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Selective alexia and agraphia sparing numbers—a case study

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Abstract

We report a patient (MT) with a highly specific alexia affecting the identification of letters and words but not numbers. He shows a corresponding deficit in writing: his letter writing is impaired while number writing and written calculation is spared. He has no aphasia, no visuo-perceptual or -constructional difficulties, or other cognitive deficits. A similar pattern of performance has to our knowledge only been reported once before [Anderson, S. W., Damasio, A. R., & Damasio, H. (1990). Troubled letters but not numbers. Domain specific cognitive impairments following focal damage in frontal cortex. *Brain*, 113, 749–766]. This study shows that letter and number reading are dependent on dissociable processes. More interestingly, it points to a common mechanism subserving the perception and production of letters. We suggest that a deficit in a visuo-motor network containing knowledge of the physical shape of letters might explain the pattern of performance displayed by MT.

Keywords: Alexia; Agraphia; Reading and writing; Letter reading; Number reading; Exner's area; Visuo-motor interaction; Number writing; Third alexia

1. Introduction

Since Dejerine's (1892) description of the selective loss of reading ability (alexia without agraphia), it has become widely accepted that reading and writing are dissociable cognitive processes. Yet in most cases, alexia is associated with agraphia as well as aphasia. In addition to describing patients with alexia with and without agraphia caused by posterior lesions, Dejerine also reported a third variety of alexia, occurring in patients with anterior lesions and Broca's aphasia (Dejerine & Mirallié, 1885). More recently Benson (1977) has shown that the third alexia can be dissociated from pure alexia and the central alexias, and that it therefore deserves to be seen as a clinical entity. In 1990 Anderson, Damasio & Damasio reported a case of isolated alexia and agraphia for letters caused by a lesion in Exner's area in the left premotor cortex. To our knowledge, this is the first patient on record suffering from the third alexia in pure form, without associated aphasic deficits. This patient was completely unable to identify single letters, while being perfectly able to read Arabic numerals. Her writing of letters was slow and laborious, while on the other hand, she was perfectly able to write numbers and perform written arithmetic. We report a patient (MT) showing a similar pattern of performance. MT is severely impaired in reading and writing of letters and words, while his number reading and written arithmetic is intact. He has no aphasia or other cognitive deficits. The pattern of performance displayed by these patients represents some interesting challenges to our understanding of the cerebral organization of visual identification and written output.

2. Case report

MT suffered a head trauma in a car accident in April 1999, when he was 18 years old. He was discharged from hospital after 24 h with a diagnosis of concussion. No post-trauma symptoms were noted. When MT got home he realized that he could no longer read. He was examined by an ophthalmologist, who found that MT had severe problems with letter-identification, but that he could still read numbers. His writing was observed to be clumsily formed. On June 8th, 1999, MT went totally blind for about 10 min,

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followed by dizziness, reduced balance and headache. He was admitted to hospital, where bilateral peripheral visual field defects were found. No other neurological symptoms were noted. This was interpreted as an ischemic attack. Six months later his visual fields were found intact. MT is fully right handed (+100 at the Edinburgh handedness inventory (Oldfield, 1971)). MT gave informed written consent according to the Helsinki Declaration to participate in this study.

Before the accident, MT was a student at a commercial college and his grades were on an average level. Of particular interest is his grade in Danish, where he got a B on his latest exam before the accident, indicating that his reading and writing abilities were not below normal premorbidly. There was no report of dyslexia or other learning disabilities, and MT had no history of neurological or psychiatric disease. MT reported that he did not read much outside school before the accident. He was able to use a computer and keyboard before the injury, but mainly used this for games, not writing.

CT- and MRI-scans, performed in June 1999, showed no abnormalities. A hyperintensity was noted on MR-angiography, in the mid portion of the basilar artery, but this might not be abnormal. Seeing that our patient's pattern of performance resembled that described by Anderson, Damasio, and Damasio (1990), we performed a new MRI-scan in November 1999, looking explicitly for a lesion in Exner's area. No abnormalities were found at that time. We also performed a SPECT scan which indicated a small flow defect in the parieto-occipital area of the right hemisphere, which may include posterior temporal regions. It should be noted that this finding is somewhat uncertain, as it is at the limit of the resolution.

2.1. Neuropsychological evaluation

The neuropsychological examination and experimental investigation was mainly undertaken in June and July 1999. MT was also examined on two later occasions, at which point he was in a language training program which may have affected the test-results. Results obtained after July 1999 will therefore be marked in the following. All test-results are shown in Table 1.

2.1.1. General abilities

The neuropsychological assessment of MT revealed a verbal IQ below the normal average and a performance IQ in the upper normal range. MT's monozygotic twin brother (BT) was also assessed with a set of tests of general abilities, and a comparison between the two reveals an almost identical pattern (see Table 1). This suggests that MT's low scores on verbal subtests reflect his premorbid abilities, and are not a result of his injury. MT is fast and efficient in tests demanding high psychomotor speed, like Block Design and Trails A. His digit span, both forwards and backwards, is above normal, and also superior to BT's.

Table 1
(A) Test results in standardised tests: MT and BT (twin brother)

	MT	BT
WAIS-subtests—raw scores (standard-scores)		
Information	14 (8)	14 (8)
Vocabulary	30 (4)	30 (4)
Similarities	11 (5)	11 (5)
Digit span	15 (17)	11 (12)
Picture arrangement	30 (12)	28 (10)
Digit symbol	36 (4)	—
Picture completion	16 (11)	20 (15)
Raven advanced progr. matrices, set I		
Scoring first response	4/12	5/12
Self corrected responses	3/12	2/12
Sum correct	7/12	7/12
Other[a]		
Sentence repetition	16/22[b]	16/22[b]
Mental arithmetic	18/20	12/20
Block design, correct	12/12	12/12
Block design, time	13 s	12 s
Trail making test A	26 s	—

(B) Results of neuropsychological tests, MT

Language	
Boston naming	48/60[b]
BORB picture naming (low freq. items)	14/15
Famous faces naming	14/15
Colour naming	10/10
Visual perception	
VOSP, shape detection	10/10
VOSP, dot counting	10/10
BORB, unusual views	13/15
Street completion test	19/20
Poppelreuter overlapping figures	15/15
Colour recognition	10/10
BIT—star cancellation	54/54
Visuoconstructive tests	
Rey's figure, copy	35/36
BORB, drawing from memory	9/9
Copy of house	3/3
MMSE, copy of figure	1/1
Memory	
Rey's figure, recall	32/36
RBMT, face recognition	10/10
Other	
Stroop—simple version	47/50[b]

VOSP, The Visual Object and Space Perception Battery (Warrington & James, 1991); BORB, Birmingham Object Recognition Battery (Riddoch & Humphreys, 1993); RBMT, Rivermead Behavioral Memory Test (Wilson, Cockburn & Baddeley, 1985); BIT, Behavioral Intattention Battery, (Wilson, Cockburn & Halligan, 1987).

[a] These tests were selected from the standard neuropsychological test-battery from Copenhagen University Hospital.

[b] This result is >2 standard deviations below the mean compared to Danish norms.

2.1.2. Visuoperceptual and -constructional abilities

The results on the visuoperceptual tests show that MT does not have difficulties in recognizing objects, faces or colors. He shows no problems with integrating fragmented pictures (Street), separating overlapping pictures (Poppelreuter) or mentally transforming images (BORB: Unusual views). His visuo-constructional abilities are also intact, as evidenced by his quick and correct copying of figures, both simple and complex, and his perfect drawings from memory (see Fig. 1).

2.1.3. Language

MT's speech was fluent and prosodic, although he generally spoke in a low voice and sometimes mumbled. He had no word-finding difficulties in conversational speech, and performance was normal on one test of confrontation-naming (from BORB). His score on the Boston naming task was two standard deviations below the mean of a normative sample, but this probably reflects MT's low premorbid verbal skills and is not interpreted as a result of his injury. Sentence repetition and his score on the vocabulary subtest of the WAIS were below normal, but at the same level as BT.

3. Experimental investigation

MT's reading and writing skills were investigated with several tests of letter identification, word reading and writing as well as tests of number identification and production.

3.1. Reading

Preliminary observations of reading revealed that MT was severely impaired in letter identification and word reading. When presented with short common words and asked to read them, MT spontaneously covered up all letters but one, and tried to identify the letters one by one. He volunteered that he had begun this strategy when he first realized he could not read. He frequently misidentified letters, and often came up with several alternatives or left letters out if he could not identify them. For instance, when presented with the word */ankel/* (ancle) he read *a*; *h* or *n*; *don't know*; *e*; *l*, and then tried to guess what the word was. (In this particular case, he failed.)

3.1.1. Letter naming

Items and procedure: 29 upper case and 29 lower case letters were presented in 48 point Times New Roman on separate cards. MT was asked to name the letters as quickly and accurately as he could. Reaction times were measured using a hand-held stop watch.

Results: During the first test-session MT was able to identify 13/29 upper case letters correctly, with an average reaction time of 6.3 s, and 18/29 lower case letters with a mean time of 10.7 s. On retest one month later, there was no improvement.

3.1.2. Tactile identification

Items and procedure: In the first task, the experimenter outlined seven letters (one by one) in MT's hand, and asked him to name the letter. MT was also presented with a small set of large wooden letters (approximately 10 cm tall), which he was allowed to feel as well as look at, and asked to identify these.

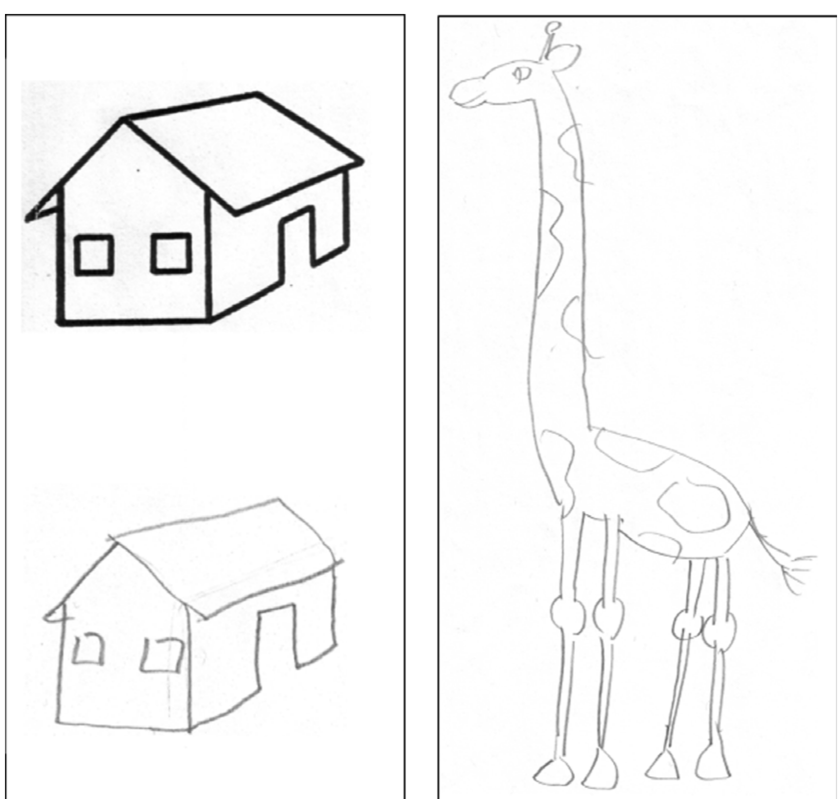

Fig. 1. MT's copy of a house (left) and his drawing of a giraffe from memory (right).

Results: When the experimenter outlined letters in MT's palm he correctly identified 4/7, claiming he did not find this any easier than identifying them by sight. Time was not measured in this task, but MT was slow and hesitant.

When allowed to feel the shape of wooden letters, as well as look at them, MT correctly identified 8/10, with a mean time of 3.9 s.

3.1.3. Imagery

Items and procedure: To investigate MT's ability to imagine letters and their shapes, he was asked to decide whether eight spoken letters had only straight lines or included curved lines.

Results: MT scored 8/8 on this test, his answers came promptly.

3.1.4. Single-letter decision

Items and procedure: MT was presented with two letter-decision tasks. The first included twelve letters and non-letters printed on the same page. The second included ten stimuli printed on the same page: four upper case letters (targets) and as distractors three mirror-reversed letters and three letters turned upside down. In both tasks MT was informed of the kind of distractors, and asked to indicate whether the stimulus was a letter or a distractor.

Results In both tasks, MT had to cover up the letters/non-letters, before judging whether it was a real letter or not. He could not be persuaded to refrain from this strategy.

In the first task, MT scored 9/12 classifying three letters as non-letters.

In the second task, MT scored 8/10, classifying two letters presented upside down as normally oriented letters.

3.1.5. Letter matching

Items and procedure: MT's ability to match letters was investigated with two letter matching tasks. In the first task the stimulus letter was presented above a string of three to five letters (including the target letter) forming either a word or a random letter string. In half the trials, the stimulus and target/distractors were printed in the same case, in the other half in the opposite case. All letters were typed in 20 point Times New Roman, and MT was asked to point to the letter corresponding to the stimulus letter. Response time was measured with a stop-watch. In another, simpler task, MT was presented with two 24 point upper case letters typed side by side, and asked if they were the same or different. He was encouraged to guess if he was unsure.

Results: In the first task, where the target letters were presented among distractors, MT covered up all letters but one, and identified them serially. The results are found in Table 2. There was no clear difference between targets presented within words versus non words. MT's response times in this task ranged from 10 to 50 s depending mostly on how far to the left the target letter was printed (he was faster with letters on the left because of his serial left-right strategy).

Table 2
Letter matching

Number of letters	Word/non-word	Same-/crosscase	No. correct
3 letters	Word	Same	2/3
3 letters	Word	Cross	2/3
5 letters	Word	Same	3/3
5 letters	Word	Cross	2/3
5 letters	Non-word	Same	3/3
5 letters	Non-word	Cross	2/3

MT was presented with one letter and asked to match this to one of three or five letters forming either a word or a non-word. In half the trials, the letters to be matched were in the same case, in the other half of the trials the stimulus letter and the target and distractors were in different cases. Response times were not formally measured, but were extremely long, as MT insisted on identifying the letters serially as he does in reading.

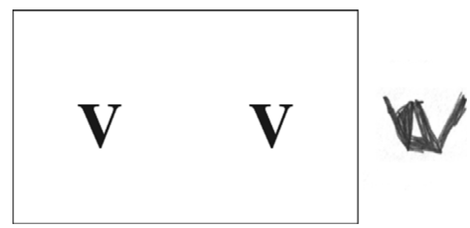

Fig. 2. A stimulus card from the simple letter matching task (left), and MT's drawing of what he is seeing when looking at it (right).

In the second task, looking at two letters simultaneously, MT was unable to judge if they were the same or different. Encouraged to guess, MT was correct on 1/5 letter pairs.

MT was asked to draw what he experienced seeing when looking at the letter pairs, and his drawing seems to suggest that he cannot separate the letters from each other. It is not clear, though, if this reflects a deficit in letter perception or in writing/copying of alphabetic material. The stimulus card and his drawing are shown in Fig. 2.

3.1.6. Word reading

Items and procedure: All words presented for reading were written in 36 point Times New Roman upper case letters, on separate cards. Word frequency measures were found in Bergenholtz (1992), and concreteness ratings are based on Paivio, Yuille, and Madigan (1968). During the first test-session, MT was presented with a list of low frequency concrete nouns, with increasing number of letters (three, five or seven letters, five words in each group). Reaction time (RT) was measured with a stop-watch.

On a later occasion (23.11.99), MT was tested on a list of ten high-frequency concrete words (three or five letters long), and five corresponding non-words. The non-words were constructed by changing one letter in words from the list of high-frequency, concrete words.

Results: On the first test-session, MT correctly read 2/5 three-letter words, with RT's at 12 and 15 s. He failed reading any five- or seven letter word correctly. Misidentification of letters accounted for all his errors, and he always substituted a visually similar letter, e.g. *ENG* was read *FNC*. On the list of concrete, high frequency words, MT correctly read 5/5 three-letter words with an average time of 26 s and 4/5 five-letter words at an average time of 38 s. He also read 5/5 three-letter non-words correctly with a mean time of 16 s. Curiously, MT's average time for reading non-words was faster than for real words. This might be because MT was told that the words presented were non-existent, so that he only had to identify and remember the letters, and not to make sense of them. This could have made the task easier for him than reading real words.

3.1.7. Whole-word reading

In the Stroop color and word test, MT scored 47/50, reading the color name on three cards, which might indicate that MT is able to read some words holistically, an ability held by many patients with the third alexia (Anderson et al., 1990; Benson, 1977).

Items and procedure: In one task, MT was presented with short "symbolic" words like *TV*, as well as words known to him, like his own name, to see whether or not he was capable of reading such words in a gestalt manner. We also attempted to test MT's whole-word reading skill using a computerized lexical decision test, in which high frequency nouns and corresponding non-words were presented too briefly to allow letter-by-letter reading. MT was instructed to attend to the whole word, and indicate whether it was a real word or a non-word. He was encouraged to guess.

Results: When prevented from covering up letters and identifying them serially, MT could not identify any of the short symbolic words presented to him. He could not guess what they were, and could not read his own name in a glance. On the lexical decision test, MT gave up after very few trials. He claimed that the test did not make any sense to him, and he had no idea whether real words or non-words were presented, as he could not read them. The test was then discontinued.

3.2. Writing

Preliminary observations revealed that MT superimposed letters on each other when writing to dictation or from memory, which made the words virtually unreadable (see Fig. 3). He did this even when writing his own name and address. He was also slow in producing single letters.

3.2.1. Writing letters and words

Procedure: In order to explore the extent to which MT would be able to separate letters from each other when writing, he was asked to write letters and words within a grid system. Furthermore he was asked to attempt writing without a grid, while trying to move his hand between letters.

Results: When presented with a grid system, MT was able to place letters within the squares, and did not superimpose. He wrote 14/14 letters slowly, but correctly, to dictation. He interchangeably wrote in upper and lower case letters. Within the grid, he could write his name and address without errors. His letters were clumsily formed, but recognizable. When asked to write the alphabet within the grid system, MT numbered the slots in which he was to write the letters. He then wrote 27/29 letters correctly, and did not superimpose (see Fig. 3, lower panel). He could not remember the shape of two letters (*g* & æ). All other letters were legible, but his response times were long. When instructed to move his hand between letters, MT was able to write a simple sentence without superimposing letters, on lined paper. There were no spelling errors, but some letters were clumsily formed. Time was not formally measured, but his production of the sentence was remarkably slow. In all the word writing tasks, MT wrote in printed letters, and was slow and hesitant in producing them. According to his family, the letters did not resemble his habitual handwriting.

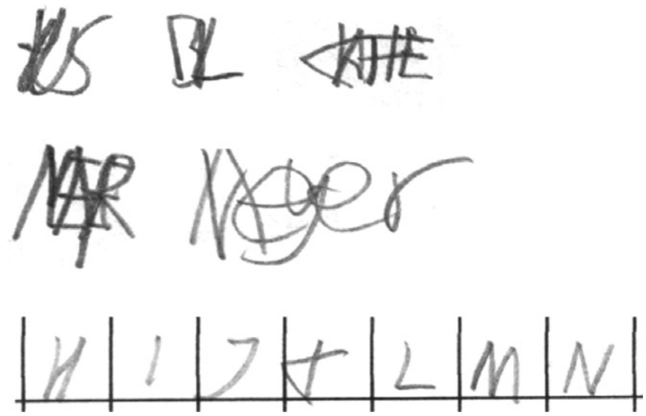

Fig. 3. MT's attempt to write the words *hus*, *bil*, and *kaffe* (top panel), and his writing of his own name in capital and lower case letters (mid panel). MT's writing of single letters when presented with a grid (lower panel).

3.2.2. Copying

Items and procedure: MT was presented with 14 upper case letters, written in 20 point Times New Roman. He was instructed to copy what he saw, rather than try to identify the letter. He was also presented with ten Greek letters for copying.

Results: In the first task, MT first tried to identify the letters, and then attempted to write the letter in question. He could not be persuaded to abandon this strategy. Using this strategy, he correctly copied (or wrote) 10/14 letters. He only abandoned this strategy when he could not identify the presented letter, and then tried to draw what he saw, the result being either the wrong letter, or (in one instance) an illegible shape. Three of the errors in this test are based on misidentification of the stimulus ($B \rightarrow R$, $Y \rightarrow V$, $a \rightarrow o$).

With Greek letters, MT did not recognize any of the letters presented. Only 1/10 letters was copied correctly, the letter "ε," which, according to MT, looks like a mirror-reversed "3." The remaining 9 copies were not recognizable.

3.2.3. Oral spelling

Items and procedure: MT was presented with ten high frequency, concrete words (from four to eight letters), as well as three seven-letter abstract words and five nine-letter abstract words (all high frequency).

Results: All words were spelled quickly and correctly.

3.2.4. Naming to oral spelling

Items and procedure: The experimenter spelled out 30 words of three to five letters. All words were high frequency nouns, 15 concrete and 15 abstract.

Results: MT named all spelled-out words correctly, without hesitation.

3.3. Number reading

3.3.1. Identification

Stimuli: Ten single digits and 15 multidigit numbers (three, five or seven digits) were presented on separate cards. All numbers were written in 48 point Times New Roman. MT was instructed to read the numbers as quickly and accurately as possible. RT's were measured with a hand-held stop watch.

Results: MT read all single digits quickly and correctly, with RT's below 1 s. (His RT's were too short to be accurately measured with a stop watch.) He read 15/15 multidigit numbers correctly, with RT's at or below 1 s.

3.3.2. Accessing semantics from numbers

Stimuli and procedure: To assess whether MT could access semantics from numbers, he was presented with a small set of well known numerals, consisting of famous historical dates, his birth date, and postalcode. He was presented with the numbers for reading, and asked what they referred to. BT was tested as a control in this test.

Results: MT scored 4/7 in this test. He read all numbers correctly out loud. He did not know what three of the historical dates referred to, but correctly recognized his own birthday and postal code as well as two historical dates. We also tested BT on the same numbers, and he obtained the same score, answering correctly on the same items as MT.

3.4. Number writing and written calculation

3.4.1. Writing single digits and multidigit numbers

Items and procedure: MT was asked to write five single digits and 21 multidigit numbers (from two to seven digits) named by the experimenter.

Results: MT wrote all presented numerals quickly and correctly. All digits were nicely formed, and MT did not superimpose digits on each other when writing multidigit numbers.

3.4.2. Written calculation

Items and procedure: The arithmetic problems used by Anderson et al. (1990, p. 758) were presented orally to MT. 14 problems were presented (three addition, three subtraction, five multiplication, and three division). He was asked to write them down, and then solve the problems in writing.

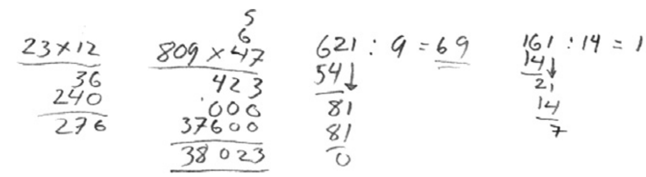

Fig. 4. Example of MT's number writing and written arithmetic.

Results: MT wrote correctly from dictation, and also solved 11/14 problems correctly. His errors were due to problems in mental arithmetic, and not caused by misidentification or miswriting of the numerals. Examples of his written arithmetic are shown in Fig. 4.

3.5. Summary of results

MT shows a selective impairment in reading and writing letters and words, while no other cognitive functions are affected. Neuropsychological evaluation of MT revealed a verbal IQ below the normal average, and a performance IQ in the upper normal range. An identical pattern of performance was observed in MT's monozygotic twin brother, indicating that this discrepancy is habitual, and not a result of MT's injury. MT's visuoperceptual and -constructional abilities are intact, as are his general language abilities.

MT is severely impaired in single-letter identification. Because he relies on a letter-by-letter strategy in reading, his response-times in word reading are extremely long. No whole-word reading was observed, except in the Stroop task, where MT read the written color names on three cards. This could have been accomplished by identifying the first letter of the written color word, and might not reflect reading of the entire word. In writing, MT superimposes letters on each other, and his letter production is slow and laborious. No spelling errors have been observed, partly because the superimposing of letters prevents identification of many of the letters and words MT has written. When presented with a grid, MT is able to separate letters from each other. Although most of his letters are clumsily formed, the majority are recognizable. MT's naming to oral spelling is good, as is his spelling of dictated words. MT is able to identify written numbers quickly and correctly, and he can access semantic knowledge from numbers. His number writing is flawless, as is his written arithmetic.

There is a striking dissociation between MT's reading and writing of letters and numbers. He is severely impaired in letter identification and word reading, and his writing of letters and words is affected, while his number reading skills and written arithmetic are intact.

4. Discussion of results

4.1. A comparison of MT with the case reported by Anderson et al. (1990)

MT's pattern of performance so closely resembles that displayed by Anderson et al.'s (1990) patient (this patient will be referred to as ADD), that a direct comparison of their performance is warranted. Both patients are severely impaired in letter recognition, including letter matching, while their other visuo-perceptual abilities, including number reading, are intact. Both patients also show a corresponding deficit in writing letters, while number writing and written arithmetic are unaffected.

ADD's impairments, although selective, seem more severe than MT's. Her writing was extremely slow, and in a letter dictation task only 2/15 of her letters were legible. MT, on the other hand, could write 26/28 letters in the alphabet correctly. ADD was also mildly impaired in naming to oral spelling, but her ability to spell words named by the examiner was intact. MT performed excellently in both these tasks. ADD was also unable to read non-words, while MT, using his letter-by-letter strategy, could read nonsense words as long as he identified the constituent letters correctly. ADD was able to read some words holistically. MT was insistent on using a letter-by-letter strategy in reading, and could not be persuaded to abolish this procedure even when instructed to focus on whole words. Yet, in the Stroop test MT made three errors–naming the written color name–and this might reflect an ability to read some words holistically.

Regarding their patient's agraphia, Anderson et al. (1990) note that "the predominant feature (…) was severely defective grapheme formation" (p. 761), and that her ability to write numbers indicated that the repertoire of movements necessary for writing was spared. MT's grapheme formation was not as severely distorted as ADD's, as most of his letters were legible. However, MT's letter writing was impaired compared to his number writing. His writing of words was slow and spatially distorted, his letters were clumsily formed, and a few letters were not recognizable.

4.2. A comment on strategy

MT consistently uses a letter-by-letter strategy in reading, that is, he serially identifies all letters in a word, before trying to identify the word itself. More than that, he insists on covering up all letters but one, and then tries to identify the letter he is looking at. His response style is very rigid, and he can not be persuaded to abolish this strategy. Although letter-by-letter reading is commonly associated with pure (occipital) alexia, it is a compensating strategy and not a diagnostic feature in itself (e.g. Price & Humphreys, 1992), and has been observed in patients with other types of alexia.

MT's response style might be related to his premorbid verbal abilities. Although his grades in Danish were on an average level before the accident, the scores in verbal subtests of the WAIS indicated verbal abilities below average for both MT and his twin brother. As pointed out by Rothi and Heilman (1981) and Price and Humphreys (1995), among others, the compensating strategy adopted after brain injury is related to the strategies and resources available premorbidly. MT's low verbal abilities might thus affect his ability to compensate for his deficits, and one can speculate that the degree of his problems might have been less dramatic had his verbal skills been on a higher level before his injury.

5. General discussion

A selective deficit in reading letters compared to numbers is evident in both Anderson et al.'s (1990) patient and in MT, and the reversed pattern has also been described (Cipolotti, 1995). Dissociations between reading and spelling of common words compared to both Arabic numerals and number words have also been reported (Butterworth, Cappelletti, & Kopelman, 2001; Denes & Signorini, 2001; Marangolo, Nasti, & Zorzi, 2004). Although curious, these latter deficits are not on the level of perception or identification of the symbols, but seem to be caused by disruption of more central processes, or even deficits on the level of spoken number output. To explain the reported dissociations, one might suggest that number and letter reading are completely separable processes from the input to the output level, and that they rely on entirely separate neural substrates. Still, given the similarity of the two types of symbols, one would expect the reading of letters and numbers to rely on the same mechanisms to some extent, at least in the early phases of visual identification.

5.1. The dissociation of number and letter reading

5.1.1. Number reading in alexia

Although there are reports of preserved number reading in pure alexia (e.g. Luhdorf & Paulson, 1977), the relation between letter and number identification has not been studied to any large degree. Dejerine's (1892) original pure alexic patient read multidigit numbers digit-by-digit (1-1-2 spelling 112), the same way most pure alexics read words (Rosenfield, 1988). Cohen and Dehaene (1995) studied the number processing skills of two patients with pure alexia. They found that these patients were more accurate in reading two digits "digit-by-digit" (e.g. 2–4) than as one number (e.g. 24), and that, in general, the patients' success in reading numbers aloud was affected by task demands. Number reading was affected to a lesser degree than letter reading, though, indicating to the authors that these functions are not entirely dependent on the same processing system. Similar cases have been reported (Cohen & Dehaene, 2000; McNeil & Warrington, 1994; Miozzo & Caramazza, 1998), suggesting that number reading is commonly affected in patients with pure alexia. It is curious that while peripheral accounts of pure alexia often claim that this disorder is caused by a more general perceptual deficit, this is usually based on studies of object processing in pure alexic patients (Farah, 1990; Friedman & Alexander, 1984). A comparison between number and letter reading in these patients might have been equally or even more informative, given the similarity of the symbols.

5.1.2. Findings in neuroimaging

While there are numerous neuropsychological and neuroimaging studies of letter identification in both patients and normals, few studies have compared number and letter reading directly.

An increasing number of studies have reported extrastriate areas that respond more to words, pseudowords and letter strings (Cohen et al., 2000; Polk et al., 2002; Polk & Farah, 2002; Puce, Allison, Asgari, Gore, & McCarthy, 1996), as well as single letters (Flowers et al., 2004; Joseph, Gathers, & Piper, 2003) than to other visual stimuli. Especially the role of the so called visual word form area (VWFA) in the left fusiform gyrus has been studied quite intensively in both normals (Cohen et al., 2000) and patients (Cohen et al., 2003; Hillis et al., 2005). Still, there is considerable controversy regarding the existence of such an area, its function, its relation to other visuo-perceptual processes, as well as the potential learning mechanisms involved (Cohen & Dehaene, 2004; Polk & Farah, 2002; Price & Devlin, 2003, 2004).

Polk et al. (2002) conducted an fMRI study aiming to test directly whether or not the neural substrates for letter and digit recognition are segregated. They report that "at least in some literate subjects, certain extrastriate areas respond significantly more to letters than digits" (Polk et al., 2002; p. 148). Polk et al. (2002) reported no area that responded more to digits than letters on a group level, although a region of interest (consisting of the fusiform, lingual and inferior temporal gyri) was associated with greater activation for digits than for letters in 3/8 patients. Allison et al. (Allison, McCarthy, Nobre, Puce, & Belger, 1994) made similar findings in an electrophysiological study of category specificity in visual perception. They identified a negative potential (N200) evoked in the fusiform and inferior temporal gyri by words and non-words, which was separable from potentials evoked by faces. They also report a "number N200" recorded from the same region, generated by the presentation of Arabic numerals compared to faces, letter strings, and false fonts. In some subjects, the number and letter N200 were recorded from the same location, indicating that "these modules may be less spatially and functionally discrete" (Allison et al., 1994, p. 544). Others have reported regions in the interparietal sulcus bilaterally to be more active during presentation of numbers compared to letters or colors (Eger, Sterzer, Russ, Giraud, & Kleinschmidt, 2003), and other studies (e.g. Simon, Mangin, Cohen, Le Bihan, & Dehaene, 2002) using less direct comparisons support this finding. This activation by numbers compared to other stimuli has been attributed to a supramodal number representation that is automatically activated by presentation (visual or verbal) of numbers (Eger et al., 2003), and its role in visual identification of the symbols—if any—is unclear.

Generally, reading disorders following smaller lesions in the VWFA or surrounding structures are selective in the sense that they leave writing unaffected. Such a lesion would therefore not be a sufficient explanation for the pattern of deficits displayed by ADD and MT. It is also not clear how the VWFA might contribute to the perception or identification of numbers—if at all—although the sparse patient data as well as Polk et al.'s (2002) and Allison et al.'s (1994) studies indicate that this area might also contribute to the identification of digits, at least in some subjects.

5.2. Exner's area

The dissociation between numbers and letters might not be as challenging to models of visual recognition or written output, as the *association* between letter reading and writing observed in ADD and MT. It is curious that a small circumscribed lesion can cause both alexia and agraphia (or at least severe writing difficulties) the way it has in Anderson et al.'s (1990) patient, and possibly in MT. Alexia can occur without agraphia (Dejerine, 1892; Friedman & Alexander, 1984; Warrington & Shallice, 1980), and some cases of pure agraphia have also been reported (Dubois, Hecaen, & Marcie, 1969; Gordinier, 1899) indicating that reading and writing are dissociable, at least at the input (reading) and output (writing) level.

ADD had a lesion in an area in the left premotor cortex often referred to as Exner's area. Given the striking similarities between the two patients, we assume that a similar lesion could be responsible for MT's impairments. Exner (1881) is usually credited with having suggested the existence of a cerebral centre for writing located at the foot of the second frontal gyrus in the dominant hemisphere: The area of premotor cortex lying directly in front of the motor area for the hand. Nielsen (1946) elaborated this idea, and speculated that Exner's area is "especially trained from childhood through the formation of engrams to function as a writing center" (p. 41). He noted that this was not an isolated centre; associations to the angular gyrus—to the mental images of letters—were necessary to constitute a writing mechanism. A recent fMRI study found consistent activation of Exner's area in copying of Japanese script, and the authors suggest that this area is involved in motor preparation for grapheme production (Matsuo et al., 2001). But what role might this "writing area" play in reading?

In a review of the third alexia, Kirshner and Webb (1982) suggested that grapheme–phoneme conversion might be a function of the anterior left hemisphere, a postulate that has been substantiated by more recent studies of transition from print to sound (Joubert et al., 2004; Pugh et al., 1996; Sergent, Zuck, Levesque, & MacDonald, 1992). A case study of a patient with a lesion in Exner's area, in whom epileptic seizures were provoked by reading (Ritaccio, Hickling, & Ramani, 1992), suggests that this area might be part of the network transforming script to sound. Speaking normally did not provoke seizures in this patient, and neither did reading when subvocalisation was prevented, suggesting that grapheme–phoneme conversion was the main precipitant of the attacks. Anderson et al.'s (1990) patient was not able to read non-words, leading the authors to compare her deficit to phonological alexia, which, in dual-route models of reading (Coltheart, 1987; Ellis & Young, 1996) is conceptualized as selective damage to the process of grapheme–phoneme conversion.

It seems that Exner's area might be important for more than the grapheme–phoneme conversion process in reading, though. Anderson et al.'s (1990) patient failed to read most words, indicating that her lexical route (as defined in dual route models of reading) is also damaged. More importantly, ADD was severely impaired not only in naming letters but also in letter matching tasks, suggesting a problem in letter perception/identification. The same is valid for MT who, while being able to read some non-words letter by letter, had severe problems in letter matching.

Circumscribed lesions in Exner's area are rare. Going through 1200 cases, Anderson et al. (1990) found only four patients with lesions restricted to this area, of which three had writing or reading deficits, at least in the acute phase. Given the scarcity of patients, exploration of the function of this area might be better achieved with other methods. A recent fMRI study (Longcamp, Anton, Roth, & Velay, 2003) reports that merely looking at visually presented letters activates a premotor area in the left hemisphere, an area corresponding to Exner's area. The same area was active when the subjects copied letters and nonsense letters, but not when they were looking at nonsense letters. A corresponding area in the right hemisphere is activated when left handed subjects are passively viewing letters but not nonsense-letters (Longcamp, Anton, Roth, & Velay, 2005). This supports the notion of Exner's area being part of a network of letter knowledge, although its role in letter identification remains unclear. Lubrano, Roux, and Demonet (2004), using direct cortical stimulation in patients with brain tumors, report that stimulation of Exner's area consistently led to writing deficits, and in some patients also to reading problems and disturbances in naming. This would suggest that (to paraphrase Polk et al. (2002)) in at least some literate adults, Exner's area is important in reading aloud. Based on the tentative but converging findings in the literature, the role of Exner's area in reading and letter identification deserves further exploration.

5.3. The relationship between letters and words

Anderson et al. (1990) attempted to explain why a lesion in the "writing area" should also affect reading, and suggested that the visual shape of letters, their sounds, and the motor patterns needed to write them become associated through learning. The "neural network" for letter knowledge will thereby contain both sensory and motor representations, and Exner's area might play a role in coactivating these representations. Rothi and Heilman (1981) presented a similar idea, based on a case study of a patient quite similar to ADD and MT. Their patient was alexic and agraphic, while his ability to spell words out loud and name to oral spelling was preserved. The authors claim that the patient's letter-recognition abilities were intact, although reading a word took him from 4 to 10 s, which is slower than many LBL-readers. In reading words, the patient would sound out each letter and then produce the word, and he could not be persuaded to use any other reading strategy (quite like MT). The patient also spelled out loud when trying to write, but often produced a letter (grapheme) not corresponding to the sound. His copying of words was impaired, as was his writing with anagram letters, although this was better than his written spelling. The patient was able to perform simple calculations, but it is not clear whether they were presented orally or in writing. He would sometimes write a wrong number in response, while saying the correct answer. Unfortunately, number reading and letter matching was not reported. Rothi and Heilman (1981) suggested that this patient's impairment was due to damage in a "graphemic area," which is "responsible for distinguishing the features of a grapheme and for guiding motor programming in grapheme production" (p. 8). A CT-scan of this patient showed no focal abnormalities, and EEG only showed mild diffuse slowing, leaving the lesion causing the impairment unknown. More recently Del Grosso Destreri and colleagues (2000) have reported a patient (FT) with severe alexia, who was disproportionally impaired in writing uppercase letters, following a large parieto-occipital lesion. FT was also impaired in number reading, but less so in number writing. Del Grosso Destreri et al. (2000) suggested that the motor aspects of the writing process can be disrupted on several levels, and that their patient's writing deficit arose at the level of *stroke sequence selection*. They interpreted Rothi and Heilman's (1981) case as reflecting a failure on the same level in the writing process, while classifying Anderson et al.'s (1990) patient, as having a deficit in the production of graphomotor patterns. They did not attempt to explain these patients' corresponding deficit in reading, which is not easily understood in terms of a disturbance in written motor output.

It seems that spelling and naming to oral spelling are not entirely dependent on the same mechanisms as reading and writing, and that visual imagery of letters is not crucial to the spelling process (Del Grosso Destreri et al., 2000). This might be because in order to spell and name to spelling one does not need to know the physical shape of letters, but in reading and writing this knowledge is crucial. On this basis, the deficits of MT and ADD (and perhaps Rothi & Heilman's (1981) patient) may be explained by suggesting a deficit in a unit or network containing visual and motor knowledge of the physical shape of letters. Such an impairment would leave reading and writing of numbers intact, while compromising letter identification and production.

Bartolomeo and colleagues (2002) have recently demonstrated a dissociation between visually and motor based knowledge of letters in a pure alexic patient, a dissociation also showed by Dejerine (1892) in his original report on Monsieur C. But in normal reading and writing these aspects will generally be integrated, and the role of Exner's area could be in the coactivation of the visual and motor representations of the physical shape of letters. One could also imagine that such a network of visuo-motor letter knowledge would exist along a posterior–anterior axis, and that lesion in different locations along this axis could produce similar deficits. It is thus possible that MT's deficit in reading and writing is related to a disturbance in this network, without assuming that his lesion is exactly similar to ADD's.

We are not suggesting that MT had lost all knowledge of the physical shape of letters, but that his deficits arise from damage or disturbance to this network. Given that MT was able to write most letters, although clumsily, some knowledge of the physical shape of letters must have been spared. On the basis of this degraded knowledge, he was also able to decide if a letter has straight or curved lines in the "letter imagery test", and even to visually identify quite a few letters, when given enough time.

5.4. Dissociations and learned abilities

The ability to read letters, words, and digits is not innately given, but learned by instruction. Thus, the brain does not contain the suggested network of letter knowledge from birth, and it is not automatically developed - it is created through learning. The same is valid for the reading and understanding of arithmetic symbols. The selective disturbance of reading letters then, suggests that the brain can create functionally specialized areas as a result of experience. Yet, as pointed out by Farah (1994), selective deficits do not necessarily imply (modular) localization of function, and one should be careful in suggesting independent brain systems on the basis of dissociations, since these can also be modeled in distributed networks (e.g. Nobre & Plunkett, 1997; Plaut, 1995).

Polk and Farah (1998) addressed this point in relation to the dissociation between letters and digits. They suggest that a correlation based (Hebbian) learning mechanism could lead to functional segregation between letters and numbers, and have modeled this in a neural network. They point out that the appearance of letters in our environment is both temporally and spatially correlated, while digits are more likely to be seen in the presence of letters or other symbols. With an input set with more letters than digits, where letters occur more frequently with other letters (as in the real world), Polk and Farah (1998) report that their network self organized to produce a segregated letter area, but no segregated area for digits. This fits neatly with their imaging study (Polk et al., 2002) as well as Allison et al.'s (1994) findings of a segregated fusiform letter area, but more variability in digit areas. Polk and Farah (1998) also report behavioral data demonstrating how experience with digits and letters can affect performance in cognitive tasks consisting of the two kinds of symbols, and interpret this as reflecting differences in the cerebral organization of these processes.

This suggests that caution is warranted when interpreting dissociations of learned abilities, as it is not certain that selective deficits reveal a common aspect of brain organization but might also reflect the individual patients' (learning) history. In this respect, the replication of the pattern of performance displayed by ADD seems important, in that it strengthens the assumption of functional selectivity for the reading of letters at least at some levels of processing.

6. Concluding remarks

We have reported a patient (MT) who has a highly specific deficit in the reading and writing of letters and words, while his ability to read and write numbers is spared. MT has no aphasia, and no other cognitive deficits have been demonstrated. This pattern of performance has, to our knowledge, only been reported once before (Anderson et al., 1990), in a patient with a lesion in Exner's area. In addition to the striking dissociation between the impaired reading and writing of letters compared to numbers seen in these patients, their pattern of performance also indicates an interesting association between the perception and production of letters. We have suggested that a deficit in coactivation of visual and motor representations of the physical shape of letters might account for the impairments displayed by our patient, and speculate that Exner's area might be contributing to this process. Further studies are needed to investigate the nature of this coactivation, and how it might be related to other cognitive domains like spelling, visual perception, number reading, and written output. The neural substrate of this process, as well as the learning mechanisms involved, also need further clarification.

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