Brain & Language xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Brain & Language

journal homepage: www.elsevier.com/locate/b&l

Covert reading of letters in a case of global alexia

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ARTICLE INFO

Article history:
Accepted 24 December 2011
Available online xxxx

We would like to dedicate this work to the memory of Lamberto Piron

Keywords:
Global alexia
Abstract letter identification
Right hemisphere contribution to word reading

ABSTRACT

This study describes the case of a global alexic patient with a severe reading deficit affecting words, letters and Arabic numbers, following a left posterior lesion. The patient (VA) could not match spoken letters to their graphic form. A preserved ability to recognize shape and canonical orientation of letters indicates intact access to the representation of letters and numbers as visual objects. A relatively preserved ability to match lowercase to uppercase letters suggests partially spared access to abstract letter identities independently of their visual forms. The patient was also unable to match spoken letters and numbers to their visual form, indicating that she could not access the graphemic representations of letters from their phonological representations. This pattern of performance suggests that the link between graphemic and phonological representations is disrupted in this patient. We hypothesize that VA' residual reading abilities are supported by the right hemisphere.

1. Introduction

Pure deficits of reading are the result of the isolation of left-hemisphere language mechanisms from visual input (Dejerine, 1892). These conditions arise from damage to posterior portions of the left hemisphere disrupting the transmission of visual information to the areas that mediate word recognition. The most severe reading disorder, known as ''Global Alexia'' (Binder & Mohr, 1992; Coslett & Saffran, 1989, 1992; Dejerine, 1892; Larsen, Baynes, & Swick, 2004; Miozzo & Caramazza, 1998; Mycroft, Hanley, & Kay, 2002) is characterized by the complete inability to read letters silently or out loud in pre-morbidly literate subjects. This pattern contrasts with the more frequent case in which patients have preserved letter identification abilities and develop a compensatory, effortful letter-by-letter reading strategy (Patterson & Kay, 1982).

One of the most detailed descriptions of global alexia, which provides information about the stages during the reading process prior to letter identification, has been reported by Miozzo and Caramazza (1998). The patient (GV) showed a severe selective deficit in reading letters, words, and numerals, following a left posterior brain lesion. While GV had intact visual processing abilities and could recognize the correct shape and orientation of letters, he could not access case-independent letter identities: he was unable to correctly determine whether a pair of letters written in different cases (uppercase and lowercase) had the same name (e.g., ''a'', ''A''). Based on GV's pattern of performance, Miozzo and Caramazza (1998) concluded that this patient's form of alexia resulted from a failure to access the abstract graphemic representations of letters and words from normally processed visual input. Chanoine et al. (1998) also reported the case of a patient (CN), affected by optic aphasia who resorted to letter by letter reading. CN could discriminate between real and pseudo letters, but was unable to categorize letters shown in different fonts as representing the same grapheme (e.g., G, C, g, t). In essence, CN and GV showed an identical functional pattern: they could access lower level visual information about letters (such as letter shapes and orientations) but could not access more abstract alphabetical representations from visual input. These findings suggest that two preliminary stages are required before accessing abstract letter representations in the orthographic input lexicon. The first stage specifies the shapes, sizes and orientations of letters. The second stage specifies the abstract letter identity or the grapheme for each individual letter shape in the letter string, independently of their font and case specific details (e.g., A, a, *A*, *a*) (Chanoine et al., 1998; Finkbeiner, Almeida, & Caramazza, 2006; Miozzo & Caramazza, 1998).

More recently, Larsen et al. (2004) investigated the reading abilities of a global alexic patient (EA) to examine the contribution of the right hemisphere in reading. EA could not access a word's phonology from visual input, nor could she overtly name letters; however, she performed above chance in lexical and semantic decision tasks showing an advantage for concrete versus abstract words. Based on her ability to access lexical and semantic information without contacting phonological representations, the authors

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doi:10.1016/j.bandl.2011.12.014

proposed that EA's implicit reading was supported by an intact right hemisphere, rather than by spared left hemisphere regions (Behrmann, Nelson, & Sekuler, 1998).

The hypothesis that the right hemisphere has a role in reading is based on data from both brain damaged patients and healthy individuals. Coslett and Saffran (1989, 1992, 1994) reported on patients CB and EM, who, like patient GV (Miozzo & Caramazza, 1998), were severely impaired in their ability to read stimuli explicitly, but could nonetheless perform lexical decision and semantic categorization tasks on the same stimuli. Another clear indication of right hemisphere involvement in the reading performance of pure alexics comes from Coslett and Monsul (1994) who transiently disrupted the residual reading abilities of a pure alexic patient by means of transcranial magnetic stimulation (TMS) on the right temporo-parietal area. More recently, in an fMRI study Cohen et al. (2003) found that, in normal subjects, alphabetic stimuli activated a bilateral and symmetrical brain network. However, only the left hemisphere showed a preference for alphabetic strings over simple chequerboards, whereas the right hemisphere reacted identically to both alphabetic and non-alphabetic stimuli. Cohen et al., 2004 reported the case of a patient who, 6 months after the surgical removal of the left occipito-temporal regions, showed a selective fMRI activation of the right fusiform gyrus to letter strings. The aforementioned findings strongly suggest that both hemispheres are equally capable of processing letter shapes and identifying abstract letter identities in the orthographic input lexicon, but only the LH can process the phonological features of words (Finkbeiner et al., 2006; Saffran & Coslett, 1998).

In the present study we report on the reading performance of a patient (VA) with global alexia following a left posterior lesion. VA was severely impaired in reading letters, words and Arabic numbers, as well as in naming pictures, but she could recognize the correct shape and canonical orientation of letters, indicating intact access to the representation of letters and numbers as visual objects with particular features. These findings resemble to a large extent the pattern described in the previously reported cases of global alexia (Larsen et al., 2004; Miozzo & Caramazza, 1998). Unlike the previous cases in the literature, however, VA showed a better-than-chance ability in matching lowercase to uppercase letters, suggesting that she had at least partially spared access to abstract letter identities independent of their visual forms. To our knowledge, there is only one other similar case (MS) reported in the literature, described by Mycroft, Hanley, and Kay (2002). MS could not read words aloud but could say that a letter was correctly oriented, and was above chance in a cross-case matching task of visually presented letters. The authors concluded that MS's reading problem reflected a difficulty at the level of letter name retrieval, stemming from a disconnection between a preserved abstract representation for letters and the representation of their names in the output lexicon.

Alternative interpretations to the ones offered by these authors will be discussed in light of the present case.

2. Case report

VA was a 69-year-old, right handed, housewife with 5 years of formal education. She suffered an ischemic lesion in the left posterior areas of the brain. An MRI (June 2007) showed damage in the left medial and lateral temporal lobe, the calcarine regions, the parahippocampal and posterior fusiform gyri, the posterior hippocampal regions, the posterolateral thalamus and the left hemisplenium of the corpus callosum. Moreover, the left frontal and parietal lobesshowed signs of atrophy. No focal lesions appeared in the right hemisphere (Fig. 1).

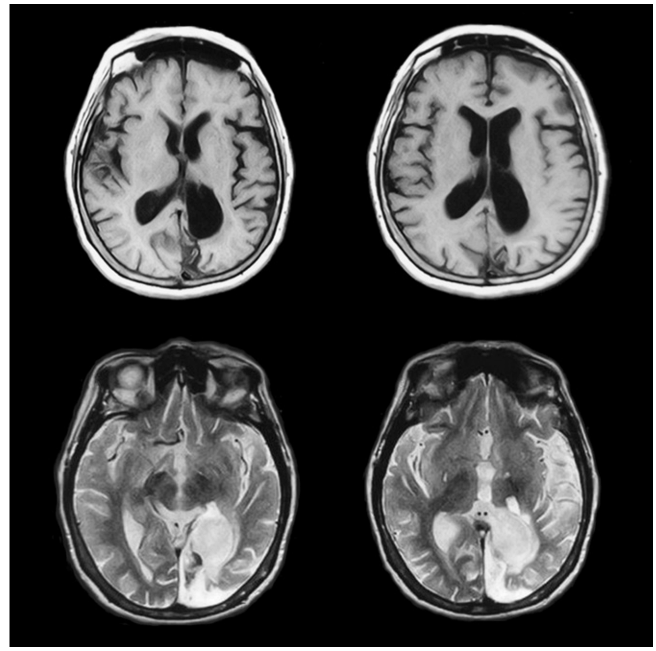

Fig. 1. Magnetic resonance images.

The neurological examination showed a right homonymous hemianopia and a mild right hemiparesis. There were no perceptual deficits and no signs of unilateral visuospatial neglect. At the time of testing VA was fully oriented and showed no signs of cognitive deterioration. She was mildly depressed, and was aware of her illness.

The patient was submitted to a comprehensive neuropsychological assessment and, for the special purpose of this study, to an exhaustive evaluation of her reading abilities. Permission for the study was obtained from the local research ethics committee and the patient consented to participate.

3. Neuropsychological assessment

Table 1 summarizes VA's neuropsychological assessment scores. Each task is described in more detail below.

3.1. Visual object processing

VA's visual-perceptual abilities were investigated in a series of tasks requiring fine-grained discrimination of perceptual features. These tasks revealed that VA's visual-perceptual object representation and processing abilities were intact.

3.1.1. Visuo-perceptual tests

VA's visuo-perceptual abilities were evaluated with a subset of tests from the Birmingham Object Recognition Battery (Riddoch & Humphreys, 1993). The tasks required discrimination of line length, size of squares, and position of small gaps in circles. Discrimination of line orientation was evaluated with the Benton Judgment of Line Orientation Test (Benton, Hamsher, Varney, & Spreen, 1983). VA's performance on all tasks did not differ from normative data.

3.1.2. Object recognition from different views

Access to the mental representation of familiar objects was evaluated with the Matching Objects from Different Views from the Birmingham Object Recognition Battery (Riddoch & Humphreys, 1993). This task requires recognizing the same object from different perspectives. VA's accuracy did not differ from normative data.

Table 1
Neuropsychological assessment.

Test	Score
Intelligence	
Raven colored progressive matrices	19/36 (cut-off = 18.96)
Visual object processing	
Length match task	27/30 (cut-off = 24)
Size match task	27/30 (cut-off = 23)
Position of gap match task	35/40 (cut-off = 27)
Benton orientation match task	21/30 (cut-off = 11)
Matching objects from different views	20/25 (cut-off = 19)
Attention	
Alertness with no warning	Reaction time = 544 (219)[a] (T scores = 26)
Alertness with no warning	Reaction time = 325 (59)[a] (T scores = 37)
Go no go	Reaction Time = 678 (185)[a] (T scores = 36)
Posner paradigm:	
Valid condition	Reaction Time = 1016 (501)[a] (T scores > 20)
No/valid condition:	Reaction Time = 1191 (585)[a] (T scores > 20)
Memory	
Digit span forward	4 (cut-off = 3)
Digit span backward	2[a] (cut-off = 3)
Corsi block test	2 [a] (PE = 2)
Memory prose:	
Immediate recall	11/28 (cut-off = 6)
Delayed recall	0/28[a] (cut-off = 8)
Gesture	
Copy of drawing	2/14[a] (PE = 0)
Ideomotor apraxia	Intransitive gesture:
	Naming = 10/17[a] (cut-off = 14)
	Description = 14/17 (cut-off = 13)
	Cartoons = 4/17[a] (cut-off = 10)
	Pantomime:
	Verbal presentation = 1/18[a] (cut-off = 12)
	Tactile presentation = 2/18[a] (cut-off = 13)
	Visual presentation = 2/18[a] (cut-off = 12)
	Recognition:
	Intransitive gestures = 40/42 (cut-off = 36)
	Pantomimes = 40/42 (cut-off = 36)
	Identification:
	Intransitive gestures = 14/17 (cut-off = 14)
	Pantomimes = 16/18 (cut-off = 14)
Language	
Aachener aphasie test:	
Token test	49[a] (severe deficit)
Written language	0[a] (severe deficit)
Naming	33[a] (severe deficit)
Comprehension	41[a] (moderate deficit)
Repetition	146 (mild deficit)
Semantic verbal fluency	5[a] (PE = 0)
Letter verbal fluency	13[a] (PE = 0)
Picture naming	13/80[a] (cut-off = 76)
Oral definition: naming	10/38[a] (PE = 0)
Semantic knowledge:	
Total score	373/480[a] (cut-off = 453.02)
Perceptual	149 (cut-off = 112.68)
Category	125[a] (cut-off = 149.6)
Associative	101[a] (cut-off = 147)

[a] Impaired performance; *cut-off*: 2 SD below the mean; *T score*: mean (SD) = 50 (10); *ES*: equivalent score, ES = 1 = pathological.

3.2. Attention

The Test for Attentional Performance (Zimmermann, North, & Fimm, 1993) was used to assess attention abilities. This test encompasses three different subtests: Alertness, Go/no go and Posner tests. VA showed delayed reaction times and higher error rates than normative data, suggesting a deficit in attentional control processes.

3.3. Memory

3.3.1. Verbal and spatial short-term memory

VA's score was within normal limits on the Digit Span Forward test (Wechsler, 1998). However, her performance was poor on the Digit Span Backward test (Wechsler, 1998). Her spatial short-term memory was also impaired (Corsi Block Tapping task, Spinnler and Tognoni, 1987).

3.3.2. Long-term memory

To evaluate verbal long-term memory, VA was given the Prose Memory Test (Mondini, Mapelli, Vestri, & Bisiacchi, 2003). She scored within normal limits on immediate recall, but she showed poor performance on delayed recall.

3.4. Gesture

3.4.1. Copying line drawings

VA showed a severe constructional apraxia. She copied correctly only 2/7 simple line drawings from the Spinnler and Tognoni's battery (1987).

3.4.2. Ideomotor apraxia

The presence of limb apraxia was assessed with a battery of tests evaluating the production, recognition and identification of gestures (Bartolo, Drei, Cubelli, & Della Sala, 2008). VA was moderately impaired in producing transitive and intransitive gestures, and pantomimes. Her recognition and identification of intransitive gestures and pantomimes was intact. Thus, VA's performance indicated an ideomotor limb apraxia in the face of preserved knowledge of meaningful actions, at least for intransitive actions.

3.5. Non-verbal intelligence

VA's non-verbal intelligence was evaluated with the Colored Progressive Matrices Test (Raven et al., 1993). She scored within normal limits.

3.6. Language

VA's speech was fluent with occasional paraphasias, perseverations, hesitations, anomias and circumlocutions. Her repetition and auditory comprehension were unimpaired; her picture naming was impaired but it improved almost to ceiling levels on phonemic cueing. VA's oral spelling of words was accurate, but her reading and writing were severely impaired. VA's performance on the AAT (Aachener Aphasie Test, Huber, Poeck, Weniger, & Willmes, 1983) was severely impaired on the Token Test, the Written Language, and the Naming subtest. The score on the Comprehension subtest was moderately pathological. However, the score included both oral and written comprehension. Oral comprehension was normal whereas tests of written comprehension could not be carried out. Her score on the Repetition subtest was mildly compromised. The AAT profile indicated anomic aphasia with severe deficits in reading and writing.

3.6.1. Premorbid reading proficiency

Family members reported that VA was proficient in reading and writing. VA had 5 years of formal education in the Italian national school system, where national standards for reading are required in third grade to pass on to the following grades. The reading tasks used in this study consisted of single word and single letter processing, and were well within the reach of someone with a 5-year elementary school education in the Italian national education system.

3.6.2. Verbal fluency

In verbal fluency tasks (Novelli et al., 1986), the patient was asked to retrieve words belonging to a specific semantic category (e.g., fruit) or beginning with a specific sound/letter (e.g., F) within the span of a minute. VA was impaired on both semantic and phonological tasks.

3.6.3. Picture naming

The patient was given a picture-naming task with 80 nouns taken from eight different semantic categories (fruits, vegetables, animals, body-parts, furniture, vehicles, musical instruments and tools (Laiacona, Barbarotto, Trivelli, & Capitani, 1993). She correctly named only 13/80 pictures. She was equally impaired across all semantic categories. In most cases, VA recognized the picture but failed to retrieve the name. However, when the examiner provided her with a phonemic cue, she named the pictures correctly, indicating intact visual recognition of objects.

3.6.4. Naming on oral definition

In an oral definition naming task (Novelli et al., 1986) VA showed poor performance (10/38 correct).

3.6.5. Color naming

VA named only 2/10 colors from the Aachener Aphasie Test (Huber et al., 1983).

3.7. Semantic knowledge

In this task VA was asked to answer oral questions about a semantic category presented in multiple-choice format (e.g., What is a butterfly? 1. a fruit, 2. an animal, 3. a body part, 4. a tool) and to give the perceptual and associative features of the object named. The same 80 items from the picture-naming test were used (Laiacona et al., 1993). VA was impaired on category and associative levels and unimpaired on perceptual level.

3.8. Summary of neuropsychological assessment

In summary, VA appeared to have preserved visual and object recognition abilities. She was severely anomic, but her naming improved dramatically on phonemic cueing, indicating that her naming deficits were not due to visuo-perceptual deficits. VA's anomia, however, impaired her ability to provide verbal responses. Her other major impairment manifested itself in reading. This is the focus of the experimental investigation reported below.

4. Experimental investigation

We examined VA's letter recognition and processing as well as her reading performance on single words. Stimulus presentation was untimed.

To obtain normative values on these tasks, 10 age- and education-matched individuals without a diagnosis of alexia were administered the tests. Modified *t*-tests to compare a single case to a control sample (Crawford & Howell, 1998) were used to evaluate VA's performance against that of the controls. Table 2 summarizes VA's and controls' performance on the experimental tasks.

4.1. Word processing

Table 2 summarizes the performance of VA and the control sample on word processing tasks. Each task is described in more detail below.

4.1.1. Reading words aloud

We presented VA with a list of 60 high frequency words, one- to three-syllables long. VA was totally unable to read the words. In most cases VA simply stated that she was incapable of reading. Occasionally, instead, she produced words that were neither semantically nor phonemically related to the target.

4.1.2. Pointing to written words on spoken input

In this task, we evaluated whether VA could recognize spoken words among three visually presented uppercase high frequency words (e.g., pointing to CANE, "dog", among: CANE, "dog", MELA, "apple", FAME, "hunger"). VA responded rapidly and intuitively and did not appear to employ a letter-based strategy. Her performance was correct only on 22/36 (61%) of the trials ($t = -13.348$, $p < .001$).

4.1.3. Oral spelling of words

VA was asked to orally spell 102 words spoken by the examiner. VA was accurate in 93/102 (92%) of the trials with some omission errors (e.g.: viso? v/s/o). The tasks also included words containing graphemes that are homophonous with other graphemes (e.g.: /q/uadro, /c/uoco or s/c/uola contain the phoneme /k/ which in Italian may be arbitrary written as q, c, ch, cq). VA never made mistakes substituting the right grapheme with another corresponding to the same sound. On the whole, her performance did not significantly differ from that of the controls.

4.1.4. Aural recognition of orally spelled words

VA was asked to recognize words orally spelled by the examiner. VA was correct only on 22/40 (55%) of the items ($t = -3.777$, $p < .005$) with substitution errors (e.g.: fata? fato).

4.1.5. Writing

VA's agraphia was extremely severe: she was unable to produce any orthographic sign.

4.2. Letter processing

In these tasks, we assessed VA's letter naming on visual, tactile and proprioceptive presentation and letter identification on oral presentation. In addition, we examined VA's access to the structural representations of letters with tasks that required her to identify letter shapes among non-letter shapes and among letters from another alphabet (Aramaic), and to identify letters in canonical and non-canonical orientation. Access to graphemic representations

Table 2
Summary of VA single score and control group mean (standard deviation) score in word tasks.

Task	VA score	Mean controls score (SD)
Reading words aloud	0/60	59.40 (1.90)[a]
Pointing to written words on spoken input	22/36	36 (0.00)
Oral spelling of words	93/102	90 (6.61)
Aural recognition of orally spelled words	22/40	36.50 (3.66)[a]
Writing words	0/20	17.90 (1.66)[a]

[a] VA score statistically different ($p < .05$) from controls.

was assessed with two different versions of a task that required matching uppercase letters to lowercase letters: one version required a verbal response (Posner & Mitchell, 1967), and one required the patient to point to the matching letter (Perri, Bartolomeo, & Silveri, 1996). Additional tasks examined her letter imagery (Table 3).

4.2.1. Letter naming on visual presentation

In several testing sessions, VA was asked to name all the letters of the Italian alphabet printed in uppercase and in lowercase format. She was incapable of correctly naming any letter, in either format. If pressed to respond, her responses were either random or perseverative on occasion, but they were always letter names.

4.2.2. Letter naming on tactile and proprioceptive input

VA was asked to name all the letters of the Italian alphabet in uppercase and in lowercase format with tactile (tracing on the patient's skin) or proprioceptive input (active tracing by the patient). Both sides of the body were probed. She was incapable of naming any letter.

4.2.3. Pointing to a letter on spoken input

VA was asked to point to the letter spoken by the examiner among three visually presented uppercase letters (e.g., point to /b/ among P, B and D). VA performed at chance performing correctly on only 22/42 (52%) of the trials ($t = -29.966$, $p < .001$).

4.2.4. Letter identification among letters, numbers and letters from a different alphabet

VA was asked to point to a spoken target letter choosing from the following three visually presented stimuli: an uppercase letter, a number, and an Aramaic grapheme (e.g., R, ϵ and 6). The characters were chosen to be perceptually similar in size and visual complexity. VA's performance was relatively successful (36/42, 86% correct responses), however, she was significantly worse than the controls ($t = -5.721$, $p < .001$).

4.2.5. Letter identification among letters and numbers

In this task VA was required to decide whether a stimulus was a number or a letter/word. We administered 40 trials, visually presented. Half of the trials consisted of one element (character and digit) (e.g., A, 2,…) and half consisted of two elements (e.g., DI, 34,...). VA was correct on 35/40 trials (88% correct responses). Her score was significantly worse than that of the control group ($t = -4.767$, $p < .001$).

Table 3
Summary of VA single score and control group mean (standard deviation) score in letter tasks.

Task	VA score	Mean controls score (SD)
Letter naming on visual input	0/42	41.90 (0.22)[a]
Letter naming on tactile input	0/42	34.80 (1.03)[a]
Letter naming on proprioceptive input	0/42	37.60 (0.84)[a]
Pointing to letters on spoken input	22/42	41.80 (0.63)[a]
Letter identification among non letter distractors	36/42	42 (0.00)[a]
Letter identification among letters and numbers	35/40	40 (0.00)[a]
Orientation decision	126/126	125.40 (0.80)
Uppercase to lowercase matching	37/42	41.20 (1.93)
Same-different decision	42/84	81.80 (2.74)[a]
Uppercase letter imagery	22/42	40.40 (2.63)[a]
Lowercase letter imagery	18/42	41.40 (1.90)[a]

[a] VA score statistically different ($p < .05$) from controls.

4.2.6. Orientation decision

In the orientation task (Cooper & Shepard, 1973), VA was asked to discriminate among normally oriented, rotated and mirror-reflected letters (e.g., R R Я). There were 42 uppercase, 42 lowercase, and 42 cursive letters. Each trial consisted of three letters, one in canonical and two in non-canonical orientation. VA performed flawlessly (126/126), and showed no hesitation in picking out the normally oriented letter.

4.2.7. Uppercase to lowercase matching

In this task (Perri et al., 1996) each trial contained an uppercase letter along with three lowercase letters, one of which was the same letter as the uppercase letter (e.g., A and e–a–c). VA was asked to point to the lowercase letter that matched the uppercase letter. All the letters of the Italian alphabet were presented twice, in random order, in two testing sessions on separate days. Each lowercase target was presented along with two foils: a perceptual foil and a phonological foil. The perceptual foils were chosen to be the most perceptually similar letters to the target, based on the similarity measures published in Boles and Clifford (1989). The phonological foil for consonant graphemes was a consonant from the same natural class (e.g., liquids, voiced stops). Phonological foils for target vowel graphemes were vowels with the same value on the front/back dimension. VA scored 37/42 (88%) correct on this task. Healthy controls on average scored 41.2/42 (98%) correct, but this difference was not statistically significant ($t = -2.750$, $p > .05$). In the first session VA made errors on Q and N; in the second session she made errors on Q, E and B. VA made errors both on letters with high similarity values (e.g., N ? m) and low similarity values (Q ? p). In each case, VA selected a foil with a lower perceptual similarity value than the target.

4.2.8. Same-different letter

This task was modeled on Posner and Mitchell (1967) (see also Miozzo & Caramazza, 1998). VA was presented with 84 pairs of letters, each consisting of one lowercase and one uppercase letter. On half of the trials the two letters were the same (e.g., A–a), on the other half of the trials they were different (e.g., A–e). VA was asked to answer "same" when the two letters were the same and "different when the two letters were different. VA answered "same" on all trials. This particular test was repeated on several occasions; however the patient's response pattern never changed.

4.2.9. Letter imagery

VA was first asked to recall from memory whether letters spoken by the examiner contained any curved lines in their uppercase format (Bartolomeo, Bachoud-Lévi, Chokron, & Degos, 2002). She was then asked to recall from memory whether letters in their lower case format contained an ascender (e.g., b), a descender (e.g., g) or neither (e.g., m). All of the letters of the Italian alphabet were presented twice, over two testing sessions. VA performed at chance (40/84, 48% correct responses).

4.3. Number processing (Table 4)

4.3.1. Counting

This ability was preserved.

4.3.2. Number repetition

One-, two-, three-, four- and five-digits numbers were used. VA was correct on 49/55 (89%) of the trials ($t = -5.721$, $p < .001$) with substitution errors (e.g.: 4655? 4635).

4.3.3. Writing of numbers

VA was incapable of writing numbers in any format.

Table 4
Summary of VA single score and control group mean (standard deviation) score in number tasks.

Task	VA score	Mean controls score (SD)
Counting	60/60	60 (0.00)
Repetition	49/55	55 (0.00)[a]
Writing	0/55	53 (2.94)[a]
Magnitude judgment (Arabic numbers)	14/16	16 /0.00)
Mental calculation		
Additions	10/30	30 (0.00)[a]
Subtractions	4/20	20 (0.00)[a]
Multiplications	1/15	15 (0.00)[a]
Parsing orally spoken complex numbers into single digits	28/35	32.80 (3.61)
Recognizing whole numbers from individually spelled single digits	23/35	32.90 (3.18)[a]
Naming	2/55	53 (2.94)[a]
Pointing to Arabic digits on spoken input	32/40	40 (0.00)[a]
Pointing across category	38/42	42 (0.00)[a]
Orientation decision	42/42	42 (0.00)
Imagery	24/40	40 (0.00)[a]

[a] VA score statistically different ($p < .05$) from controls.

4.3.4. Number magnitude judgment

VA was asked to judge which of two visually presented Arabic numbers was larger. Numbers were up to five digits long. She was correct on 14/16 (88%) of the trials and her performance did not statistically differ from the controls.

4.3.5. Mental calculation

In this task VA was orally asked to mentally perform 30 additions, 20 subtractions and 15 multiplications involving numbers with one or two digits. She provided the correct answer to only 10/30 (33%) additions ($t = -19.069$, $p < .001$), 4/20 (20%) subtractions ($t = -15.255$, $p < .001$) and 1/15 (7%) multiplications ($t = -13.248$, $p < .001$).

4.3.6. Parsing orally spoken complex numbers into single digits

VA was asked to sound out loud each digit in a complex number spoken by the examiner (e.g.: stimulus "thirty-two", response "three, two"). Numbers were up to four digits long. VA was accurate on 28/35 (80%) of the trials and her score did not statistically differ from the control group. She committed some substitution errors (e.g.: 5429? 5–4–9–0).

4.3.7. Recognizing whole numbers from individually spelled single digits

A list of 35 two, three and four digit numbers was used to test VA's ability to recognize numbers individually spelled by the examiner. In this task VA performed correctly on 23/35 (66%) items and her score was significantly different from healthy participants ($t = -2.968$, $p < .05$). She performed worse on three- and four-digit numbers, with omission errors (e.g.: 1–4–4 = 44).

4.3.8. Naming Arabic numbers

VA was asked to name a list of 55 one, two, three, four and five digit numbers. She was able to correctly name only 2/55 (<1%) one digit numbers ($t = -16.540$, $p < .001$). If pressed to respond, her responses were at random. She occasionally perseverated.

4.3.9. Pointing to Arabic digits on spoken input

In this task VA was asked to indicate the number named by the examiner choosing from three visually presented numbers (e.g., pointing to number 3 among 4, 9 and 3). Although her score was significantly worse than that of the control sample ($t = -7.628$, $p < .001$), VA responded correctly on 32/40 (80%) trials.

4.3.10. Number identification among letters, numbers and letters from a different alphabet

In this task VA was asked to point to the number named by the examiner choosing from three visually presented stimuli: an uppercase letter, a number, and an Aramaic grapheme (e.g., pointing to the number, among G, ϵ and 6). VA performed correctly on 38/42 (90%) trials, but her score was statistically lower than that of the controls ($t = -3.814$, $p < .004$).

4.3.11. Orientation decision

This task required VA to discriminate between normally oriented, rotated and mirror-reflected numbers (e.g., 2 ~ ƨ). VA performed flawlessly.

4.3.12. Imagery

VA was asked to remember whether numbers named by the examiner contained any curved lines. She answered at chance (24/40, 60% correct responses) ($t = -15.255$, $p < .005$).

5. Discussion

VA's case fits the definition of "global alexia" (Binder & Mohr, 1992) as the patient she was incapable of reading aloud single letters or digits. VA showed no evidence of a low-level perceptual deficit that could account for her reading problem. In fact, her performance on a battery of tests requiring object recognition and more fine-grained perceptual processing was within the normal range. VA's oral spelling of words was relatively accurate, suggesting that, while her reading and writing were severely impaired, she had spared access to the orthographic structure of words. VA also exhibited severe anomia, and other non-linguistic disturbances (i.e., apraxia), but, again, none of these deficits can account for her reading impairment.

In contrast with her inability to read letters and words (as well as Arabic numbers) and to match spoken letters (and, to a lesser degree, numbers) to their graphic form, VA could: (a) recognize a letter shape among numbers and unfamiliar graphemes; (b) recognize the canonical orientation of letters and numbers; (c) match lowercase to uppercase letters when the task did not require an overt verbal response. Her performance suggests an intact ability to process letter shapes and orientations, and, importantly, sufficiently preserved access to abstract letter identities to allow her to categorize letters shown in different fonts (R with r) as representing the same grapheme (e.g., the grapheme ⟨r⟩).

A similar case (MS) was described by Mycroft et al. (2002). MS performed well on cross-case matching despite being unable to name letters. MS and VA thus provide an interesting dissociation with the global alexic patients described by Miozzo and Caramazza (GV) (1998) and Larsen, Baynes, and Swick (EA) (2004). Although all four patients recognized correct letter shape and orientation, MS and VA, unlike GV and EA, could also match visually distinct (uppercase and lowercase) graphemes representing an identical abstract letter.

Mycroft et al. (2002) proposed that MS suffered from a disconnection between preserved abstract letter representations and the representation of their names in the output lexicon (e.g., "t" ? /ti/), resulting in a deficit in letter name retrieval specific to the visual modality. Another possibility, which we favor, is that the deficit in letter naming results from a disconnection between the grapheme and the representation of the corresponding spoken form (the phoneme /t/).

Despite her relatively preserved access to grapheme identity, VA could not use grapheme-to-phoneme correspondence rules to translate graphemic input into its corresponding phonological code. VA's inability to link graphemes to phonemes appears to be bi-directional. VA could not match spoken letters and numbers to their visual form (the same finding holds for patient MS, but the implications of this finding are not further elaborated on). Importantly for our purposes, VA exhibits a disconnection between orthography and phonology (Bowers, Arguin, & Bub, 1996). The phonological representation is not accessible from the graphemic stage, and, in turn, the visual form cannot be accessed from the phonological representation.

VA's relative success at the uppercase to lowercase matching task when the response requires pointing among alternatives is in contrast to her severe problems with the version of the task, used in Miozzo and Caramazza (1998), requiring an overt verbal response. One possibility is that task demands account for this difference. VA, like GV was incapable of matching uppercase to lowercase letters in a task requiring her to say whether two letters were the same or different. Note that, unlike GV, who performed just above chance, VA answered "same" on all trials across several sessions. This behavior is in all likelihood due to a verbal perseveration pattern known as 'recurrent' perseveration. Recurrent perseveration consists of the repetition of a previously produced response when processing a series of consecutive stimuli. This type of perseveration has been often reported in aphasic patients (Papagno & Basso, 1996) and has been interpreted by Cohen and Dehaene (1998) as an effect of the disconnection between the left hemisphere from the right hemisphere input. In VA, verbal perseverations could reflect the persistent activity determined by previous trials in the (damaged) left-hemisphere verbal system which, failing to receive adequate stimulus information from the right hemisphere, keeps repeating a previous response.

One possibility is that VA's accurate performance on the cross-case matching task is due in part to the visual similarity between upper case and lower case letters. Using Boles' and Clifford's (1989) measures of perceptual similarity between letters, we found that VA performed correctly both in cases where the uppercase and lowercase letters were similar and in cases where the uppercase and lowercase letters were dissimilar. Conversely, her few errors occurred on both perceptually similar and dissimilar letters. Importantly, her errors consisted invariably in choosing a less perceptually similar letter, suggesting that VA was not using perceptual similarity as a strategy to perform the task. VA's performance on the upper-to-lower matching task is thus unlikely to be due to the perceptual similarity between uppercase and lowercase letters. It may seem somewhat paradoxical that the patient was at random when asked to point to a letter on spoken input, but was way above chance when asked to point written words. Although the tasks differ in a number of ways, this may reflect some lexical/semantic strategy available for "implicit reading" of meaningful words only.

With respect to the anatomical substrate of the representation of abstract letter identities, invariant for spatial location, case and font, a bihemispheric model of letter recognition has been proposed by Epelbaum et al. (2008). In this model, inspired by Dehaene, Cohen, Sigman, and Vinckier (2005), an invariant representation of letter strings is computed in the Visual Word Form Area (VWFA) lying in the left occipito-temporal sulcus (see also Cohen et al., 2000, 2002, 2003; Cohen & Dehaene, 2004; Dehaene et al., 2001, 2002; Henry et al., 2005; Polk & Farah, 2002). There is also evidence for the existence of a homologous area in the right hemisphere supporting abstract letter identification, albeit with large individual variability in normal subjects. Cohen et al. (2002) found right VWFA activation for alphabetic stimuli in two out of seven subjects (although this activation was always weaker than in the VWFA proper).

The role of the right hemisphere (RH) in the early stages of the reading process is essential to our understanding of VA's performance. There is converging evidence that alphabetic identification is within the reach of the RH, even if this process is not needed for normal reading (Coslett & Saffran, 1998). This evidence comes from studies of split-brain patients (Baynes, Eliassen, Lutsep, & Gazzaniga, 1998), left-hemispherectomized patients (Patterson, Vargha-Khadem, & Polkey, 1989), deep dyslexic patients with extensive left hemisphere lesions (Coltheart, 1980) and patients with pure alexia (Cohen et al., 2003; Coslett & Monsul, 1994; Coslett & Saffran, 1989, 1992, 1994). However, we do not know whether the patients in these studies had preserved case-invariant letter representations, because they were not tested on cross-case matching tasks. Functional imaging findings with normal subjects have also found that alphabetic stimuli activated a bilateral and symmetrical brain network (Cohen et al., 2003). Taken together with the case presented here, the clinical and neuroimaging studies suggest that during reading, letters are processed in the contralateral hemisphere (including the RH) up to a case invariant level.

As already mentioned, our patient VA and patient MS described by Mycroft et al. (2002), in contrast to the global alexic patients described by Miozzo and Caramazza (GV) (1998) and Larsen et al. (EA) (2004), performed successfully on the cross-case matching task, suggesting a preservation of abstract letter identities. The extensive damage in the left hemisphere of our patient suggests a likely role of the right hemisphere in abstract letter identification. How do we account for the discrepant findings with previously reported cases of global alexia? One possible explanation for the lack of concordance in the performance of different alexic patients is that the substitution of the critical areas responsible for reading abilities (VWFA) by the right hemisphere structures may not be perfect. In fact, the existence of alphabetic activations in the corresponding right VWFA in alexic patients might depend on premorbid functional dispositions and subject to individual variability (Cohen et al., 2002). Such adaptations could reflect neural plasticity processes in the right VWFA following the stroke. Right hemisphere involvement in language recovery is also supported by recent functional imaging studies in aphasics, showing increased activity, relative to controls, in regions of the right hemisphere that are homotopic to language areas on the left (Cardebat et al., 1994; Crinion & Leff, 2007; Weiller et al., 1995). In the absence of functional imaging data from VA, however, we can only speculate that her residual reading abilities, including access to case-independent letter representations, were mediated by the right hemisphere.

Otherwise, access to phonology from visual input was interrupted in our patient, probably because of the extensive damage in the left hemisphere and the corpus callosum, which isolated the language processing systems in the left hemisphere from visual input. This is in line with the data on global alexic patients reported in Binder and Mohr (1992) showing extensive lesions affecting the callosal pathways (splenium and forceps major) and the dorsal white matter above the horn of the lateral ventricles and posterior to the forceps major. These lesions may block the transmission of visual information from the right to the left hemisphere where phonological processing likely takes place. Several functional imaging studies, indeed, are consistent in showing that phonological demands elicit increased activity in left posterior superior ("dorsal stream") cortical areas, including the lateral inferior parietal and posterior superior temporal cortices (Hagoort et al., 1999; Herbster, Mintun, Nebes, & Becker, 1997; Price, Moore, & Frackowiak, 1996; Pugh et al., 1996; Rumsey et al., 1997; Simos et al., 2002). The role of the left inferior parietal/posterior superior temporal cortex as the anatomical substrate of the grapheme-to-phoneme process has also been shown in a number of studies (Brunswick, McCrory, Price, Frith, & Frith, 1999; Fiez, Balota, Raichle, & Petersen, 1999; Hagoort et al., 1999; Herbster et al., 1997; Poldrack et al., 1999; Pugh et al., 1996; Rumsey et al., 1997; Zurowski et al., 2002).

Please cite this article in press as: Volpato, C., et al. Covert reading of letters in a case of global alexia. *Brain & Language* (2012), doi:10.1016/j.bandl.2011.12.014

VA's processing of Arabic numbers seems to be quite similar to that of letters. Note that not all global alexics behave the same in this respect: for example, Dejerine's (1892) original global alexia patient, Monsieur C, could read numbers quite well. VA was, in fact, incapable of reading aloud or writing numbers in any format, however, she performed better in recognizing digits on multiple-choice presentation. She could also recognize the correct shape and orientation of Arabic numbers. As in previously reported patients (Cohen & Dehaene, 1995; McNeil & Warrington, 1994; Miozzo & Caramazza, 1998), VA had an almost intact ability to perform magnitude judgements with Arabic numbers, despite her difficulty in naming them. One possible explanation is that the right hemisphere is capable of representing number magnitude information (as well as various conceptual features of objects) but not complete semantic representations. Thus, semantic information in the right hemisphere is insufficient to drive the lexical system in the left hemisphere without error, either because the semantic information is incomplete or because it becomes degraded during inter-hemispheric transfer (Miozzo & Caramazza, 1998). The same pattern held for the two patients studied by Cohen and Dehaene (1995) who failed to identify two-digit numbers correctly, but had no difficulty at all judging the relative magnitude of pairs of these numbers. To account for this pattern of performance, the authors suggested that magnitude comparisons are carried out by the right hemisphere, whereas explicit report is based on information transferred to the left hemisphere.

In conclusion, VA's reading performance strongly suggests preserved access to abstract letter identities in a case of global alexia and supports the hypothesis that, at least in some brain-damaged individuals, the right hemisphere has the ability to process letters as abstract alphabetic objects, and not just shapes. This finding is in line with the results previously reported by Mycroft et al. (2002). Together, these studies indicate that in alexic patients the right hemisphere can take over some of the functional properties normally specific to the left hemisphere, providing the anatomical substrate to the recovery from alexia (Cohen et al., 2003). The somewhat inconsistent patterns of reading performance among the previously reported cases of global alexia so far discussed may likely be due to variability across individuals in the neuroanatomical localization of the different stages of reading process.

Acknowledgments

The authors thank VA for her cooperation on this study. Thanks to the three anonymous reviewers for their helpful comments on a previous version of this paper. Portions of this work were presented at the XXVII European Workshop on Cognitive Neuropsychology (2009). Funding was provided from a MIUR Grant to Carlo Semenza.

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