was flawless in the dictation test. She made 2/36 errors in the word identification test, proposing responses close to the target (e.g. MUSIQUE \rightarrow Munich).

3.2. Reading

The patient was asked to read aloud a short story of about 15 lines. She made essentially no errors (pâte \rightarrow pâté), but it took her more than 11 min to complete this task, while normal subjects need on average 35 s (Cohen et al., 2003).

Six months after surgery, C.Z. was presented with 79 lower-case familiar nouns, three to nine letters and one to

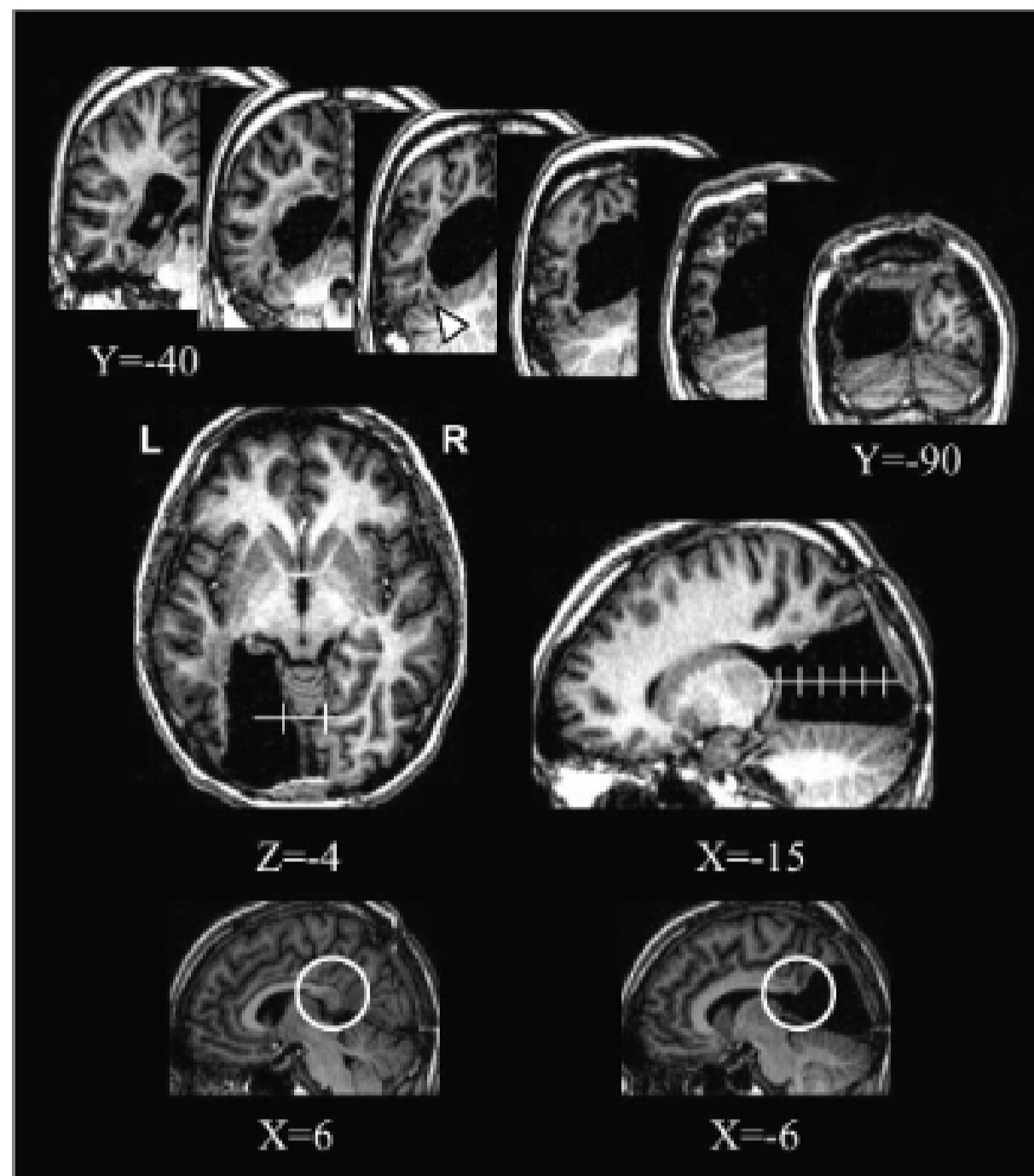


Fig. 1. Normalized T1-weighted MRI of patient C.Z., showing the surgical resection of most of the left occipital lobe including the left half of the splenium, the posterior hemispheric white matter, the hippocampal and parahippocampal gyri. The white arrowhead points to the spared mid-fusiform cortex.

four syllables in length. Stimuli were presented centrally on a computer screen, subtending a maximum angle of 4° on each side of fixation, using the Courier New font. Stimuli remained visible until a response was produced. Latencies were measured using a voice key. C.Z. was asked to read each word aloud as rapidly as she could, while minimizing errors. She made no errors, but her mean reading time was 8196 ms (excluding 2 outliers beyond 20 s), and was strongly correlated with word length (Fig. 2), with a slope of 1181 ms per letter ($r(5 \text{ d.f.}) = 0.94$; $P < 0.002$). Five months later, at about the time of the imaging experiment, her speed had improved, as reading the short text took her 7 min, while the slope of the word length effect had diminished to 431 ms per letter.

All upper- and lower-case letters were presented randomly using the same technique. C.Z. made no error out of 52 trials, but was significantly slowed down (mean reading time = 1964 ms, excluding one outlier at 12 s). In order to assess her mental imagery for letters, the patient was orally presented with the name of all letters, and was asked to decide whether the upper-case letter included a curve or not. She made no error. In a similar task, she was asked to decide

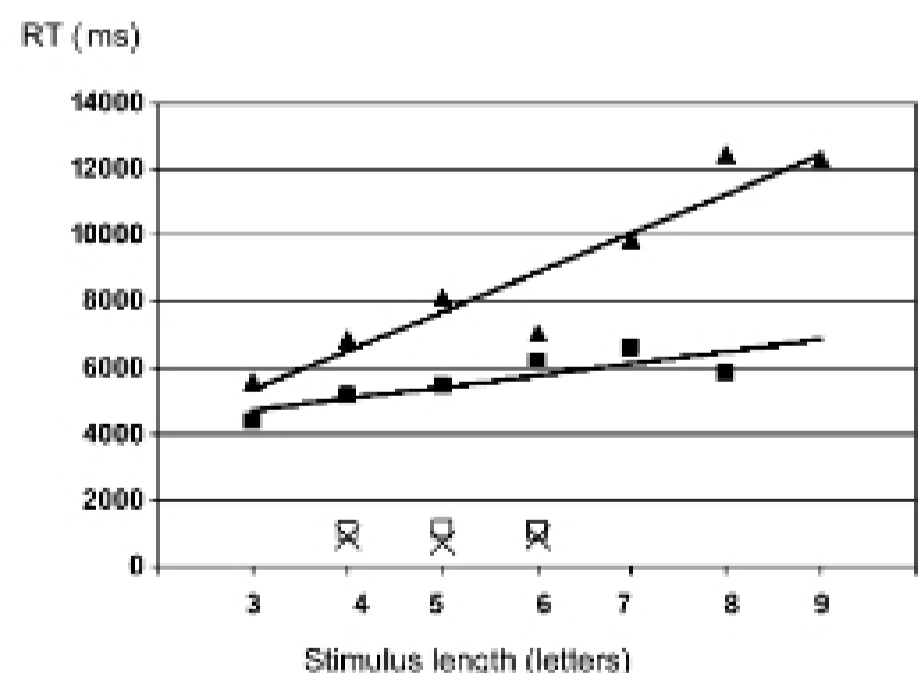


Fig. 2. Patient C.Z.'s correct response latencies in the initial word reading test (triangles), in word reading at the time of the imaging experiment (solid squares), and in lexical decision (real words: crosses; consonant strings: open squares). She showed a letter-by-letter reading pattern, with a slope of 1181 ms per letter. In contrast, she could discriminate real words from consonant strings rapidly and with no effect of length.