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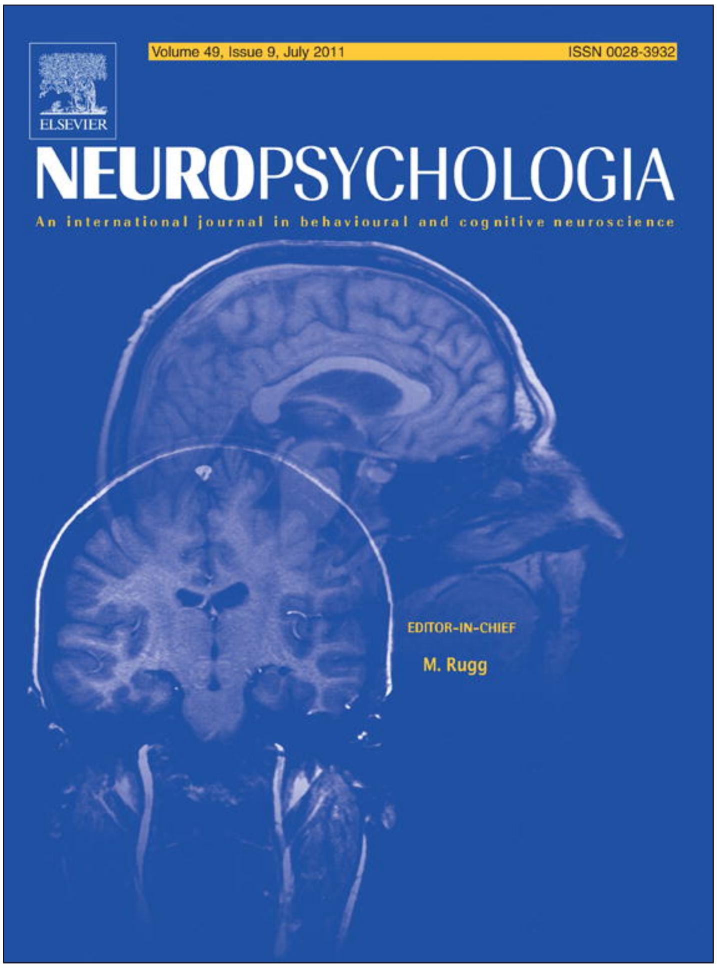
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Reviews and perspectives

Number reading in pure alexia—A review

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ABSTRACT

It is commonly assumed that number reading can be intact in patients with pure alexia, and that this dissociation between letter/word recognition and number reading strongly constrains theories of visual word processing. A truly selective deficit in letter/word processing would strongly support the hypothesis that there is a specialized system or area dedicated to the processing of written words. To date, however, there has not been a systematic review of studies investigating number reading in pure alexia and so the status of this assumed dissociation is unclear. We review the literature on pure alexia from 1892 to 2010, and find no well-documented classical dissociation between intact number reading and impaired letter identification in a patient with pure alexia. A few studies report strong dissociations, with number reading less impaired than letter reading, but when we apply rigorous statistical criteria to evaluate these dissociations, the difference in performance across domains is not statistically significant. There is a trend in many cases of pure alexia, however, for number reading to be less affected than letter identification and word reading. We shed new light on this asymmetry by showing that, under conditions of brief exposure, normal participants are also better at identifying digits than letters. We suggest that the difference observed in some pure alexic patients may possibly reflect an amplification of this normal difference in the processing of letters and digits, and we relate this asymmetry to intrinsic differences between the two types of symbols.

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1. Introduction

Pure alexia is an acquired disorder of reading that leaves writing and other language skills unaffected (hence the term 'pure'). The disorder is characterized by slow and effortful but mostly correct reading, with a pronounced effect of word length on reading latency: Reaction times increase linearly with word length, often with hundreds of milliseconds per letter. Pure alexia is associated with a lesion impacting occipito-temporal areas of the left hemisphere, and damage to the left mid-fusiform gyrus, in particular, seems to play a causal role in this disorder (Leff, Spitsyna, Plant, & Wise, 2006). Other forms of acquired reading disorders, commonly termed *central alexias*, are seen following more widespread damage to temporo-parietal areas in the left hemisphere, and are associated with more general deficits in language like aphasia and agraphia. A question that continues to plague theories of pure alexia is whether the disorder is specific to alphabetic characters, and is caused by damage to or disconnection of a cerebral area dedicated to visual letter or word recognition (the so-called Visual Word Form Area; Cohen et al., 2003, 2004; Gaillard et al., 2006), or whether it emerges from a more general visuoperceptual deficit (Behrmann, Nelson, & Sekuler, 1998; Farah & Wallace, 1991; Starrfelt, Habekost, & Leff, 2009).

One way to adjudicate between these alternatives is to examine the performance of pure alexic patients when presented with other visual stimuli. It has often been suggested that number reading can be intact in patients with pure alexia (e.g.,Dehaene, 2009; Leff et al., 2001), but, to date, there has not been a systematic review of the evidence regarding number reading in these patients. If number reading can remain intact following a lesion causing pure alexia, this would offer convincing evidence of the specificity and selectivity of the disorder, and would support the hypothesis that pure alexia affects the processing of alphabetic material only. If, on the other hand, number reading is invariably impaired in patients with pure alexia, this would suggest a more general (visual) deficit being at the core of the disorder. In this paper, we review the literature on pure alexia from 1892 until 2010, and select for further investigation all papers that describe a pure alexic patient's reading of numbers. Our aim is to characterize the relationship between the reading of letters/words and numbers in pure alexia, and, in particular, to search for a possible dissociation of performance between these two symbol types.

An immediate challenge concerns the demarcation of pure alexia: although the definition of pure alexia is quite straightforward, different labels have been used for this disorder over the last century or so. Thus, all the following terms have been used to describe the same, or very similar, disorders: *pure alexia, global alexia, alexia without agraphia, visual alexia, verbal alexia, word blindness,* and *letter-by-letter (LBL) reading*. Some of the labels describe a variation in severity, for instance 'global alexia' refers to a total inability to read letters and words, while 'pure alexia' usually (but not consistently) refers to patients who are still able to read, although at an abnormal speed (and presumably using an abnormal strategy). Also, many different patients have been grouped under the heading of 'LBL reading', regardless of whether or not they are pure alexic. Many patients with LBL-reading have accompanying deficits in writing (e.g., Ingles & Eskes, 2008; Lambon Ralph, Hesketh, & Sage, 2004) and/or naming (e.g., Lambon Ralph et al., 2004), and/or make reading errors commonly seen in more central types of alexia (e.g., Friedman & Hadley, 1992; Ingles & Eskes, 2008). We have chosen to include all patients with disorders referred to by any of the labels mentioned above, and we comment on this issue in the results section.

Another challenge concerns what constitutes a dissociation. As clearly laid out by Shallice (1988), there are (at least) three types of dissociations in neuropsychology: (i) A *trend dissociation*, where a patient's score on task I is markedly lower than on task II, but where performance is not compared to a control group; (ii) a *strong dissociation*, where "neither task is performed at a normal level, but task I is performed very much better than task II" (p. 228). In this case, performance is commonly compared to a normal control group, but a patient's performance on tasks where normal controls would be expected to perform at ceiling may also constitute evidence for a strong dissociation (i.e., in the absence of directly comparing the patient to a control, one assumes perfect or near-perfect performance for normal individuals); and (iii) a *classical dissociation*, where – relative to normal controls – performance on task I is impaired while performance on task II is within normal limits. While trend dissociations are taken as a weak form of evidence, both strong and classical dissociations have been interpreted as suggestive of specialized functions or modularity. Recently, more refined (and operational) criteria specifying statistical demands for dissociations have been suggested (e.g., Crawford & Garthwaite, 2005, 2007; Crawford, Garthwaite, & Grey, 2003). In brief, this approach demands that, in order to conclude that there is a *classical* dissociation, the patient's scores should differ significantly from the control group on one of two tasks, while performance should be within the normal range on the other task, and – importantly – the difference between the patient's standardized scores in the two tasks should be significant. For the less stringent *strong* dissociation, there should be a significant difference between the patient's standardized scores on the two tasks in question, while both scores may differ significantly from the mean of the control group.

The presence of a clear classical dissociation would provide strong theoretical support for the independence or segregation of the system subserving processing of letters or words from the system(s) subserving the visual processing of numbers. The absence of a classical dissociation but evidence for a strong dissociation or a trend dissociation would require further explication—numbers and letters/words might be mediated by separate systems, both of which are damaged albeit differentially, or the two domains might potentially be subserved by the same system. If the latter were true, an explanation that accounts for the differential impairment between the two domains will be required. Clear evidence for separated areas or modules responsible for letter and digit processing must be supported by a pattern of *double dissociation* in which the complementary pattern of impaired and preserved abilities is observed. Thus, if we find a clear dissociation between letter and number reading in a patient with pure alexia, searching for a patient showing the opposite pattern (number reading impaired, letters spared) would be the obvious and necessary next step.

In sum, the goal of our investigation is to determine whether a dissociation between the reading of numbers and letters/words can be found in pure alexia, and if so, to examine the strength of the dissociation using Shallice's classifications and the operational criteria specified by Crawford et al. (2003), Crawford and Garthwaite (2005, 2007). We start by conducting an extensive review of the existing literature on pure alexia, focusing on studies reporting results from number reading tasks. We then go on to present new data from a psychophysical study of letter and digit identification in normal subjects, and, finally, we report an analysis of differences in image statistics between the two symbol types.

2. Literature review

2.1. Methods

For this review of the neuropsychological literature, we have included all studies of patients with *pure alexia, global alexia, alexia without agraphia, visual alexia, verbal alexia, or letter-by-letter (LBL) reading.* As mentioned above, these labels are often (but not always) used to refer to the same type of reading disorder, and, to ensure that no cases were missed, we adopted a policy of overinclusion in this first step. A thorough search of Web of Science, PubMed, PsychInfo, and ScienceDirect, as well as The Copenhagen Neuropsychology Database (www.gade.psy.ku.dk/database), using the above-mentioned keywords was performed. The latest search was conducted on August 27th 2010. Of the retrieved references, only studies of patients reading a script using Latin letters were included. Although interesting, associations and dissociations between reading of different Asian orthographies like Japanese Kanji and Kana are difficult to interpret in the current context. Only papers published in English were included, with one exception: because of its importance, we include Dejerine's (1892) original patient study (translated in Bub, Arguin, & Lecours, 1993; Rosenfield, 1988). Conference abstracts were generally disregarded, but one (Henderson, 1987) specifically describing a study of number reading in pure alexia, was included. Because of our focus on acquired deficits in the mature visual system, studies of children, including reports of developmental dyslexia, were also excluded.

From the assembled list, containing a total of 223 references, we selected all studies mentioning patients' performance with digits or Arabic numerals, whether formally assessed or just mentioned in the descriptive background information. This resulted in 76 papers reporting a total of 90 different patients, all of whom are included in this review. An overview of these papers and summary of the patient data can be found in Table A1 in Appendix A, which also lists (as far as possible) diagnosis given, aetiology, lesion site, visual field defect, and whether the patient was reported to have aphasia or agraphia.

2.2. Results

Many of the reviewed papers only summarize patient performance briefly, without presenting details of assessment methods or specific results. Further, even when details are presented, most studies lack a control group against whose performance the patient data can be compared. The absence of the normal benchmark makes it difficult to judge whether any observed difference between patients' performance with letters and digits reflects a normal pattern or asymmetry, or whether it is indicative of a true dissociation. Also, in many of the reviewed studies (as in most neuropsychological case studies in general), tasks are often quite simple in the sense that normal subjects would be expected to perform at ceiling. On the one hand, using simple tasks makes it unlikely that a difference between the tasks would be observed in the normal population, but, on the other hand, we do not know whether a difference in performance might be observed in normal participants under more difficult tasks (when the ceiling effect is removed). Most normal subjects do not make errors in naming letters and digits under conditions of free vision, but differences in performance with the two kinds of characters might still be revealed by more sensitive and taxing measures.

On this basis, we have grouped the individual case reports according to two parameters; whether or not they report a dissociation between performance with letters/words and digits, and, for those cases where a possible dissociation is present, how well supported this dissociation is by the evidence at hand. This has resulted in the four main groups of patients that will be described in the following sections (2.2.1–2.2.2.2.). Table A1 in Appendix A includes a numbered list of patients; these numbers are used for reference in the following sections as some papers report more than one patient, and patients reported in the same paper may show different patterns of performance.

As mentioned in the introduction, pure alexia may be referred to by different labels, and patients with associated deficits like anomia or agnosia may be referred to by some of these labels, too (e.g., LBL-reading). We include in our literature review all patients referred to by any of these different labels, and find no systematic pattern in the type of diagnosis/label for the patients' reading deficit and associated deficits, in relation to patients' performance with numbers. We have thus kept all patients in the analysis, although some have associated deficits like agraphia (and thus do not strictly conform to a diagnosis of alexia without agraphia or pure alexia). In the discussion of individual patients in the following sections, their associated deficits are commented on, and these are also listed in Table A1.

2.2.1. No dissociation

In 46 of the 90 reviewed patients, no dissociation between performance with letters and digits is reported. For 36 of these 46 individuals, both letter reading and number reading are reported to be impaired (cases 1–36 in Table A1). In many of these cases, the tasks administered to assess letter reading and number reading are not directly comparable, but roughly the same level of impairment is noted with both kinds of symbols. The majority of these patients will not be considered further (but see section 3.1. for a discussion of cases 33–36 reported by Starrfelt et al., 2009). In the remaining ten patients, the processing of (single) letters and of digits is reported to be unaffected (cases 37–46 in Table A1). For seven of these patients, no details of assessment are presented, and it is merely stated that the patient is able to name letters and numbers (cases 37, 38, 40, 42, 43, 44, 45), which makes it difficult to evaluate whether more subtle deficits were present in these patients and/or whether any deficits might have been uncovered with more sensitive testing. The remaining three patients are presented in some detail below.

Caffara (1987; case 39) reports flawless naming of single letters with 30 ms tachistoscopic presentation, in a patient with alexia following a left occipito-temporal hematoma. Naming of single digits was without error (12 trials) with 50 ms presentation. The exposure durations were chosen to "obtain the best approximate performance with the lowest presentation time" (p. 68). No normal data are presented, so it is unknown whether normal participants would be able to report letters or digits at even lower exposure durations, but at least the patients' performance on both stimulus types is good at relatively brief presentations times. These tests were performed three weeks after onset, and this patient's alexia remitted within ten months.

Relatively intact identification of letters and numbers was also noted in patient ROC reported by Warrington and Langdon (1994; 2002; case 41), who was diagnosed with spelling dyslexia following a large occipito-parietal stroke. ROC had a left uniocular nasal quadrantanopia. ROC's threshold for single letter identification was 35 ms, which is at the same level as a non-alexic control patient with spelling problems (Warrington & Langdon, 2002). No normal controls were tested, so it remains unknown whether ROC's performance is within normal bounds. At the very least, ROC's single letter recognition ability is superior to that commonly observed in pure alexia. ROC also performed speeded number copying at normal age level, relative to control subjects tested in another study. As the two tasks (recognition and copying) are not directly comparable, it is difficult to evaluate whether processing of both kinds of symbols were (un)affected to the same degree, but the presented data at least indicates that both letter and number reading was relatively normal.

Patient FC, reported by Rosazza, Appollonio, Isella, and Shallice (2007; case 46), suffered from pure alexia and a right homonymous hemianopia following stroke. His main lesion affected the left occipito-temporal region, but occipito-temporal structures in the right hemisphere were also affected, in addition to multiple, diffuse foci of chronic ischemic encephalopathy. FC had reaction times (RTs) within the normal range for both letter and digit naming, and was also within normal limits on letter identification under rapid conditions. No accuracy scores are given for the letter and digit naming tasks, so we cannot know whether the patient made more errors than controls. Assuming that accuracy was also within the normal range, this patient seems to have intact letter and digit identification skills. FC's RTs in word reading were slow (mean RT was approximately 1500 ms for words of 4–10 letters), with a modest word length effect of 70–90 ms per letter. He was impaired in some visual tasks (the object decision task from BORB and the silhouette task from VOSP). Rosazza et al. (2007) argue that FC has a deficit in integrating letters into letter groups and words, and that this deficit in itself is sufficient to give rise to pure alexia. This case is noteworthy because it may be the only one on record demonstrating normal RTs in both letter and digit naming in pure alexia, in spite of other visual deficits being present.[1] For our primary purposes, it is important to note the reported data show no dissociation between performance with letters and digits. The same is true for the two patients discussed above (Caffarra, 1987; Warrington & Langdon, 1994, 2002).

2.2.2. Possible dissociations

Findings that may indicate a dissociation between performance with letters and digits are reported in the remaining 44 patients (cases 47–90 in Appendix A). For 33 of these, the original papers lack the details necessary to reach any conclusions about the type of dissociation, either because tasks with letters and digits are not comparable ($N=5$; cases 47–51), or, more often, because too few details are given about assessment methods and stimuli ($N=28$; cases 52–79). We note that for all the 33 patients, performance is reported to be better with digits than letters, a point to which we return in the discussion, but these patients will not be considered in further detail here. Six patients (cases 80–85, discussed in section 2.2.2.1.) fulfil the criteria for a trend dissociation, with letter reading being more severely impaired than number reading. These studies lack a control group or use rather coarse tasks, and statistical comparison between tasks is not conducted. Four papers (five patients; cases 86–90, section 2.2.2.2.) report a strong dissociation, with the patients being impaired with both letters and digits, but disproportionately affected with letters. Two of these papers relate performance to that of normal controls, but as the patients do not perform within the normal range with digits, criteria for a classical dissociation (numbers spared, letters impaired) are not met.

2.2.2.1. Trend dissociations. Dejerine's (1892; case 80) original patient, Oscar C, is commonly described as having a massive pure (or global) alexia with spared number reading (e.g.,Dehaene, 2009; Geschwind, 1966). However, it is clear from the translation of Dejerine's work, and, in particular, from his quotes from the ophthalmological evaluation by Landolt (Rosenfield, 1988; see also Bub et al., 1993) that Monsieur C's number reading was far from perfect. Landolt noted that "if one shows him numbers, he is able to distinguish them, after some hesitation, from the letters" (Rosenfield, 1988; p. 34). He further reported that Monsieur C "reads the numbers poorly, since he cannot recognize the value of several numbers at once. When shown the number 112, he says, "It is a 1, a 1, and a 2", and only when he writes the number can he say "one hundred and twelve" (p. 35). This latter strategy resembles the letter-by-letter method employed by many pure alexic patients in word reading in which they spell out the individual letters sequentially and then assemble the pronunciation from this sequence ("C" "A" "T" and then 'cat'). There seems to be no doubt that Monsieur C was impaired not only in letter identification, but also in number reading. It is also clear, however, that his ability to recognize digits was superior to his letter recognition, as, according to the description, he was not able to name even a single letter from visual input alone. The information available about Monsieur C's number reading is limited, making it difficult to classify definitively the type of dissociation present in this case. As he was impaired in both tasks, and there was no comparison to a control group, we have tentatively classified this case as representing a trend dissociation, but we note that there seems to be a quite large discrepancy between his letter and digit identification skills.

Other studies report a pattern similar to the one observed in Monsieur C. Ajax (1977; case 81) reported a patient who was able to read multidigit numbers up to 10 digits correctly, while he showed difficulties with unisyllabic words, and was unable to read multisyllabic words. No further details from the reading assessment are presented. In another study, Landis, Regard, and Serrat (1980; case 82) reported a patient with alexia without agraphia following a glioblastoma affecting the left occipital lobe. They noted that "when presented with combinations of letters and numbers, he named the letters slowly but the numbers at normal speed" (p. 48). Grossi, Fragassi, Orsini, De Falco, and Sepe (1984; case 83) studied a patient diagnosed with alexia without agraphia, who was nonetheless impaired in writing single letters both spontaneously and to dictation. This patient could accurately name 30/30 "simple numbers" and 16/20 "complex numbers", while his scores with printed single letters and words were 38/42 and 2/50, respectively. In this case, the trend may be weak, as the major difference observed is between 'complex numbers' (not further specified) and words, but as there is an indication of dissociation of performance, we have included the study here.

A quite clear dissociation between number and letter reading was reported in the pure alexic patient VT (case 84; Maher, Clayton, Barrett, Schober Peterson, & Gonzalez Rothi, 1998). VT scored within the normal range on tests of visual perception (the VOSP or MVPT-V batteries), and scored 59/60 on the Boston naming task. She was able to match physically identical words, but was unable to match letters or words to stimuli presented in a different case or font. No single letter naming data are presented, but it is stated that VT "was not able to name individual letters from visual input alone" (p. 641), while she could read aloud numbers with one to five digits "accurately and without hesitation" (p. 639). In a search task, VT was able to detect the presence of an *X* in a string of letters, but RTs were slow and increased when the *X* appeared towards the end of the string. When searching for an *X* or a *0* in a string of numbers, VT's performance was "rapid and flawless, and there was no indication of an effect of place" (Maher et al., 1998; p. 639). Thus, it seems that the patient was better able to perceive several digits in a glance, but had to search letter sequences serially. In this case, the difference in performance with letters and numbers seems quite convincing at first glance, but unfortunately no details of assessment procedure (instructions, stimuli, order of tasks, etc.), response times or normal data are presented, which makes it impossible to judge fully the (ab)normality of VT's performance.

VT's inability to name single letters resembles the performance of Monsieur C (Dejerine, 1892; case 80), who, by today's criteria, would be classified as having global alexia (Binder & Mohr, 1992). In both patients, number naming seems better preserved than letter naming. A similar pattern is also evident in the global alexic patient (EA) reported by Larsen, Baynes, and Swick (2004; case 85). EA could name only 24% (6/25) of single letters at 500 ms exposure, while she named 84% (21/25) of single digits correctly. She was unable to read three letter common words presented for 2 s. She could name 60% (*N* not given) of two-digit numbers at 500 ms exposure, while performance deteriorated to 5% correct (1/20) with

[1] We are concerned by this patient's multiple lesions, and by his modest word length effect, which is lower than most pure alexic patients, and closer to the level commonly reported in hemianopic alexia (Leff et al., 2001). Future studies replicating this finding in other patients would be highly informative.

Table 1
Statistical comparison of processing speed (*C*) for single letters and single digits for (a) Patient NN and controls ($N = 5$; Starrfelt et al., 2010), and (b) Three patients and controls ($N = 9$) from Starrfelt et al. (2009). * marks performance significantly reduced compared to controls ($p < 0.05$; Crawford & Howell's test).

(a)	NN	Control mean (SD)		
Single letter C	22*	143 (47)[a]		
Single digit C	42°	138 (48)[a]		
(b)	TJ	JT	JH	Control mean (SD)
Single letter C	31*	27*	22*	117 (23)[b]
Single digit C	44*	47*	79*	119 (16)[b]

° $p = .07$, Crawford & Howell's test.
[a] Correlation between scores in the control group = 0.915.
[b] Correlation between scores in the control group = −0.130.

four-digit numbers. In sum, EA was obviously impaired in reading numbers, but at least naming of single digits seems relatively preserved compared to single letters.

In general, number reading seems relatively less impaired compared with letter reading, in all the six patients mentioned above. However, the tasks used are not very sensitive and most comparisons are based on accuracy scores, which, while useful, might not be sufficiently discriminatory. Also, performance is not compared to normal or patient (other lesion site) controls. Thus, although these studies suggest that number reading may be less affected than letter identification in these case of pure alexia, no definitive evidence is presented.

2.2.2.2. Strong dissociations. Very few studies of pure alexic patients have explicitly aimed to compare performance with letters and digits, and few make formal comparisons of patients' performance with the two types of symbols. We have identified four studies (reporting five patients, cases 86–90 Table A1) that do make such a comparison and find a significant difference between patients' performance with letters and digits. Only two of these studies compare patient performance to normal controls (Perri, Bartolomeo, & Silveri, 1996; Starrfelt, Habekost, & Gerlach, 2010), while one includes a group of patient controls (Ingles & Eskes, 2008). The fourth study (Cohen & Dehaene, 1995) may only meet the formal criteria for a trend dissociation as they do not compare the patients' performance to controls. We have chosen to include the study here, as it had as its stated goal the investigation of number processing skills in pure alexia, and the patients' performance with letters and digits in the same task was statistically compared. Also, the authors mostly used tasks where normal participants would be expected to perform at ceiling. We consider these four studies in greater detail below.

In a comprehensive study of two pure alexic patients, Cohen and Dehaene (1995; cases 86–87 in Table A1) showed that both patients made significantly more errors in naming single letters than single digits when compared using the Yates chi-square test ($p = 0.0004$ and 0.021 for the two patients, respectively). Both patients were also impaired in naming digits, but they were disproportionately impaired in reading words and letters compared to single- and multidigit numbers. Cohen and Dehaene (1995) also showed that their patients' accuracy in number reading depended on task demands. For instance, they noted significantly more reading errors *per digit* when patients were to read multidigit numbers as compared to single digits. This may be interpreted as an effect of task difficulty (reading two numbers at the same time is more difficult than reading one at a time). They also report that both patients were better at reading out digits in the context of a comparison task than in an addition task even though the exact same digits were used in both conditions. A similar effect was not observed when number words ('one' 'three') were used as stimuli. It is important to note that although performance with digits was better in the 'reading for comparison' than in the 'reading for addition' task, it was not perfect. Rather, the patients performed at the same level in the 'reading for comparison' task as they did in the single digit identification task. It seems then, that a general deficit in digit reading may be present in all conditions in Cohen and Dehaene's (1995) study, and that some additional factor (perhaps level of difficulty) contributes to the patients' error scores in the addition task compared to the more straightforward comparison task and the simple reading task. For the present purposes, the most important finding is that both patients were significantly better at reading digits than letters, although their performance with digits was also impaired. Whether or not this finding constitutes a strong dissociation in a strict sense (Crawford & Garthwaite, 2005) remains unknown, as performance was not compared to a control group. In addition, Cohen and Dehaene (1995) report that their patients' performance was far better in comparison tasks than in reading out loud: their patients could often decide which of two numbers was the larger, even when they misnamed the very same digits. They interpret this as reflecting the processing abilities of a (spared) right hemisphere system capable of identifying (but not naming) single digits, and of accessing magnitude information. As accuracy was the only dependent measure in this comparison tasks, it remains unknown if the patients' performance was at a normal level.

Perri et al. (1996) report a LBL-reader, SP, who, in addition to the impaired reading, also showed signs of agraphia and anomia (case 88 in Table A1). SP, unlike most pure alexics, made many errors in word reading, mostly due to letter confusions or misidentifications. SP also made errors in letter matching and pointing tasks. He identified 90% of single digits correctly, while he was 70 and 80% correct with lower and upper case letters respectively. No statistical tests on these data were presented in the paper, but a comparison of SP's performance with letters and digits using a chi-square test (data from Table 1 and text, Perri et al., 1996; p. 394) reveals a significant difference in performance with lower case letters vs. digits ($\chi^2 = 8.351$, $p = 0.004$), while the difference in performance with upper case letters vs. digits is only borderline significant ($\chi^2 = 3.676$, $p = 0.055$). No normal controls were tested in these tasks, but one would expect normal observers to perform at ceiling with all stimulus types, and thus it is unlikely that a similar difference in performance would be observed in normal individuals in these exact tests. SP was also tested on a "perceptual speed" task where a single target was to be identified in a row of five stimuli from the same category. This task used letters, digits and figures as stimuli (in separate conditions). Performance was compared to two normal controls, and to a non-alexic patient with a left parietal lesion. SP's accuracy was similar to that of normal controls for all three stimulus types, but he was slower to complete the test in all conditions. In addition, he was disproportionately slow in the letter condition, compared to the number and figure conditions (Numbers 115s.; Letters 210s.; Figures 130s. The two normal controls spent 60s. (SD = 0); 66s. (SD = 8.5); 62.5s. (SD = 3.5)). No statistical analyses were presented in the paper, but using Crawford and Howell's (1998) test on the reported data (Perri et al., 1996, Table 5) reveals that SP's performance with letters was indeed significantly slower than that of the controls ($p = 0.023$). He was, however, significantly slowed in the number ($p = 0.01$) and figure ($p = 0.018$) conditions too.[2] The control patient without alexia also performed better with digits than with letters (both in accuracy and RT), while his error rates in all three conditions were higher than for SP. This makes the interpretation of the difference in performance with letters and digits observed in SP difficult, and, in the words of the authors: "This finding suggests that these types of tasks may also be sensitive to deficits other than the ones affecting reading mechanisms" (Perri et al., 1996; p. 399).

Ingles and Eskes (2008) present patient GM (case 89 in Table A1), whom they classify as a letter-by-letter surface dyslexic (or Type 2 pure alexic) patient. GM also had surface agraphia and anomia. GM's accuracy in naming digits was significantly superior to his performance with letters in a RSVP (rapid serial visual presentation) paradigm ($p < 0.01$). This pattern was also found in a group of non-alexic patient controls, but the discrepancy between digits and letters was more pronounced in GM. In a speeded matching task, GM's RTs were elevated for letters compared with digits ($p < 0.01$), a pattern not found in the control patients. Importantly, GM's performance with digits in the matching task was impaired relative to patient controls, as was his performance with letters, and his performance in both conditions is likely to be far below the normal level (no normal controls were tested in this study). Again, while a difference in performance with digits and letters seems evident, the lack of a normal control group prevents us from deciding whether the patient's pattern of performance meets the criteria for a strong dissociation. Critically, as we discuss below, the data presented might well be accounted for by an intrinsic difference between letters and numbers (in terms of guess rate, visual confusability, nature of representation) rather than necessarily compelling an interpretation in terms of a letter/word-specific module.

Starrfelt et al. (2010) studied the performance of a pure alexic patent (NN; case 90 in Table A1) on psychophysical tasks using letters and digits as stimuli. Besides his alexia, NN showed no other impairments in language or cognition. This study was performed within the framework of the Theory of Visual Attention (TVA; Bundesen, 1990), which is described in some detail here, as it is also relevant for the analysis presented in the next section. TVA is a computational theory, and based on simple psychophysical tasks and mathematical modelling, several parameters in visual processing can be estimated. The two main parameters of interest in the study of NN was visual processing speed (or recognition efficiency) and visual apprehension span (the number of items that can be encoded into visual short term memory simultaneously), which were measured for letters and digits separately. NN participated in two experiments (single item report and whole report), which both make use of brief, masked stimulus presentation. After mask onset, subjects have unlimited time to name the stimuli, and thus naming latency does not affect scores within this paradigm. It should be noted that NN's accuracy in naming letters and digits in free vision was perfect.

In single item report, a letter or digit (in separate conditions) is presented briefly and then masked. Exposure durations are chosen individually, so that the subject's performance from floor (zero correct) to ceiling (100% correct) can be assessed (usually between 7 ms and 50 ms for normal observers). This enables the determination of the perceptual threshold (the exposure duration below which recognition is zero), and processing speed (indicating the speed of processing in items per second). In the whole report experiment, five stimuli are presented simultaneously in either the left or right field (usually left for pure alexic patients, as they commonly have a right visual field defect). Whole report also uses brief exposures (30–200 ms in these case studies), and requires the subject to name as many of the presented letters/digits as possible. Again, several parameters can be measured using data from a single experiment. Processing speed (now in the parafoveal visual field) and visual apprehension span are the most important parameters in the current context. Using this method, Starrfelt et al. (2010) found that NN's visual apprehension span was uniformly reduced for letters and digits, but that his processing speed at fixation was significantly reduced only for letters (data are presented in Table 1).[3] NN's central processing speed was comparatively better with single digits than single letters, and the ratio between the two scores was significantly different from the pattern observed in the controls (assessed with Crawford and Howell's test), strongly suggesting an asymmetry in letter/digit recognition. However, with respect to overall accuracy in the single digit report task, NN was significantly impaired compared to controls, indicating that his number reading was also not entirely normal.

2.3. A new analysis of published data

In a study of four pure alexic patients using the same TVA-based experiments and analyses described above, Starrfelt et al. (2009) found impaired performance with both letters and digits for all patients, compared to controls. Although no dissociations in single item processing speed were discussed in this paper (and the patients are listed as showing no dissociation of performance in Table A1; cases 33–36), a closer inspection of the patients' scores reveals that three of the patients did show better performance with single digits than with letters in the single item report task. For the purposes of the current review, we have re-analysed the data from these three patients (cases 34–36 in Table A1), along with data from patient NN mentioned above (Starrfelt et al., 2010), to explore possible dissociations using methods suggested by Crawford and Garthwaite (2005). This analysis first compares the scores of the patient to the control mean, using Crawford and Howell's (1998) test for a deficit. As is evident from Table 1, and also as reported in the original papers, all patients are significantly impaired with letters, and all but NN are also impaired with digits. Then the patient's scores are converted to z-scores based on the control-group results, and the z-scores are compared using the Revised Standardized Difference Test (RSDT, Crawford & Garthwaite, 2005), and the criteria for a dissociation (strong or classical) are met only if this difference is statistically significant. The patient and control data are presented in Table 1, and to illustrate the procedure, the analysis of patient NN's results can be seen in Fig. 1.

The analysis reveals that none of the four patients fulfils the criteria for either a strong or a classical dissociation in performance between single letters and digits, because the difference between their standardized scores on the two tests is not statistically significant. This means that a similar discrepancy in scores could be found in the normal population with a probability of $p > 0.05$. Even for the patient with the largest difference in performance (case 34 in Table A1; JH, Starrfelt et al., 2009), whose processing speed was

[2] The standard deviation for controls was set to 0.1 in the number conditions, to be able to perform this analysis. As we do not know the correlation between tasks in the controls, we cannot use Crawford and Garthwaite's (2005) methods for deciding whether a dissociation in present. Also, only two controls were tested, which further renders this analysis problematic. Thus, we do not know if SP's performance with letters was disproportionally impaired compared to his performance with digits.

[3] In the single digit test, one normal control performed at a very high level, creating quite large standard deviations in the small control sample ($N = 5$). The authors thus suggest that NN's processing speed may well be reduced for numbers also, but that this failed to reach significance due to the large SD's in the control group.

Step 1: Compares performance on Task I (single letter processing speed) to controls using Crawford & Howell's (1998) test for a deficit.

NN's score of 22 compared to 138 (SD = 48) for controls; t = - 2.35 (df = 4); p(one-tailed) = 0.03925

NN meets the criterion for a deficit on Task I.

Step 2: Compares performance on Task 2 (single digit processing speed) to controls using Crawford & Howell's (1998) test for a deficit..

NN's score of 42 compared to 143 (SD = 47) for controls; t = - 1.826 (df = 4); p(one tailed) = 0.07096

NN does not meet the criterion for a deficit on Task II.

Step 3: Compares the patient's z-scores on Task I and II using the Revised Standardized Difference Test (Crawford & Garthwaite, 2005), to test if the patient' s discrepancy between scores is greater than what could be expected in the control population.

Task I z-score = - 2.574
Task II z-score = - 2.00
t = -0.973 (df = 4); p(two-tailed) = 0.3858

The difference between the patient's standardized scores is n ot significant.

Step 4: Conclusion
The patient does not meet the criteria for either a strong or a classical dissociation.

Fig. 1. Illustration of procedure for analysing dissociations using Crawford & Garthwaite's (2005) method. NN's data compared to 5 controls (Starrfelt et al., 2010). Data are listed in Table 1.

about 3.5 times slower for letters than digits, the difference does not meet the statistical criteria for a dissociation: While she performs significantly differently from controls both with letters and digits, the difference between her standardized scores on the two tasks does not even approach significance (*z-digits* = −2.5, *z-letters* = 4.1, $t = 0.969$, $p = 0.36$). The same is true for patient NN, whose processing speed for single digits was within the low normal range: As the difference between his performance on the two tasks is not significant ($p = 0.39$), the results do not fulfil Crawford and Garthwaite's (2005) criteria for a strong or classical dissociation (see Fig. 1 for the full analysis). In sum, these data show that even quite substantial differences in performance with letters and digits may not constitute a dissociation in the statistical sense, as such differences may also be found in the normal population. Indeed, one of our controls had processing speed for letters at 83 letters/s and for digits at 123 digits/s, corresponding to *z*-scores of −2.25 and 0.261, respectively, and a larger *z*-score difference than both of the patients mentioned above (NN and JH).

2.4. Summary of results

The most important finding of our review is that there is not a single *well-documented* classical dissociation between a pure alexic patient's reading of letters and digits in the literature to date. "Normal", "fluent" or "unimpaired" reading of numbers have been reported, but only in papers where details of assessment are not given, or where the tasks presented are not comparable in any meaningful way. While it remains a possibility that one of these patients really does have normal number reading, this would represent a departure from the general findings in this review. Some papers do report strong dissociations between number and letter reading, but when stringent statistical criteria for dissociations are applied to the data from these studies, we find that the observed difference in performance does not meet the criteria for either a strong or a classical dissociation. Thus, there is no obvious evidence presented in any of the reviewed studies that demands an explanation on the level of a cerebral area dedicated to processing letters or words but not numbers. What we are left with then, are some cases that show a trend dissociation, which, as mentioned in the introduction, is generally thought of as a weak form of evidence for independence. Still, as the trend in all these studies points in the same direction (number reading is comparatively better than letter or word reading), one is left with the impression that number reading, in some cases, has been spared to a degree, and that this asymmetry needs to be explained.

3. Normal performance and visual similarity

3.1. Normal recognition of letters and digits

One possible explanation for the somewhat better reading of digits than letters in some pure alexic patients is that digits are simply easier to process, and that this may be true even for normal individuals. We start by investigating whether this is so and report findings from a psychophysical study in which normal recognition of single letters and single digits was recorded at varying, short exposure durations. We demonstrate that accuracy is higher for digits than letters and then, in the next section, we go on to investigate possible sources of this asymmetry.

3.1.1. Methods

In order to explore the recognition performance of normal observers with letters and digits, we have analysed data from a single item report task that was part of a larger study of visual attention (unpublished data, the study was conducted by the first author in

Table 2
A comparison of mean (SD) proportion correct responses in the single item report task for digits vs. letters for the six exposure durations, and the overall mean correct. Data are from 20 normal subjects, and were analysed using paired-samples *t*-test.

	Digits	Letters	t (df = 19)	p
13 ms	0.39 (0.25)	0.29 (0.22)	4.3	<.001
20 ms	0.74 (0.19)	0.58 (0.26)	5.6	<.001
27 ms	0.91 (0.09)	0.78 (0.21)	3.5	<.01
33 ms	0.95 (0.05)	0.88 (0.14)	2.8	<.02
40 ms	0.97 (0.03)	0.91 (0.11)	3.0	<.01
53 ms	0.98 (0.03)	0.97 (0.05)	0.77	.454
Total	0.82 (0.10)	0.73 (0.15)	4.8	<.001

collaboration with T. Habekost and K.I. Karstoft at the Center for Visual Cognition, Copenhagen University). The subjects (university students, $N = 20$, 10 female) performed a single item report task similar to the one described in section 2.2 (Starrfelt et al., 2009, 2010). Digits (0–9) and upper case letters (A–J) were run in separate blocks of 120 trials in a ABBA–BAAB design ($N = 480$ trials per stimulus type per subject; half the subjects did letters first, half did digits first). Before the start of the experiment, the participants were shown the 10 digits and the 10 letters, and were asked to read through them. Subjects were told that only the letters A–J would be used as stimuli in the letter condition. Stimuli were computer generated, and did not conform to any known typefont (but resemble the Rumelhart and Siple font, see Starrfelt et al., 2010 for images of stimuli and mask). Stimuli were presented in white on a black background.

On each trial, a single item, either digit or letter, was flashed briefly using six different exposure durations randomly intermixed (range 13–53 ms) and immediately followed by a pattern mask for 500 ms (screen refresh rate was set so there was no delay between stimulus and mask). Subjects were to report the stimulus if they were fairly certain of its identity and there was no requirement to report the stimulus at speed. Accuracy was recorded.

3.1.2. Results

Mean accuracy scores were computed for letters and digits separately for all six exposure durations, and an overall correct score (summed over all exposure durations) was also computed for letters and digits separately. Data are presented in Table 2. A comparison using a paired-samples *t*-test shows that overall accuracy was significantly higher for digits than letters ($t_{19} = 4.78$, $p < .001$). Also, subjects performed significantly better with digits than letters on average in the five conditions with the shortest exposure durations (13–40 ms; see Table 2). In the condition with the longest exposure duration (53 ms), there was no difference in accuracy for letters and digits, as performance with both was at ceiling, with mean accuracy of 97% and 98%, respectively.

In sum, these findings indicate that digits are significantly easier to identify than letters for normal subjects under conditions of brief, masked exposure, that is, when the perceptual information about the stimuli is limited. Also, the findings show that normal observers reach ceiling performance with both letters and digits at relatively brief exposure durations. This pattern of results is important as it suggests that the tendency towards better performance with digits than letters in pure alexic patients might reflect an amplification of a normal difference in symbol processing. This still, however, begs the question of where this difference originates.

3.2. Visual similarity for letters and digits

There are a number of potential sources for the asymmetry in performance with letters and digits. One is that the guessing rate differs for the two types of symbols. With pure guessing, the chance of getting the correct digit is 1/10, while it is only 1/26 in letters, thereby affording better guessing with digits than letters. Guessing may be invoked under difficult encoding conditions, such as the very brief exposure conditions reported in section 3.1. However, we do not usually proceed with wild (unconstrained) guessing when identifying visual stimuli. Rather, we commonly have at least some information available, on which we base a ‘qualified perceptual guess’, and the degree of within-category visual similarity is likely to be important in this process. Specifically, under conditions of insufficient evidence for a particular target, the number of within-category competitors (other letters or digits) that resemble the target become important. Here we explore whether visual similarity or discriminability differs between letters and digits, using two different methods: First, we compare image-based pairwise similarity for the two categories and, second, we measure the number of within-category competitors as a function of different levels of discriminability. In the latter analysis, we also take into consideration that, as a raw number, there are potentially more competitors for letters than for digits.

3.2.1. Methods

There are many ways to compare the image properties of letters and digits – for example, one might count absolute strokes per symbol or the number of curved vs. straight strokes. To avoid making any a priori assumptions on how to carve up the symbols, we computed letter and digit image-based similarity using one of the simplest methods for template matching and similarity estimation: normalized cross-correlation (Lewis, 1995). To do so, we cross-correlated each pair of symbol images, and found the peak of the cross-correlation map, that is, the horizontal/vertical translation of one image with respect to the other that maximizes their alignment. We then recorded the respective correlation coefficient (i.e., degree of overlap between the two images, see Fig. 2a) as an estimate of similarity: the higher the correlation, the more similar the images of the two symbols. This provides an estimate of maximal similarity between two symbols, and the cross-correlation coefficient can be thought of as the worst-case scenario when discrimination of a symbol from its competitors is most difficult. This analysis was done separately for letters and digits displayed in high contrast (black against white background) and it was done for two

Fig. 2. Illustration of physical overlap (cross-correlation) between symbols. On the left we have overlaid an Arial font ‘9’ (dark grey) on ‘0’, and ‘0’ (dark grey) on ‘9’; these symbols have a very high cross-correlation of 0.85. On the right an illustration of overlaying ‘v’ (dark grey) with ‘n’, and ‘n’ (dark grey) on ‘v’, respectively; these two letters have a quite low cross-correlation of 0.37.

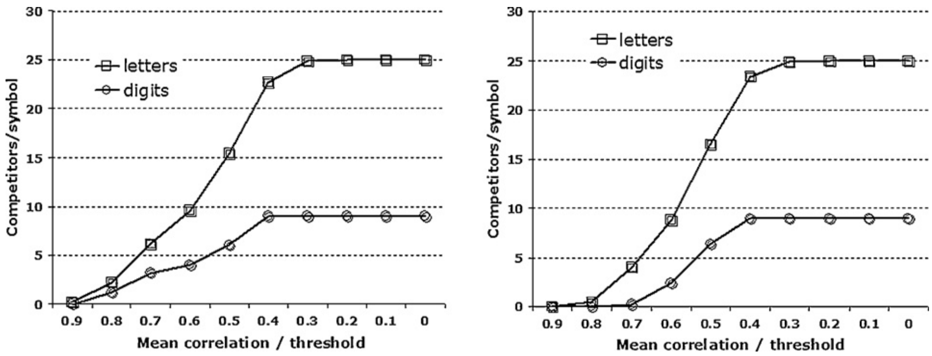

Fig. 3. Illustration of the number of competitors for letters and digits in Arial (left panel) and Times (right panel) fonts, based on the pairwise cross-correlation analysis of the symbols. 'Mean correlation/threshold' refers to the interval of pairwise cross-correlation coefficients, and within each interval the average number of competitors per symbol are shown, separately for letters and digits. The higher the number of competitors per symbol, the higher the confusability.

different fonts, Times and Arial. Letters were in lower case as this is the more common case encountered in text reading and captures the perceiver's task more veridically.

3.2.2. Results

In Arial, the mean similarity (cross-correlation) across symbol pairs was 0.58 (SD = 0.15) for letters and 0.61 (SD = 0.15) for digits, and the corresponding values for Times were 0.57 (SD = 0.12) and 0.55 (SD = 0.08). A t-test conducted within each font reveals no significant differences between the two symbols types, indicating that, with this measure, the within-category similarity for letters and digits is about equal. This result does not support an explanation of the behavioural asymmetry based on pairwise symbol similarity (although it is possible such a difference might exist for types of font other than those tested here). However, this comparison may not be the most informative, since letters and digits are normally recognized as part of the entire set of letters and digits, respectively, rather than as a forced choice between just two alternatives. Thus, a more meaningful comparison should take into account the visual similarity of all potential competitors and should also factor in the category set.

Therefore, the procedure we adopted was to determine the average number of competitors as a function of discriminability threshold separately for letters and digits, where discriminability is indexed by a given cross-correlation threshold. For example, using the pairwise similarity values previously computed, we find that the letter 'a' has two competitors if the discriminability threshold lies in the 0.7–1 range, i.e., two letters have a pairwise cross-correlation with 'a' higher than 0.7 ('n' and 'u'). This rises with eight competitors if the discrimination threshold is lowered to 0.6–1 (including 'o', 'c' and 'e'), another 12 for 0.5–1 (such as 'm', 'p' and 'b'), and all letters when we drop the discrimination threshold to 0.4 (adding the last two 'y' and 'v' to the set). For each symbol, we added up the average number of confusable stimuli within each threshold interval, as plotted in Fig. 3 for the Times and Arial symbols (the actual numbers are shown in Table 3). Looking at the Times figure, we see that, on average, every letter starts with no competitors if the discriminability threshold is high, but acquires systematically more competitors as we lower the discriminability threshold (e.g., 4 within the 0.7–1 range) and ends up with the entire letter set when the threshold is low enough. The same is true for the Arial font analysis.

The important point here is that letters have more competitors than digits for any given discriminability threshold below the most optimal. This has to be the case with low thresholds, because there are more letters than digits and thus many more possible competitors. However, Fig. 3 shows that this asymmetry is also present when discriminability threshold is high enough to exclude many of the items in the total stimulus set. For instance, if we index confusability as the number of symbol pairs achieving a similarity score above a 0.7 threshold, then the confusability of letters is about twice the confusability for digits. In conclusion, when an observer encounters a single letter, there are more possible competitors (average of all pairwise confusability measures) than is the case for digits and this is true even when one holds constant the discriminability threshold to equate for the set size for letters and digits. On this basis, single symbol identification should be more difficult for letters than for digits (at least for the fonts we have investigated here), when the amount of available visual information is limited.

Table 3
Average cumulative frequency of letters and digits (per symbol) in the different ranges of cross-correlation for (a) Times and (b) Arial. See also Fig. 2 for a graphical illustration.

Cross-correlation threshold	Letter	Digit
(a)		
0.9	0	0
0.8	0.5	0
0.7	4	0.2
0.6	8.9	2.4
0.5	16.5	6.4
0.4	23.4	9
0.3	24.9	9
0.2	25	9
0.1	25	9
0	25	9
(b)		
0.9	0.2	0
0.8	2.2	1.2
0.7	6.2	3.2
0.6	9.6	4
0.5	15.4	6
0.4	22.7	9
0.3	24.9	9
0.2	25	9
0.1	25	9
0	25	9

4. Discussion

This aim of this paper is to examine whether number reading can be intact in pure alexia. If so, this would support the hypothesis that pure alexia is a domain-specific deficit in visual word- and letter-processing. Understanding the mechanism(s) underlying pure alexia would not only elucidate the origin of this particular disorder but, more generally, would shed light on an ongoing debate about the nature of brain-behaviour organization. Specifically, much recent literature argues in favour of a circumscribed word recognition system (the so-called Visual Word Form Area; VWFA), which is specialized for or even selectively dedicated to processing alphabetical input (Cohen et al., 2003, 2004). Intact number reading in patients with pure alexia, whose damage is usually to the VWFA and surrounding structures (Leff et al., 2006) would provide compelling evidence for cerebral specialization for visual word recognition. Such a finding would be particularly informative because there are so many similarities between letters and digits; hence if the deficit affected letters selectively, this would strongly endorse the view of a domain-specific orthographic system. An alternative proposal is that the mechanism mediating visual word processing is somewhat more general-purpose and capable of representing multiple types of input, but is perhaps optimized for word recognition (e.g., Behrmann, Nelson et al., 1998; Behrmann, Plaut, & Nelson, 1998; Starrfelt & Gerlach, 2007; Starrfelt et al., 2009). On one recent account, the VWFA serves to bridge between higher-order visual areas and language areas and, while this cortical region is not dedicated for letter/word recognition per se, the bidirectional connectivity between these regions fine-tunes the VWFA for maximal efficiency in representing alphanumeric symbols (Plaut & Behrmann, in press).

To assess the evidence for a dissociation between number and letter reading in pure alexia, we undertook a comprehensive review of the literature on pure alexia from 1892 to 2010. We adopted a stringent classification system based on Shallice's (1988) definitions of dissociations, coupled with recent guidelines for assessing the statistical legitimacy of the empirical observations (i.e., testing statistically if the observed difference in performance is larger than what could be expected in the normal population, Crawford et al., 2003). Interestingly, we did not find a single study documenting a classical dissociation in which letter or word reading is impaired while number reading is fully preserved. Several studies do report better performance with digits than letters (40 of the 76 reviewed studies, reporting a total of 44 patients), but most of these (30 studies reporting 33 patients) do not report sufficient details about methods or results for us to evaluate the status of the reported dissociations. Some studies show a statistically significant difference between processing of letters and numbers in pure alexic patients (e.g., Cohen & Dehaene, 1995; Ingles & Eskes, 2008), but none of these studies conform to stringent statistical criteria for a strong dissociation (Crawford et al., 2003). In some cases ($N = 10$), letter and number reading are both reported to be intact, but, in nine of these, a control group is lacking. The exception is a study by Rosazza et al. (2007). They show that their patient FC had normal reaction times in naming both letters and digits, but do not present accuracy data for these tasks. In other tests of visual recognition, the patient was impaired.

Thus, within the bounds of our stringent framework, we are left with a few studies (10 studies reporting 11 patients) that show a *trend* dissociation, with number reading being less affected than letter and word reading. This does not constitute evidence for selectivity or cerebral specialization for visual word processing, but it is remarkable that the trend points in the same direction in almost all cases of pure alexia; performance with digits is better than with letters.[4]

Inferences about separability of systems not only demand a single dissociation (independent of its strength) but also the complementary pattern of preservation and loss. In some patients with more general language disorders following lesions to temporo-parietal areas in the left hemisphere, a pattern of performance opposite to the trend in pure alexia, has been reported: impaired reading of numbers and even of number words, with relatively preserved word reading (e.g., Marangolo, Nasti, & Zorzi, 2004; see Piras & Marangolo, 2009 for an overview). This has led to a discussion about a separate semantic system for numbers, and even a separate output lexicon for number names (e.g., Marangolo et al., 2004), and to theorizing about the relation between language and number processing at levels involving conceptual (rather than perceptual) representations (e.g., Gelman & Butterworth, 2005). However, to our knowledge, there are no reports of a number reading deficit with spared letter reading following damage to perceptual/temporo-occipital areas of the brain, akin to the locus underlying pure alexia.[5] Thus, there is no extant evidence from lesion studies, including the ones we have reviewed, for a strong or classical single dissociation (and therefore no double dissociation) between visual identification of letters and numbers. And yet there is this trend...

One possible account of a difference in performance between any two tasks, and indeed the first explanation to consider for a single dissociation observed in brain injured subjects (Shallice, 1988), is that one task is merely more difficult than the other. This might be the case here: When we investigated the performance of normal observers required to identify letters and digits under brief exposure durations, we found better identification of digits than letters at all but the longest exposure duration, at which point performance was approaching ceiling in both cases. Our interpretation of this observed superiority for digits in normal subjects is that the relative preservation of digit over letter processing in pure alexic patients might simply reflect damage to a common system for processing of alphanumeric symbols. The difference in performance observed in patients seems larger than that demonstrated in normal subjects, perhaps because the difference observed in normals may be be exacerbated following brain injury; thus, when the system is perturbed, the more vulnerable of the two domains is disproportionately affected. This still leaves the question, however, of *why* digits are more easily identified than letters when visual information is limited.

One contributing factor could be the difference in *guessing rate*, given that there are simply more letters than digits. When visual information is limited or degraded, and thus accuracy < 100%, the probability of correct guessing may influence the proportion of correct responses. In our study reported in section 3.1, the normal participants were informed that the target digit would be one of 10 digits and the target letter would be one of 10 possible letters. They were familiarized with the stimuli prior the experiment to minimize the difference in guessing rate between the two stimulus types. Even under these conditions, performance was better for digits than letters. There is the possibility that the entire character set, rather than the specific subset, might automatically be activated or accessible even under these 'equated' conditions, a point that illustrates how difficult it is to create comparable experimental conditions for letters and digits. There is also the possibility that digits are simply easier to recognize than letters regardless of the size of the character set, but perhaps because of structural aspects. On the basis of our analysis of image statistics, where we performed a normalized cross-correlation pairwise for all letters and for all digits, we suggest that the superiority of digits over letters may be related to the number of visually similar competitors for the two sets of symbols. This analysis showed that digits are more

[4] Judd et al. (1983) report a rare exception: They note that in their patient "number reading was worse than his letter reading" (p. 445), but no further details are provided.

[5] Searching the literature for a selective number reading deficit is more difficult than a search for pure alexia, as there is no syndrome label for a primary deficit in number reading with intact writing and calculation, or for a pattern of performance with impaired number reading and intact letter reading. We have performed a search for the keywords 'number alexia' and 'number agnosia' in Web of Science, which retrieved no references.

discriminable than letters in the sense that letters have more visually similar competitors even when the discriminability threshold is very high, e.g., when only symbols cross-correlating 0.7 or more with the target symbol are defined as competitors. This index of discriminability would be expected to be most important for symbol identification when the amount of available visual information is suboptimal, as is the case when stimulus presentation is experimentally degraded, or – as may be the case in pure alexia – when it is degraded by a lesion affecting visual perception. Thus, even if both numbers and letters were processed by a single system for visual recognition, and this system was affected by the lesion causing pure alexia, the differential demands of processing numbers vs. letters could give rise to the apparent superiority of numbers over letters.

We have focused thus far on perceptual differences between letters and digits, but there are also high level, semantic differences between numbers and letters that may affect perceptual processing of these stimuli. Digits have a concrete referent (amount), and thus may be associated with semantic value or semantic representations in a different way than single letters, that are commonly only meaningful in strings (see Cohen & Dehaene, 1995). This could give rise to greater top-down effects on the speed and accuracy of digit recognition compared with letter recognition, particularly in cases where visual information is limited. In a similar vein, it has been suggested that top-down effects on word recognition in pure alexia, both in reading and lexical decision tasks, may interact with the severity of the patients' reading problems (Behrmann, Plaut et al., 1998; Roberts, Lambon Ralph, & Woollams, 2010). The general hypothesis is that for mildly affected patients, bottom-up activation is sufficient to generate the correct response, while for moderately affected patients in whom bottom-up input is slow and error prone, top-down effects may significantly aid recognition. For the most severely affected patients, because the bottom-up activation generated by the stimuli will be too weak, top-down processing will be of no assistance. It is possible that such an account might also explain the trend towards better reading of digits, which may have more semantic (top-down) support, than letters. This account makes a counterintuitive prediction that there will be relatively greater divergence between digit and letter recognition in more moderately than more mildly affected pure alexic patients since the former will benefit more from top-down support for digits. Thus, the relationship between performance and the suggested visuoperceptual impairment in pure alexia may not always be straightforward, and we suggest that the differences between letter and digit processing may be explained by an account in which stimulus characteristics (e.g., visual discriminability and semantic value) interact with task type (e.g., naming vs. magnitude comparison) and impairment severity.

Other explanations also remain possible. For instance, the hypothesis that number reading is more bilaterally distributed than letter and word reading, and therefore more likely to be relatively preserved in pure alexia (Cohen & Dehaene, 1995, 2000) cannot be ruled out by the presented findings. However, even if there is a right hemisphere system with capabilities for number recognition, it seems clear from the present review that the left hemisphere damage associated with impaired letter processing in pure alexia also affects number reading. We suggest that this is caused by a visuoperceptual impairment that impacts alphanumeric processing more generally. Determining the nature of this visuoperceptual impairment has been the subject of many previous papers (for some examples, see Behrmann, Nelson et al., 1998; Farah & Wallace, 1991; Fiset, Gosselin, Blais, & Arguin, 2006; Starrfelt et al., 2010). While there seems to be general consensus that the problem arises at higher levels of visual representation rather than in early visual cortices, and the typical lesion site is consistent with this claim, the exact nature of the impairment remains ill-specified. One possibility is that the lesion impacts fine-grained discriminations between homogenous symbols. The siting of the lesion associated with pure alexia in what would be the anterior extrapolation of the fovea (Hasson, Levy, Behrmann, Hendler, & Malach, 2002; Plaut & Behrmann, in press) is consistent with this. Suffice it to say that this difficulty in pattern recognition can slow down the speed of visual processing, reduce visual span, and give rise to visual confusions and various crowding effects. This problem in pattern discrimination functionally compromises the representations of both letters/words and numbers, but the emergent pattern of relatively less impaired digit over alphabetic symbol recognition may nevertheless persist.

This paper focuses on dissociations between digits and letters, but it would be fruitful to explore the extent to which the suggested perceptual deficit in pure alexia affects processing of other classes of visual stimuli. For instance, the ability of pure alexic patients to read musical notation – which we would expect to be affected by the perceptual deficit suggested above – is largely unexplored. The few studies on record investigating this issue present contradictory findings (see Horikoshi et al., 1997 for an overview), much in the same way that the literature on number reading has seemed contradictory. Picture naming has been quite extensively studied in pure alexia, but here too the findings are inconsistent. Normal picture naming has been reported in some pure alexic patients with regards to accuracy (e.g., Gaillard et al., 2006; Maher et al., 1998; Starrfelt et al., 2010), while in tasks measuring RTs (e.g., Starrfelt et al., 2009) or where subtle object discrimination is required (Sekuler & Behrmann, 1996; Starrfelt et al., 2010), performance is commonly impaired. As the severity of visuo-perceptual problems in pure alexia has been found to be related to reading skills (Mycroft, Behrmann, & Kay, 2009), further exploration of the nature of these problems seems important. In general, investigating apparent dissociations, e.g., between recognition of words and other objects in pure alexia, using sensitive tests and the statistical methods applied here, could provide important insight into the workings of the cerebral systems underlying visual recognition and offer further constraints on theories of brain-behaviour correspondences.

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Appendix A.

A complete list of references mentioning alexic patients' performance with numbers are listed in Table A1. Studies are listed in groups, defined by whether a dissociation in performance with letters and digits seems to be present, and how well supported this dissocation is by the presented data. The column labels and abbreviations used are listed and explained below the table.

Aetiology: The reported cause of the observed reading deficit. Abbreviations: (h) = hemorrhagic/hematoma; (surg) = following surgery; AVM = Arterio-venous malformation; CJD = Creutzfeldt-Jakob disease; HSV = Herpes simplex virus: MS = Multiple sclerosis; NR = not reported; TBI = Traumatic brain injury; ? = uncertain diagnosis.

Diagnosis: The label for the observed reading disorder provided by the authors of the original papers. Abbreviations:

Table A1

	Author (year; patient)	Aetiology	Diagnosis	Lesion	Visual field	Agraphia	Aphasia
Ia. Number and letter reading both impaired at roughly same level.							
1	Joy (1947; CS)	Trauma	AWA(ag)	NR	URQ	no	an
2	Kinsbourne and Warrington (1963; Mrs.B)	h_surg	SD	L STG; ITG	RH (ambl.)	no	no
3	Collignon (1972; Mrs.B.L.)	Stroke	PA	L posterior	RH	no	NR
4	Caplan and Hedley-Whyte (1974; XX)	Stroke	AWA	L temp-occ; Scc; Hi; Th; LG	RH	slight	an
5	Woods and Pöppel (1974; XX)	TBI or stroke	AWA	NR	RH (partial)	no	nam
6	Vincent, Sadowsky, Saunders, and Reeves (1977; XX)	Meningioma	AWA	L inf temp-occ.	None	no	no
7	Holtzman, Rudel, and Goldensohn (1978; XX)	Meningioma(surg)	AWA	L inf temp-occ; AnG	None.	no	no
8	Levin and Rose (1979; XX)	Meningioma(surg)	AWA	L occ-temp; Scc	RH	slight	an
9	Shipkin, Grey, Daroff, and Glaser (1981; XX)	Atrophy	AWA	Diffuse	LH	no	no
10	Judd, Gardner, and Geschwind (1983; BL)	Stroke(h)	AWA	L occ-temp	RH	yes	nam; comp
11	Henderson, Friedman, Teng, and Weiner (1985; XX)	Stroke(h)	PA	L FuG; ITG; O2	None	no	no
12	Henderson (1987; Pt.1)	NR	PA	NR	NR	NR	NR
13	Henderson (1987; Pt.2)	NR	PA	NR	NR	NR	NR
14	Henderson (1987; Pt.3)	NR	PA	NR	NR	NR	NR
15	Coslett and Saffran (1989; JG)	Multiple strokes	PA	LG; or; Scc	RH	no	no
16	Coslett and Saffran (1989; TL)	Stroke	PA	L occ; fmj	RH	NR	no
17	Coslett and Saffran (1989; JC)	Stroke	PA	L occ.; fmj; pic	RH	yes	no
18	Farah and Wallace (1991; TU)	AVM/stroke	PA	L temp	RH	NR	an
19	Iragui and Kritchevsky (1991; XX)	Stroke	AWA	L subangular	None	yes	nam; comp
20	Price and Humphreys (1992; EW)	Stroke	LBL	NR	RH	NR	dys
21	Price and Humphreys (1992; HT)	TBI(surg)	LBL	L par-occ	None.	yes	nam
22	Coslett, Saffran, Greenbaum, and Schwartz (1993; JWC)	Stroke	PA	L med occ; PHG; pic	RH	NR	nam
23	Buxbaum and Coslett (1996; JH)	Stroke	LBL(deep)	L inf temp-occ; PHG; LG	RH	no	no
24	Sekuler and Behrmann (1996; MA)	TBI	PA	Bilat	RH	surface	nam(RT)
25	Sekuler and Behrmann (1996; DS)	Stroke	PA	L occ	URQ	no	nam
26	Sekuler and Behrmann (1996; MW)	Stroke	PA	L occ	?	NR	nam(RT)
26	Behrmann, Plaut et al., (1998; EL)	Stroke	PA	L inf temp; lat temp; dor par	URQ	no	nam(RT)
27	Miozzo and Caramazza (1998; GV)	Stroke	PA	L occ-temp; Scc; R par	RH	no	Optic aph.
28	Cohen and Dehane (2000; VOL)	Stroke	PA	L inf med occ-temp	RH	no	nam; comp
29	Dalmas and Dansilio (2000; AA)	Stroke	AWA(vg)	L ccs; LgG; FuG; Scc; Hi; PHG; Th	RH	no	no
30	Lambon Ralph et al. (2004; FD)	Stroke(h)	PA	Multiple: L occ; L par-temp; R par; R occ	RH	yes	an
31	Armbruster and Wijdiks (2006; XX)	Stroke	PA	L occ-temp	RH	no	nam
32	Rosazza et al. (2007; LDS)	Stroke	PA	L ITG; FuG; ots; O4 + bilat front	RH	no	no
33	Starrfelt et al. (2009; BA)	TBI(h)	PA	L ITG; FuG; PHG	RH	no	nam(RT)
34	Starrfelt et al. (2009; JH)	AVM(h)	PA	L 17; O2; O3; O4; LgG; MTG; ITG; FuG	RH	no	nam(RT)
35	Starrfelt et al. (2009; JT)	Stroke	PA	L 17; O2; O3; O4; LgG; ITG; FuG; PHG	RH	no	nam(RT)
36	Starrfelt et al. (2009; TJ)	Stroke	PA	L O2; FuG; PHG	none	no	nam(RT)
Ib. Number and letter reading both reported normal or intact.							
37	Greeblatt (1976; XX)	AVM(surg)	AWA(trans)	L temp-par	None (R extinction)	no	no

Table A1 (*Continued*)

	Author (year; patient)	Aetiology	Diagnosis	Lesion	Visual field	Agraphia	Aphasia
38	Rosati, Debastiani, Aiello, and Agnetti (1984; XX)	Stroke(h)	AWA	L ITG; O2	URQ	no	no
39	Caffarra (1987; MR)	Stroke(h)	AWA	L post LOTG	None	no	no
40	Daniel, Bolter, and Long (1992; KV)	Stroke(h)	AWA	L temp-par-occ	URQ + LoRQ (partial)	yes	an
41	Warrington and Langdon (1994, 2002; ROC)	Stroke	SD	L occ-par	L eye nasQ	no	no
42	Dogulu, Kansu, and Karabudak (1996; XX)	MS	AWA	L occ.; Scc; Bilat ic	RH	no	no
43	Mao-Draayer and Panitch (2004; XX)	MS	AWA	L occ; Scc	RH	no	no
44	Verma, Singh, and Misra (2004; XX)	Neurocysticercosis	AWA(trans)	L occ	RH	no	no
45	Celebisoy, Sagduyu, and Atac (2005; XX)	Stroke(h)	PA	L occ	RH	no	no
46	Rosazza et al. (2007; FC)	Stroke	PA	L OcP; LgG; PHG; O4; R O2 + O4	RH	no	no
IIa. Possible dissociation (numbers > letters). Tasks not directly comparable.							
47	Warrington and Shallice (1980; RAV)	Stroke(h)	WFD	L temp-par	RH	no	an
48	Patterson and Kay (1982; TP)	Angioma(h)	LBL	L occ-temp-par	RH	surface	an
49	Leegaard, Riis, and Andersen (1988; XX)	Stroke(h)	PA	L dors lat occ	URQ	no	wfd
50	Di Pace, Guariglia, Judica, Spinelli, and Zoccolotti (1995; GM)	TBI	LBL	Bilat front; L occ; ox; R occ	R scotoma right eye; left eye 10/1200	NR	no
51	Chialant and Caramazza (1998; MJ)	Stroke	LBL	Multiple wm lesions; or; cc	RH	no	no
IIb. Possible dissociation (numbers > letters). Poorly described or tested.							
52	Geschwind and Fusillo (1966)	Stroke	PA/AWA	L ccs; Scc; or; Hi; VPL	RH	no	no
53	Lee (1966)	Trauma?	AWA	NR	RH	no	an
54	Cumming, Hurwitz, and Perl (1970; WL)	Stroke	AWA	L occ; Scc	RH	no	no
55	Benson, Brown, and Tomlinson (1971; Case 1)	Stroke	AWA	L post med	RH	no	an
56	Goldstein, Joynt, and Goldblatt (1971; XX)	CO-poisoning	AWA	Diffuse	None	no	no
57	Wechsler, Weinstein, and Antin (1972; Case 1)	Stroke(h)	PA	L occ-temp	RH	no	an
58	Wechsler et al. (1972; Case 2)	AVM(h)	PA	L post temp-occ	RH	no	nam
59	Wechsler et al. (1972; Case 3)	Stroke(h)	PA	L occ-par	RH	no	an
60	Greenblatt (1973; XX)	Glioblastoma	AWA	L FuG; LgG; wm	None	yes	nam
61	Fincham, Nibbelink, and Aschenbrener (1975; XX)	Metastases	AWA	L PrG; SMG; R multiple	LH	no	no
62	Luhdorf and Paulson (1977; XX)	NR	PA	NR	Incomplete RH	no	nam
63	Karanth (1981; NR)	NR	PA	NR	RH	slight	nam
64	Winkelman and Glasson (1984; XX)	Stroke	AWA	R temp; occ; par; Th; fmj; Scc;	LH	no	nam/wfd
65	Lang (1985; XX)	Stroke (multiple)	AWA	L MOTG; LOTG; O2; PHG; Scc; basal ganglia	URQ	slight	nam/wfd
66	Pena Casanova, Roig Rovira, Bermudez, and Tolosa Sarro (1985; AR)	Stroke	AWA	L med temp	LH	no	no
67	Regard, Landis, and Hess (1985; XX)	Metastases	PA	L occ; front; R par	RH	no	nam
68	Marks and DeVito (1987; Case1)	Stroke	AWA	L inf occ; post temp; R occ-temp	None	no	wfd
69	Pillon, Bakchine, and Lhermitte (1987; XX)	Stroke	AWA	R occ-temp	LH	no	nam
70	Katz (1990; Case 1)	Stroke	LBL	Multiple	RH	no	an
71	Katz (1990; Case 2)	Stroke	LBL	Multiple	RH	yes	an
72	Duffield, Desilva, and Grant (1994; XX)	Stroke	AWA	L occ	None	no	no

Table A1 (*Continued*)

	Author (year; patient)	Aetiology	Diagnosis	Lesion	Visual field	Agraphia	Aphasia
73	Erdem and Kansu (1995; XX)	HSV	AWA	L temp (OTG); L front-temp	None	no	an; wfd
74	Lanzinger, Weder, Oettli, and Fretz (1999; XX)	Stroke	GA/SD	L inf med temp	URQ	no	an
75	Goodglass, Lindfield, and Alexander (2000; RH)	Stroke	PWB	L occ-temp-par; Scc; L FrP	RH	no	an
76	Imtiaz, Nirodi, and Khaleeli (2001; XX)	Stroke	AWA	L par-occ	URQ	no	nam; wfd
77	Leff et al. (2001; AR)	Stroke(h)	PA	L med lat occ	None	no	no
78	Adair, Cooke, and Jankovic (2007; XX)	CJD	PA	L temp-par (atrophy)	None	no	nam; comp
79	Miglis and Levine (2010; XX)	Stroke(h)	PA	L post inf temp	None	no	nam
III. Trend dissociation (numbers > letters).							
80	Dejerine (1892; MC)	Stroke	AWA	L occ; Scc	URQ, LoRQachrom	no	no
81	Ajax, Schenkenberg, and Kosteljanetz (1977; Mr A)	Stroke?	PA	L O4; LgG; PHG; Hi; Scc; fmj	RH	no	no
82	Landis et al. (1980; XX)	Glioblastoma	AWA	L temp-par-occ	RH	no	no
83	Grossi et al. (1984; XX)	Stroke	AWA	L occ; temp-occ; Scc; Th	RH	NR	no
84	Maher et al (1998; VT)	Stroke	PA	L temp; LgG; FuG; Cun; Cb	RH	no	no
85	Larsen et al. (2004; EA)	Stroke	GA	L temp-occ; Hi; Scc	RH	slight	an; wfd
IV. Strong dissociation (numbers > letters).							
86	Cohen and Dehane (1995; GOD)	Stroke	PA	L ccs; LgG; FuG	RH	no	wfd
87	Cohen and Dehane (1995; SMA)	Stroke	PA	L ccs; LgG; FuG; Th	RH	no	no
88	Perri et al. (1996; SP)	Stroke(h)	LBL	L occ-par	RH	slight	nam
89	Ingles and Eskes (2008; GL)	Stroke(h)	LBL(sur)	L temp-occ	Remitted URQ	surface	an
90	Starrfelt et al. (2010; NN)	Stroke(h)	PA	L 17; O2; inf LgG; FuG; SFG; Md	URQ	no	no

(ag) = agnosic; (deep) = deep dyslexia; (surf) = surface dyslexia; (trans) = transitory; (vg) = visuographemic; AWA = alexia without agraphia: GA; Global alexia; LBL = letter by letter reading; PA = pure alexia; PWB = pure word blindness; SD = spelling dyslexia; WFD = word form dyslexia.

Lesion: Lists the reported anatomical location of cerebral lesions. Some patients have multiple lesions. The methods used to determine lesions vary from post mortem examinations, through angiograms and computerized tomography, to magnetic resonance imaging, and the level of detail in lesion description varies accordingly. Abbreviations for specific areas are based on Mai et al. (1997).

General abbreviations: L = left; R = right; bilat = bilateral; inf = inferior; sup = superior; post = posterior; med = medial; lat = lateral; dor = dorsal; front = frontal; occ = occipital; par = parietal; temp = temporal; wm = white matter; NR = not reported.

Specific abbreviations (in alphabetical order): AnG = angular gyrus; Cb = cerebellum; cc = corpus callosum; ccs = calcarine sulcus/cortex; Cun = cuneus; fmj = forceps major; FrP = frontal pole; FuG = fusiform gyrus; Hi = Hippocampus; ic = internal capsule; ITG = inferior temporal gyrus; LgG = lingual gyrus; LG = lateral geniculate nucleus; LOTG = lateral occipito-temporal gyrus; Md = medulla; MOTG = middle occipito-temporal gyrus; MTG = middle temporal gyrus; O2 = middle/lateral occipital gyrus; O3 = inferior occipital gyrus; O4 = fourth occipital gyrus (posterior fusiform gyrus); OcP = occipital pole; or = optic radiation; ots = occipito-temporal sulcus; ox = optic chiasm; PHG = parahippocampal gyrus; pic = posterior limb of internal capsule; PrG = precentral gyrus; Scc = splenium of corpus callosum; SFG = superior frontal gyrus; SMG = supramarginal gyrus; STG = superior temporal gyrus; Th = thalamus; VPL = ventroposterolateral nucleus of the thalamus; 17 = striate area/primary visual cortex.

Visual field: Lists the type of visual field defect reported in the original papers. Note that method of assesment of visual fields differs between studies, and some patients reported to have "none" may have had defects not detected by e.g., confrontation testing. Abbreviations: R = right; L = left; U = upper; Lo = lower; achrom = achromatopsia; H = hemianopia; nas = nasal; Q = quadrantanopia; NR = not reported.

Agraphia: Lists whether deficits in writing are reported in the original papers. yes = writing impaired; no = writing intact; slight = minor writing problems; NR = writing scores not reported; surface = surface agraphia.

Aphasia: Lists whether language deficits are reported in the original papers. Again methods and sensitiviy of assessment differ widely between studies, and where no deficits are reported, some deficits may have been present but not assessed. Abbreviations: an = anomia; nam = naming deficit; nam(RT) = elevated RTs in naming; wfd = word finding deficit; dys = dysnomia; comp = comprehension deficit; Optic aph. = optic aphasia; NR = not reported.

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