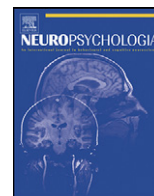




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Reading words, seeing style: The neuropsychology of word, font and handwriting perception

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ABSTRACT

The reading of text is predominantly a left hemisphere function. However, it is also possible to process text for attributes other than word or letter identity, such as style of font or handwriting. Anecdotal observations have suggested that processing the latter may involve the right hemisphere. We devised a test that, using the identical stimuli, required subjects first to match on the basis of word identity and second to match on the basis of script style. We presented two versions, one using various computer fonts, and the other using the handwriting of different individuals. We tested four subjects with unilateral lesions who had been well characterized by neuropsychological testing and structural and/or functional MRI. We found that two prosopagnosic subjects with right lateral fusiform damage eliminating the fusiform face area and likely the right visual word form area were impaired in completion times and/or accuracy when sorting for script style, but performed better when sorting for word identity. In contrast, one alexic subject with left fusiform damage showed normal accuracy for sorting by script style and normal or mildly elevated completion times for sorting by style, but markedly prolonged reading times for sorting by word identity. A prosopagnosic subject with right medial occipitotemporal damage sparing areas in the lateral fusiform gyrus performed well on both tasks. The contrast in the performance of patients with right versus left fusiform damage suggests an important distinction in hemispheric processing that reflects not the type of stimulus but the nature of processing required.

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Neuroimaging studies have showed that the processing of written text is associated with activation of a network of cortical regions (Jobard, Crivello, & Tzourio-Mazoyer, 2003; Reinke, Fernandes, Schwindt, O'Craven, & Grady, 2008). Among others, these include the fusiform gyri, middle temporal gyri, angular gyri, and inferior frontal gyri, more prominently but not exclusively in the left hemisphere. In particular, numerous reports have studied the potential contributions to text-processing of a region in the left lateral fusiform gyrus, which has been named the visual word form area (VWFA), as it responds more to words than to other visual stimuli (Cohen et al., 2000; McCandliss, Cohen, & Dehaene, 2003).

Most behavioural and neuroimaging investigations of text-processing have focused naturally on the reading of text – that is, the extraction of word and letter identity with the goal of

deriving meaning and pronunciation for language. Indeed, lesion studies have long supported a left-hemisphere dominance for reading, confirmed by modern neuroimaging (Damasio & Damasio, 1983; Kleinschmidt & Cohen, 2006; Leff, Spitsyna, Plant, & Wise, 2006) with rare exceptions (Henderson, Alexander, & Naeser, 1982; Hirose, Kin, & Murakami, 1977). However, like faces, written texts are complex visual stimuli with multiple dimensions. Text has colour, shape, size and intensity, from which it is possible to infer higher-order forms of information, such as the style of font, the identity of the human scribe or the typewriter used (as in detective fiction) and perhaps even the emotional state of the writer. The degree to which these additional 'non-reading' aspects of text share resources in common with the reading of text for word meaning, and the degree to which they diverge, remains unknown.

One possibility is that the reading and the non-reading aspects of text processing are differentially lateralized in the human brain. Indeed, neuroimaging studies show that text also activates an area in the right fusiform gyrus that approximately mirrors the location of the left VWFA, although this right-sided region is smaller, less significant, and seen in fewer participants than that on the left

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(Cohen et al., 2002). In the neuropsychological literature there are a few anecdotes suggesting a dissociation between reading and processing for handwriting identification. The first was a remark that two alexic patients could still recognize handwriting (Alajouanine, Lhermitte, & de Ribaucourt-Ducarne, 1960). The possibility that this dissociation may be related to hemispheric lateralization was suggested by a report that one patient with prosopagnosia but not alexia following a right posterior cerebral artery infarct had trouble recognizing handwriting, whereas another patient with alexia but not prosopagnosia following a left occipital lesion did not (Campbell, Landis, & Regard, 1986; Landis & Regard, 1988; Rentschler, Treutwein, & Landis, 1994). These observations, however, were never formally tested. Also, they appear to be at odds with a recent functional MRI study that found sensitivity to handwriting style in both the left and right VWFA (Barton, Fox, Sekunova, & Iaria, 2010). This study found evidence for adaptation to handwriting style in both the right and left VWFA, but not adaptation to word content of text, for which a trend was not found until the level of the inferior temporal gyrus. The results for handwriting adaptation in that report might suggest that style encoding may not be a lateralized aspect of text processing. However, functional neuroimaging studies can only show whether certain perceptual processes modulate the activity in a region. Assertions that a region plays a key role in that perceptual processing are best confirmed by evidence from subjects in whom that region has been disabled or destroyed.

In this report we describe two tests designed to examine the ability to process text for word and stylistic properties separately. One test examines recognition using computer fonts, the other uses handwritten text. After characterizing the ability of healthy subjects to sort the stimuli by word identity and then by style identity, we tested four patients with lesions causing object recognition deficits affecting reading or face recognition. While rare, these syndromes can occur with unilateral lesions. Our four patients were selected because they all had unilateral lesions involving the fusiform gyri: three had right-sided lesions and had presented with prosopagnosia, while one had a left fusiform lesion and had presented with alexia without agraphia. All four patients had detailed neuropsychological and neuroimaging profiles. Our hypothesis was that the identification of words would be impaired more by left than by right hemispheric lesions, while the recognition of script style would show the converse pattern, being impaired more by right than by left hemispheric lesions.

1. Methods

1.1. Subjects

10 healthy subjects participated (4 male, 6 female), with mean age of 40.1 years (s.d. 16.1, range 15–72), all with normal corrected vision. These included the spouses of patients R-IOT3, R-IOT4 and L-IOT1, who thus acted as controls of similar age and background. The Institutional Review Boards of the University of British Columbia and Vancouver Hospital approved the protocol. All subjects gave informed consent in accordance with the principles of the Declaration of Helsinki.

We tested four subjects with brain damage, recruited because all complained of some type of difficulty with object recognition. Three had noted problems with face recognition, and all had had structural and functional MRI imaging (Fox, Iaria, Duchaine, & Barton, 2008), a complete neuro-ophthalmologic examination including Goldmann perimetry, as well as a battery of standardized neuropsychological tests (Table 1). The last subject had difficulty reading and had a similar evaluation, with the exception that because of possible metal fragments from his work at an autobody shop he was

not eligible for functional neuroimaging on the research 3T MRI scanner, despite having had medical scans on a clinical 1.5T MRI scanner.

R-IOT3 is a 70 year-old right-handed male, a retired car mechanic who had two sequential right occipital strokes 2 years prior. Since then he has had trouble recognizing faces, which initially he had attributed simply to his hemianopia. He relies on voice to identify people. He has visual acuity of 20/25, normal colour vision, and a macula-sparing left homonymous hemianopia. During reading, he has some trouble finding the start of the next line.

R-IOT4 is a 57 year-old man, an accounting executive who had a right carotid dissection 6 months prior to testing, which caused a right posterior cerebral arterial infarction because of a fetal pattern of circulation at the circle of Willis. Within a few hours of onset, he was aware that he could recognize his wife's voice but not her face. Though he feels this has improved, he still feels uncertain whether the face before him is familiar or not, and states that faces lack the 'crispness and clarity' they had prior to his stroke. He relies on voice recognition and is helped by context, if he knows which people he will see at a meeting. He also noted trouble recognizing his own house and getting lost in familiar surroundings, particularly the interior of the houses of friends. He had some initial problems with short-term memory, often forgetting where he had put things, but this recovered quickly. Initially when reading he omitted the letters on the left side of words: this has also improved but still occurs at times. He has visual acuity of 20/25, normal colour vision, and a macula-sparing left superior quadrantanopia.

R-AT2 is a 30 year-old left-handed female who had herpes simplex encephalitis five years prior. Since her recovery she has trouble recognizing faces, relying on body habitus, gait and voice cues instead. She has difficulty recognizing buildings in her environment. She has mild problems with forgetfulness but continues to function well in her work at a bank. She reads and writes well. In her previous administrative position she had to recognize the handwriting of invoices from co-workers who often neglected to sign their paperwork, and feels that she was able to do so. She has visual acuity of 20/15 and normal peripheral visual fields. She had mild difficulty with recall on the Rey-Osterreith figure, but did well on tests of verbal, episodic and spatial memory.

L-IOT1 is a 41 year-old male, an engineer who suffered a stroke in the left posterior cerebral arterial territory 15 months prior, from paradoxical emboli in conjunction with a patent foramen ovale. He had transient right-sided numbness and suffered a single seizure, and was taking leviracetam at the time of testing. He complains of laborious and error-prone reading. He also reports some difficulty recognizing tools by sight at the autobody shop he owns and operates, but not with recognizing familiar faces, although he occasionally has trouble recalling their names. He has visual acuity of 20/20, normal colour vision, and a complete right homonymous hemianopia. His neuropsychological testing showed good performance on tests of face recognition and perception (Table 1): on the Warrington Recognition Memory test he was poor for words and good for faces, the reverse of the pattern seen in the prosopagnosic subjects. His reading and writing were assessed with a protocol that we have described elsewhere (Sheldon, Malcolm, & Barton, 2008). He read successfully 96% of the words presented. His errors were primarily omissions or substitutions for the right-most portion of words. He was able to read pseudo-words and real-words with equal success. Similarly, there was no effect of word class or word regularity. His reading was slowed with a significant word-length effect: the slope of the relationship between reading time and number of letters in a word was 1.3 s per letter. This is greater than that seen in hemianopic dyslexia, which is usually less than 100 ms per letter, and more consistent with letter-by-letter read-

Table 1
Neuropsychological testing (asterisks indicate abnormal scores).

| Test | Max | R-IOT3 | R-IOT4 | R-AT2 | L-IOT1 |
|------------------------------|------|--------|--------|-------|--------|
| Edinburgh handedness | | 100 | 95 | 10 | 100 |
| Visual perception | | | | | |
| Hooper Visual Organization | 30 | 27 | 22 | 28 | 36 |
| Benton Line Orientation | 30 | 25 | 24 | 28 | 28 |
| Boston Naming | 15 | 14 | 15 | 15 | 15 |
| VOSP | | | | | |
| Object perception | | | | | |
| Screening | 20 | 20 | 18 | 20 | 20 |
| Incomplete letters | 20 | 19 | 19 | 20 | 17 |
| Silhouettes | 30 | 21 | 18 | 18 | 19 |
| Object decision | 20 | 19 | 19 | 20 | 17 |
| Progressive silhouettes | 20 | 16* | 13 | 10 | 6 |
| Space perception | | | | | |
| Dot counting | 10 | 9 | 9 | 10 | 10 |
| Position discrimination | 20 | 18 | 19 | 20 | 20 |
| Number Location | 10 | 9 | 10 | 9 | 10 |
| Cube analysis | 10 | 9 | 10 | 10 | 10 |
| Imagery | | | | | |
| Mental rotation | 10 | 9 | 10 | 9 | 10 |
| Attention | | | | | |
| Star cancellation | 54 | 54 | 54 | 54 | 54 |
| Visual search | 60 | 32* | 45 | 59 | 22* |
| Memory | | | | | |
| Digit Span – forward | 16 | 7* | 8 | 13 | 6* |
| Spatial Span – forward | 16 | 6 | 10 | 9 | 8 |
| Word Memory | | | | | |
| Word list | 48 | 31 | 37 | 35 | 26* |
| Words, Warrington RMT | 50 | 47 | 50 | 47 | 37* |
| Face processing | | | | | |
| Benton face recognition test | 54 | 49 | 46 | 47 | 49 |
| Faces, Warrington RMT | 50 | 33* | 39* | 27* | 50 |
| Cambridge face memory test | 72 | 38* | 27* | 30* | 45 |
| Famous face recognition (d') | 3.92 | 0.29* | 1.28* | 0.65* | 2.31 |
| Face imagery (%) | 100 | 85 | 84 | 73* | 87 |

Due to poor knowledge of celebrities, a version of this test using personally familiar faces. FAB: Florida Affect Battery; RMT: Recognition Memory Test; VOSP: Visual Object and Space Perception.

ing in pure alexia (Cohen et al., 2003; Leff et al., 2006). His writing was flawless, with no evidence of surface dysgraphia.

1.2. Neuroimaging protocol

All scans were acquired in a 3.0T Philips scanner, except for that of L-IOT1, who because of possible metal fragments was scanned with a Siemens Magnetom Avanto 1.5T scanner. Stimuli were presented using Presentation 9.81 software and rear-projected onto a mirror mounted on the head coil. With the 3.0T scanner, whole brain anatomical scans were acquired using a T1-weighted echoplanar imaging (EPI) sequence, consisting of 170 axial slices of 1 mm thickness with an in-plane resolution of 1 mm × 1 mm (FOV = 256). T2*-weighted functional scans (TR = 2 s; TE = 30 ms) were acquired using an interleaved ascending EPI sequence, consisting of 36 axial slices of 3 mm thickness (1 mm gap) with an in-plane resolution of 1.875 mm × 1.875 mm (FOV = 240). The first volume of each functional scan was discarded to allow for scanner equilibration. With the 1.5T scanner, the anatomical scan consisted of 160 slices with 1 mm isotropic voxels, and the T2*-weighted functional scans with BOLD contrast were collected for 36 axial slices using a TR of 3 s, and an in-plane resolution of 3.44 mm.

We performed two functional localizer runs. The first functional localizer was designed to identify word- and/or letter-selective regions of cortex. Currently there is ongoing debate on the optimum localizer for word-selective areas, particularly regarding the control condition (Cohen & Dehaene, 2004). We used a method reported in our prior study (Barton et al., 2010), contrasting English text with Korean text in subjects literate for English but not Korean, similar to the use of Chinese characters as a baseline in other studies

(Baker et al., 2007; James, James, Jobard, Wong, & Gauthier, 2005). This is based on the argument that a reasonable control for the low-level properties of text would be text from another language: written texts share an emphasis on two-tone contrasts, on line form rather than surface, with approximately similar variations in curvature, orientation and length of segments. Studies have also shown that activation in the VWFA is greater for a language text for which a participant is literate, than for one that they cannot read (Baker et al., 2007). Participants performed an irrelevant 'one-back task', pressing a button if an image was identical to the previous one – that is, if the same word in the same handwriting was seen twice in a row, a task that was easily performed by all subjects. Fixation blocks, which consisted of a cross in the centre of an otherwise blank screen, were alternated with text blocks, all blocks lasting 12 s (18 s for the 1.5T scanner; equivalent to 6 TR intervals in all cases). Six text blocks of each text category were presented in a counterbalanced order. Each text block consisted of 15 images presenting a single word at a time (12 novel and 3 repeated), all sized to a standard width of 400 pixels and presented at screen center for 500 ms, with an inter-stimulus-interval of 300 ms. The word-localizer consisted of 224 functional volumes.

The second functional localizer identified face-selective regions-of-interest, with a protocol using dynamic images that we reported recently as having a greater ability to identify all core regions of the face processing network in single subjects, compared to standard localizers using static facial images (Fox, Iaria, & Barton, 2009). Participants viewed video-clips of non-living objects and faces presented in separate blocks. Video-clips of faces displayed dynamic changes in facial expression, and video-clips of objects displayed types of motion that did not create large translations in position. Video-clips of objects were gathered from the Inter-

net, and video-clips of faces were provided by Chris Benton (Department of Experimental Psychology, University of Bristol, UK). All video-clips were resized to a width of 400 pixels. Participants again performed a one-back task. Identical fixation blocks began and ended the session and were alternated with image blocks, with all blocks lasting 12 s (18 s for the 1.5 T scanner). Eight blocks of each image category (object, face) were presented in a counterbalanced order. Each image block consisted of 6 video-clips (5 novel and 1 repeated) presented centrally for 2000 ms each. The dynamic localizer consisted of 199 functional volumes.

The first volume of each functional scan was discarded to allow for scanner equilibration. All MRI data were analyzed using BrainVoyager QX Version 1.8 (www.brainvoyager.com). Anatomical scans were not preprocessed. Preprocessing of functional scans consisted of corrections for slice scan time acquisition, head motion (trilinear interpolation), and temporal filtering with a high pass filter in order to remove frequencies less than 3 cycles/time course. For each participant, functional scans were individually co-registered to their respective anatomical scan, using the first retained functional volume to generate the co-registration matrix, and were resliced (1 mm³) to match the anatomical scan.

For the word-localizer data, English words (ENG) and Korean words (KOR) were used as predictors. An analysis of ENG > KOR was overlaid on the whole brain and significance was set at a false discovery rate (FDR) of $q < 0.01$, with FDR correction for multiple comparisons. The time course of the face localizer time course was analyzed with a single subject general linear model (GLM), with objects (O) and faces (F) as predictors. Analysis of F > O was overlaid on the whole brain and significance was set at $q < 0.01$, with FDR correction for multiple comparisons.

Although our dynamic face localizer was able to localize the FFA in right and left hemispheres in almost all healthy subjects in our prior study, our word localizer revealed a right VWFA in only about half of subjects, as is true in most neuroimaging studies of word processing (Barton et al., 2010). Therefore it is more difficult to know in any given subject whether their lesion had destroyed the right VWFA. In the absence of any word-activation in the right fusiform gyrus, we judged the probable status of the right VWFA according to two additional criteria. First, we examined whether the lesion involved cortex at the mean Tailairach coordinates of the peak voxel of the right VWFA found in our prior study ($x = 44, y = -43, z = -22$). Second, we noted the relation of the lesion to the right FFA, if present, which is more reliably localized. In our prior study, the mean location of the peak voxel for the right VWFA was 7 voxels lateral, 6 voxels anterior, and 2 voxels superior to the mean location of the peak voxel of the right FFA. In those subjects in whom the two localizers were able to find both a right VWFA and FFA, the peak voxel of the VWFA was on average 6 voxels lateral (range 0–14), 5 voxels anterior (range -7 to 11) and 2 voxels superior (range -8 to 7) to the peak voxel of the FFA. Therefore, if a subject had preservation of the FFA and cortex lateral to it, it is likely that the right VWFA was also spared, even if no word-selective voxels had been seen on the functional word-localizer.

1.3. Behavioural protocol

We devised two paper-based tests of word reading and script processing. Both used a sorting task. Sorting was chosen over naming or pronunciation for the word reading task for two reasons: first, to maintain an equivalent task to that used to probe script processing, and second, to minimize left hemispheric contributions from grapheme-to-phoneme conversion or comprehension of meaning (Chiarello, 1988; Hellige & Adamson, 2007). Subjects were seated at a table in standard well-lit conditions.

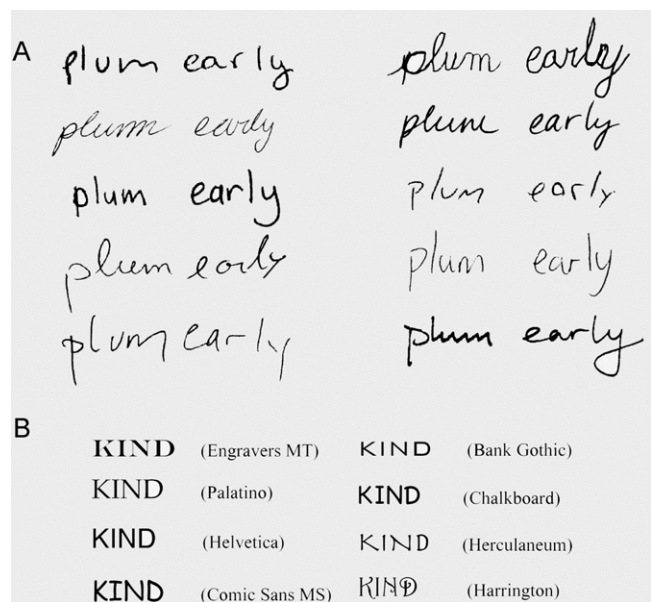


Fig. 1. Examples of text stimuli. (A) samples of the 10 different handwriting styles. (B) samples of the 8 different font styles, with their names in brackets.

1.3.1. Handwritten text-processing

1.3.1.1. Stimuli. We used word stimuli developed for a recent fMRI-adaptation study of healthy subjects (Barton et al., 2010). (None of the control subjects in this study had been subjects in that experiment.) We had selected 10 items from word databases (Coltheart, 1981; Marchand & Friedman, 2005), chosen to maximize both linguistic and perceptual differences between stimuli. Thus each word had a different number of letters, ranging from 2 to 11, with examples of both high and low frequency words, concrete and abstract words, regular and irregular words, and of different parts of speech (nouns, verbs, modifiers and functors). The words were: “go, but, plum, early, island, because, ambulate, orchestra, vigorously, maintenance”. We then had 16 individuals ranging in age from 8 to 49, with different educational and ethnic backgrounds, write each of the 10 words in lower case. We then had a panel of 10 participants compare these handwritten lists to identify which handwriting samples were most similar to one or more samples in the set. The 6 samples most frequently identified as sharing similarities to other samples were removed, leaving us with a set of 10 handwriting styles that, like the words, were chosen to maximize differences. The end result was 100 stimuli, 10 words each written in 10 different handwriting styles (Fig. 1A). All words were legible to all participants in our prior imaging study. For this behavioural study, all 100 words were scanned, converted to greyscale, and printed as high-contrast black type on white paper and fixed to white cards of 102 mm × 63 mm size. The main bodies of these lower-case words were approximately 3–5 mm in height.

1.3.1.2. Protocol. The cards were shuffled beforehand to randomize their order, and the deck was handed to the subject with instructions to sort the cards as accurately and quickly as possible into piles of different words, regardless of handwriting. Subjects were not told how many different words were present. They were timed with a stopwatch by the examiner.

Following this the 10 cards with the word “maintenance” were taken and placed side by side on the table as exemplars of the 10 different handwriting styles. The subject was allowed to arrange these as they wished. The subject was told that they were again to sort the remaining cards into piles, but now matching them for handwriting style rather than word. They were to place each card they were

given underneath the “maintenance” exemplar card whose handwriting most resembled that of the card in their hand. After placing the card in that pile they would not be able to review it again. Each of the 90 remaining cards were handed one by one to the subject by the experimenter, in random order, with the one rule being that no card was followed immediately by a card with the same word. (This and the rule against review were used to minimize the ability of subjects to place cards by using the logic that, since a pile already had a card with a certain word, another card with the same word should not be placed in that pile. The fact that all control subjects and patients had several instances in which they placed one or more cards of the same word in the same pile testifies to the success of these maneuvers.) The examiner always had the next card ready before the subject completed their card assignment, so that no examiner-related delays confounded completion times. The time to complete this test was also timed by a stopwatch.

1.3.2. Computer-font text-processing

1.3.2.1. Stimuli. For this test we kept word length uniform, so that one could not deduce word identity simply by the number of letters. The seven words were: “NICE, EAST, KIND, ZONE, SOON, BUNS, HAIR”. For font we chose 8 different styles provided in Microsoft Word 2004, which were Engravers MT, Palatino, Helvetica, Comic Sans MS, Bank Gothic, Herculeum, Chalkboard and Harrington (Fig. 1B). All were printed in upper case. The end result was 56 stimuli, 7 words each printed in 8 different styles. We varied font size between 16, 18 and 20 point to minimize cues to font identity from letter height. These upper-case words were 4–5 mm in height. All words were printed in black type on white paper and fixed to white cards of 50 mm × 60 mm size.

1.3.2.2. Protocol. This followed a nearly identical procedure as that used for the test with handwritten text. The first stage involved sorting of the cards by word identity, timed with a stopwatch. Following this the 8 cards with the word “HAIR” were taken and placed side by side on the table, as exemplars of the different fonts. The subject now sorted the remaining 48 cards for font style, as quickly and accurately as possible, again placing each card underneath the chosen “HAIR” exemplar card without possibility of review. Again, the cards were handed one by one to the subject by the examiner, and performance timed by a stopwatch.

1.3.2.3. Analysis. Both Font and Handwriting tests were analyzed in a similar manner. We calculated a per-item completion time by dividing the total test completion time by the number of items in the test (for word-sorting: 56 for computer font, 100 for handwriting; for script-sorting: 48 for computer font, 90 for handwriting). Per-item completion time was the main index of performance for word-sorting as, with one notable exception (L-IOT1), subjects made no errors.

For script-sorting, we also measured two indices of accuracy. The first was a simple ‘fraction correct’ measure, where the numbers of correct and incorrect assignments to the “maintenance” or “HAIR” exemplars were tabulated. However, this score does not capture potential evidence of script recognition within the erroneous assignments. Consider the case of two subjects who make 5 errors in a particular pile. If the 5 errors made by the first subject all belong to one script style, this is still evidence of some recognition of stylistic elements in script, even if they are errors. In contrast, if the 5 errors of the second subject all belong to different script styles, this would suggest a more random error, with low recognition of script properties. Both subjects would have the same ‘fraction-correct’ score, though.

To create a metric that captures evidence of script recognition in both errors and correct scores, we generated contingency tables that would assess the degree of clustering in the subject’s

responses. For handwriting, this was a 10 × 10 table, in which the Rows represent the handwriting style of the “maintenance” exemplars provided, and hence the classification given by the subjects to each card, whereas the Columns represent the actual handwriting style of the cards. From the number of cards placed in each pile, we can calculate the expected number of cards in each cell of this table if assortment were random. The square of the difference between the observed and the expected value of each cell is calculated and summed over the entire table to give an uncorrected cluster score. A similar procedure was followed for the computer font test, with an 8 × 6 table. To make the computer font and handwriting scores comparable, we then divided the uncorrected cluster scores by the number of items in the test (48 for computer font, 90 for handwriting), to give a final ‘cluster index’. The ability of subjects to cluster cards of the same script style would be reflected in a high cluster index, regardless of the fraction-correct score.

All completion time and accuracy scores for patients were converted to z-scores based on the control data: for the completion time data, quantifying deficits by z-scores is more appropriate than quantifying deficits in time units because of the asymmetry in completion times between word and style sorting, reflecting the differences in task difficulty. We calculated prediction limits for z-scores for each of the two tests, using Sidak’s correction for multiple comparisons, adjusted for the mean correlation between the different outputs (Sankoh, Huque, & Dubey, 1997). This gave a cut-off score of $z = 2.673$ for a one-way test set to an alpha value of 0.05, which would be the equivalent of lowering the p -value to 0.0127.

2. Results

2.1. Neuroimaging data

Structural imaging showed that both R-IOT3 and R-IOT4 had suffered right occipitotemporal strokes that had damaged the lateral fusiform gyrus (Fig. 2). Functional imaging showed that in both subjects there was face-related and word-related activity in the left but not the right fusiform gyrus. Given the location of their lesions it is highly likely that both subjects had loss of the right FFA and right VWFA. Concerning the other components of the core face network, the right occipital face area was spared in R-IOT4 but destroyed in R-IOT3, while the right superior temporal sulcus was preserved in both.

R-AT2 had a right anterior temporal lobe lesion extending to the medial aspect of the fusiform gyrus, sparing its lateral component (Fig. 2). Functional MRI showed preservation of the right FFA, occipital face area and superior temporal sulcus components of the core face network. The word localizer showed some activation in the right hemisphere, suggesting that the right VWFA has at least partially survived. This is also supported by the fact that her lesion is medial to an intact FFA, since in our prior study (Barton et al., 2010) the right VWFA was anterior and lateral to the right FFA.

L-IOT1 had a left occipital infarct involving the middle portion of the fusiform gyrus and white matter (Fig. 2). The word localizer revealed activation of the left middle temporal gyrus, as seen in control subjects (Barton et al., 2010), as well as a region of activation in the proximity of the left fusiform gyrus. Compared to the usual location of the VWFA (Cohen et al., 2002), this area is in the depths of a sulcus rather than on the fusiform surface. Whether this represents a normal variation of VWFA location or an adaptive effect after the damage of his lesion is uncertain. More detailed structural assessment also showed that his lesion damaged not just the cortex but also eliminated the white matter between cortex and the posterior horn of the lateral ventricle (Fig. 3), where fibers projecting to the VWFA from occipital cortex travel (Damasio & Damasio, 1983; Epelbaum et al., 2008; Erdem & Kansu, 1995; Molko et al., 2002).

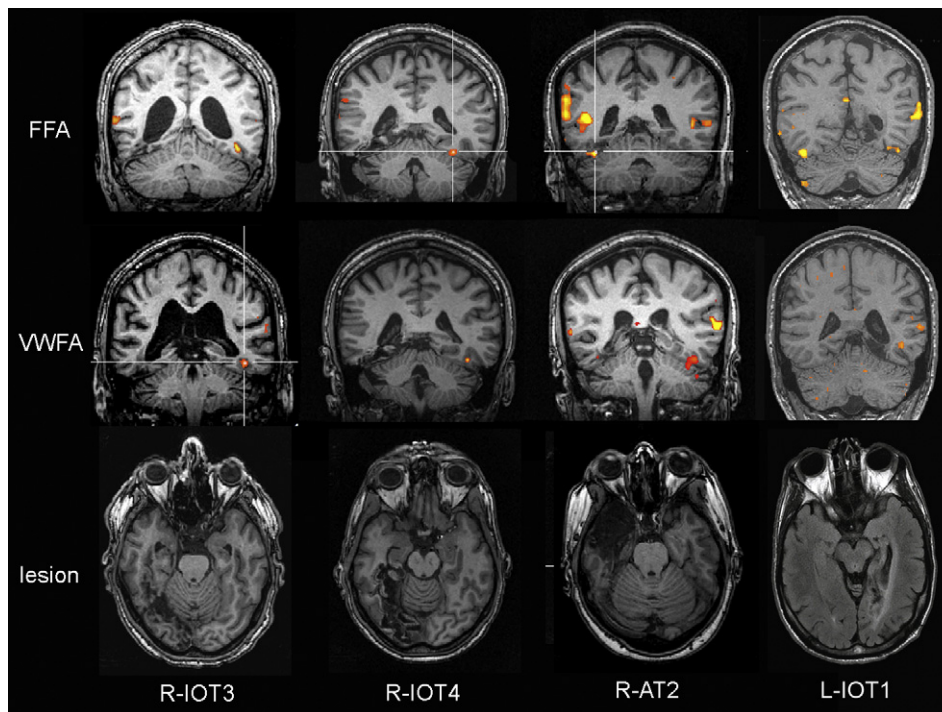


Fig. 2. Functional and structural imaging of subjects. Yellow-orange regions indicate areas significantly activated during the functional localizers. Top row shows coronal images for data from the functional localizer for faces, at the level of the FFA. In R-IOT3 and R-IOT4 the left FFA is evident but the mirror location on the right is encompassed by the hypointense lesion. R-AT2 has a right FFA still, just lateral to the small posterior extent of her lesion. L-IOT has activation of both a dominant right FFA and a minor left FFA. Middle row shows coronal images with the functional localizer for words superimposed on structural images at the level of the VWFA. Again, in R-IOT3 and R-IOT4 the left VWFA is present but the mirror location on the right has been destroyed by the lesion. A small degree of word-activation is present lateral to the lesion of R-AT2. L-IOT1 has a region of activation that is in the depths of a sulcus rather than on the fusiform surface: whether this represents an anomalously located VWFA or post-lesion re-organization is unclear. Bottom row shows axial structural images of their lesions.

Hence it is likely that his alexia stems from either disconnection of the VWFA or damage to it.

2.2. Behavioural data – control subjects

For both computerized print and handwriting, word-sorting was rapid and flawless, requiring about 2.2 s per item. This did not differ between computer font and handwriting. Script-sorting required more time than word-sorting in both tests. Subjects required about 9 s per item for computer font and 13 s per item for handwriting,

which was a significant difference between the two styles. No subjects achieved perfect accuracy in script-sorting in either test. The mean accuracy was 0.86 (s.d. 0.06) for computer fonts and 0.61 (s.d. 0.05) for handwriting, showing that handwriting sorting was more difficult.

The fact that word-sorting is easier than script-sorting is not surprising, given that humans are more practiced at deciphering text for words than for style. This creates an asymmetry in perceptual difficulty in our tests. However, this minor disadvantage is outweighed by the significant benefit of using the identical stimuli for

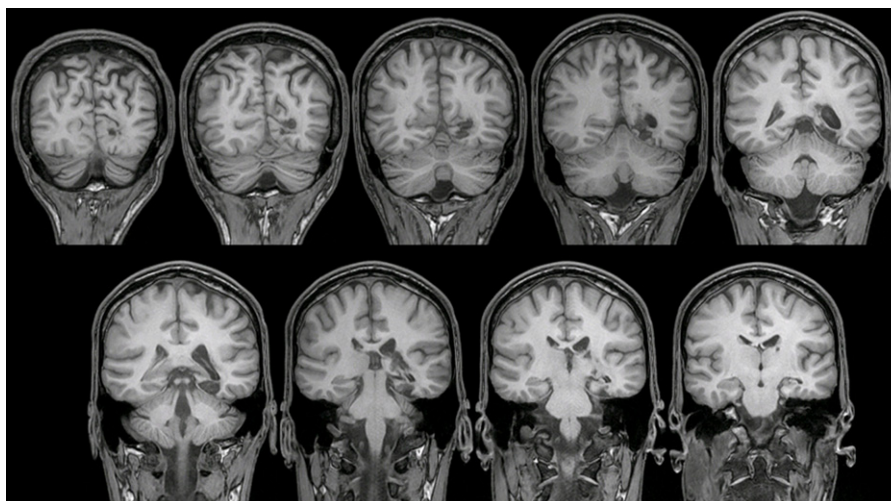


Fig. 3. Structural imaging in alexic subject L-IOT1. Coronal images show the involvement of the fusiform gyrus, near but probably slightly medial to the typical location of the VWFA, as well as destruction of white matter between the cortical surface and the ventricle.

Table 2
 Spouse-matched data.

| Subject | Age | Word processing | Script processing | | |
|----------------------|-----|--------------------------|--------------------------|------------------|---------------|
| | | Completion time (s/item) | Completion time (s/item) | Fraction correct | Cluster index |
| Computer font | | | | | |
| R-IOT3 | 70 | 4.5 | 36.3 | 0.60 | 2.80 |
| R-IOT3(spouse) | 72 | 4.1 | 13.1 | 0.79 | 3.75 |
| R-IOT4 | 57 | 2.6 | 17.4 | 0.75 | 3.13 |
| R-IOT4(spouse) | 56 | 1.6 | 7.5 | 0.79 | 3.55 |
| L-IOT1 | 41 | 6.8 | 10.7 | 0.88 | 4.45 |
| L-IOT1(spouse) | 45 | 1.4 | 8.3 | 0.92 | 4.61 |
| Handwriting | | | | | |
| R-IOT3 | | 6.8 | 60.7 | 0.39 | 1.51 |
| R-IOT3(spouse) | | 6.5 | 13.9 | 0.58 | 3.43 |
| R-IOT4 | | 3.2 | 19.2 | 0.39 | 1.91 |
| R-IOT4(spouse) | | 2.2 | 10.4 | 0.63 | 3.74 |
| L-IOT1 | | 10.9 | 23.7 | 0.61 | 3.75 |
| L-IOT1(spouse) | | 1.5 | 16.5 | 0.71 | 4.41 |

both word- and script-sorting, which eliminates the possibility that stimulus-related differences might account for any discrepancies in performance. The practical implication, though, is that completion time is the main index of performance on word-sorting, while both speed and accuracy can be assessed for script-sorting.

2.3. Prosopagnosic patients with right hemisphere lesions

R-IOT-3 and R-IOT4 had similar lesions, with destruction of the right FFA and likely also the right VWFA. For word-sorting, R-IOT3 had slightly longer completion times (font = 4.5 s, $z = 2.56$; handwriting = 6.8 s, $z = 3.00$), but he was the oldest of our subjects and his completion times for word-sorting were comparable to those of his wife (Table 2), who was of a similar age (72 years) and also performed the slowest of the controls. For script-sorting, R-IOT3 had markedly prolonged completion times (font = 36.3 s, $z = 11.56$; handwriting = 60.7 s, $z = 16.14$; Fig. 4), which were about three to four times as long as those of his wife. He was impaired in all fraction-correct scores (font = 60.4%, $z = 3.31$; handwriting = 38.9%, $z = 3.60$), and cluster indices (font = 2.80, $z = 2.74$; handwriting = 1.51, $z = 3.73$; Fig. 5).

R-IOT4 showed normal completion times on both tests of word-sorting. For script-sorting, R-IOT4 had prolonged completion times (font = 17.4 s, $z = 3.79$; handwriting = 19.2 s, $z = 2.37$), though not as dramatically so as R-IOT3. For font, his fraction-correct score (75.0%, $z = 1.28$) was normal and his cluster index was in the borderline normal range (3.12, $z = 2.04$). However, for handwriting his fraction correct score (38.9%, $z = 3.60$) and cluster index (1.91, $z = 3.04$) were both clearly abnormal.

R-AT2 differed from R-IOT3 and R-IOT4 in that she had a medial lesion that spared the right FFA and thus most likely also spared the right VWFA. She had normal completion times in word-sorting and script-sorting, and normal fraction-correct scores and cluster indices for script-sorting (Figs. 4 and 5).

2.4. Alexic patient with a left hemisphere lesion

In contrast to the patients with right hemispheric lesions, L-IOT1 showed markedly prolonged completion times for word-sorting, taking 3–4 times longer than the mean control time to accomplish the task (font = 6.8 s, $z = 5.14$; handwriting = 10.9 s, $z = 5.71$; Fig. 4). Also, L-IOT1 was the only subject to make an error on word-sorting, in that he created two separate piles for the word 'orchestra' for the handwritten sample without realizing it. For script-sorting, his fraction-correct scores and cluster indices were normal (Fig. 5), and his completion time was normal for computer fonts (10.7 s, $z = 1.01$) though slightly increased for handwriting (23.7 s, $z = 3.88$).

3. Discussion

Our findings show that the two prosopagnosic subjects with lesions involving the right lateral fusiform gyrus have a deficit in processing text for style of script, with minimal or no slowing in processing text for word content. In contrast, the alexic subject with a lesion of the left fusiform gyrus showed markedly prolonged completion times in sorting for word content, but normal accuracy in sorting for script style. This suggests a differential impairment that supports a lateralization of mechanisms involved in reading

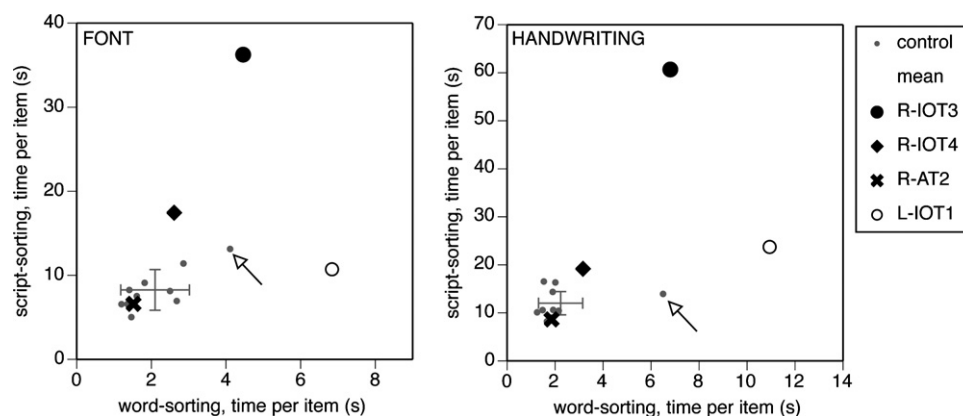


Fig. 4. Completion time data. Time per-item is plotted for script-sorting on the y-axis and for word-sorting on the x-axis, for computer font (left graph) and handwriting (right graph). Error bars indicate one standard deviation for the control data, which are plotted individually also as small grey discs. The arrow indicates the data for the wife of R-IOT3, who serves as an age-matched control for him.

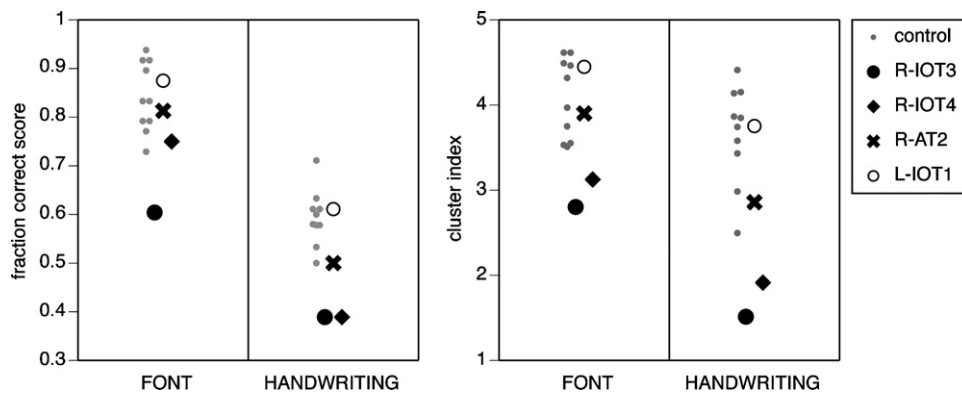


Fig. 5. Accuracy data for script-sorting. Left graph: Fraction-correct scores for computer font and handwriting. Right graph: Cluster indices for computer font and handwriting.

words versus processing writing style for the same textual stimuli, validating two anecdotal observations in the older literature (Alajouanine et al., 1960; Landis & Regard, 1988).

The fact that the patient with a left hemispheric lesion showed some minor slowing in sorting for handwriting style, and one patient (R-IOT3) with a right hemispheric lesion showed some slowing (at least partly age-appropriate) in sorting for words in font or handwriting, may suggest that the dissociation is not quite complete. However, these two were the only subjects with a complete hemianopia. This low-level limitation of vision may have lengthened processing times in general, which is supported by the fact that these two subjects alone had difficulty on the test of visual search (Table 1). Indeed, our previous studies of face-processing tasks have shown that hemianopia in the absence of prosopagnosia or alexia is associated with highly accurate but somewhat delayed responses (Barton, 2008).

Our control data showed that healthy subjects were equally proficient at reading for word content with either computer fonts or handwriting. This finding contrasts with other studies that show longer reaction times for identifying briefly viewed letters or words with handwriting than with computer fonts (Corcoran & Rouse, 1970; Hellige & Adamson, 2007). It may be that our procedure obscured the small temporal differences seen in these tachistoscopic studies. We did find that the processing of script style required more time with handwritten text than with computer fonts. This likely relates to the greater variability of handwritten letters compared to computer-generated ones. As others have noted (Wing, 1979), handwritten letters can vary considerably, even when written by the same individual: the same letter may have a different appearance when the context of its surrounding letters changes, while different letters may resemble each other because of similar production routines. Furthermore, even the same letter in the same context is subject to random variation. None of these variations appear in the very regular letters of a single computer font. As a result, analysis of handwriting style may demand a greater abstraction of general stylistic properties than analysis of computer font, an abstraction that may involve a form of texture processing (Busch, Boles, & Sridharan, 2005).

There is a paucity of studies on the processing of textual style for style's sake. Rather, most studies have focused upon the impact of style on the processing of word or letters. Thus one study concluded that handwritten script and type-face used different cognitive word recognition programs because identification of briefly seen words was reduced when print and handwriting were randomly mixed within a block, but not affected when the mix involved either upper versus lower case type or two different handwritings (Corcoran & Rouse, 1970). A few split-field tachistoscopic studies have gone further to suggest that, while reading of print-like fonts showed the expected right hemifield/left hemisphere superiority, cursive fonts

showed a left hemifield/right hemisphere superiority, and that this is due specifically to the script-like properties of cursive (Bryden & Allard, 1976; Wagner & Harris, 1994). It was suggested that in reading the right hemisphere may serve to “segregate the relevant components of the visual input” and “get rid of irrelevant detail” (Bryden & Allard, 1976). Likewise, a study comparing computer font with handwriting in the identification of letter triplets showed a smaller right hemifield/left hemisphere advantage in both accuracy and latency, and concluded that there was a “greater contribution of the right hemisphere to the identification of handwritten cursive” (Hellige & Adamson, 2007). On the other hand, these works are countered by a study of 20 aphasic patients with left-sided lesions that found that whether handwritten words were printed or cursive in style had no overall impact on reading accuracy or latency (Williams, 1984).

A number of priming studies have varied font or case to examine the proposal that the left hemisphere represents text at an abstract level for word identity while the right represents text in a more form-specific manner. This has parallels with other suggestions that the left fusiform gyrus may represent objects at a categorical level, while the right represents specific exemplars (Koutstaal et al., 2001). One tachistoscopic study found that priming across different fonts (“abstractive priming”) was better in the left hemisphere, but priming for names in the same font (font-specific priming) was equivalent in the two hemifields (Schweinberger, Lisa Ramsay, & Kaufmann, 2006). This also reported event-related potential data showing modest font-specific priming effect in the N200 potential, but priming whether the font was changed or not in the left lateralized N250, which may originate in the left fusiform gyrus. Again, one somewhat indirect conclusion was that the “right hemisphere represents written names in a more form-specific manner”. Studies varying case rather than font have generally reached similar conclusions. Case-specific priming was greater in the left hemifield/right hemisphere than the right hemifield/left hemisphere in several split-field tachistoscopic studies (Burgund & Marsolek, 1997; Marsolek, Kosslyn, & Squire, 1992) but not in another (Kroll, Rocha, Yonelinas, Baynes, & Frederick, 2001). Transcranial magnetic stimulation of the right but not the left occipital lobe disrupted case-specific priming but not priming across different fonts (Pobric, Schweinberger, & Lavidor, 2007). Last, font-specific priming was also reported absent in a patient with right occipital damage (Vaidya, Gabrieli, Verfaellie, Fleischman, & Askari, 1998).

The above studies promote a view of hemispheric specialization as a contrast between abstract text representations on the left and style-specific (or exemplar-specific) text representations on the right. Our results do not address or negate the possibility of exemplar-specific representations, but suggest at the very least an additional type of hemispheric specialization. Rather than a difference in exemplar specificity, our findings imply that contrasting

types of abstraction are also being performed by the two fusiform gyri, the left abstracting word and letter identity across variations in style, and the right abstracting style across variations in word and letter identity. One might argue that in the case of our font stimuli, exemplar-specific *letter* processing could be used to facilitate script-sorting for words (for instance, recognizing the specific form of the 'N' in 'BUNS', 'KIND' and 'NICE'). However, this is less plausible for our handwritten stimuli, given the large variability in production of the same letter in different or even the same contexts, as described above (Wing, 1979). Note for example the differences in how the same individual wrote the letter 'l' in the words 'plum' and 'early' in Fig. 1A. For these reasons we suggest that our script-sorting test does not probe exemplar-specific text representations but representations of stylistic properties of text, the abstraction of which is probably just as sophisticated and complex as the decoding of text for word content.

More recently we examined this possibility of diverging hemispheric representations of text with an fMRI-adaptation study (Barton et al., 2010). Using the same handwritten stimuli as in this report, we studied adaptation for word identity across variations in handwriting style, and adaptation for handwriting style across variations in word identity. Surprisingly, we found that both the right and left VWFA showed adaptation for handwriting style but not word identity, while adaptation for word identity only emerged as a trend in the left superior temporal gyrus. The current finding that right fusiform damage impairs handwriting discrimination but not word discrimination is consistent with the finding of adaptation for handwriting in the right VWFA. However, the fact that our alexic patient discriminates handwriting and font style accurately and has normal completion times for sorting font style suggests that the left fusiform gyrus may not make a critical contribution to the perception of stylistic properties of text, despite the fact that the fMRI-adaptation study showed that the left VWFA was also sensitive to handwriting style. The possibility remains of a minor contribution that may be recruited when style processing is more demanding, given that he has slightly elevated completion times for sorting handwriting style, although, as considered above, this is obscured by the possible impact of his hemianopia on the speed of scanning over multiple items required by our test. An alternate interpretation of our prior fMRI results is that the left fusiform gyrus encodes stylistic elements, not for the purpose of representing style, but to facilitate extraction of word identity. If so, this could explain a scenario where the left VWFA shows sensitivity to style on functional neuroimaging but the perception of style is minimally affected by a lesion encompassing this region.

As with other complex stimuli like faces, it is not yet clear what dimensions best support the ability to discriminate one font or handwriting from another. One can conceive of several candidate properties, such as slant, convexity, regularity, aspect ratios and so on, which may vary in importance according to the specific samples to be discriminated. It is suggested that these may fall under a general rubric of texture perception (Busch et al., 2005), which raises an interesting parallel with another observation that prosopagnosia following a right hemispheric lesion may be accompanied by deficits in global texture processing (Rentschler et al., 1994).

In a broader sense, a deficit in handwriting recognition in our prosopagnosic subjects also parallels other reports that these subjects can have trouble discriminating members of other non-face object categories, such as cars, flowers, animals, clothing or buildings (Assal, Favre, & Anderes, 1984; Bornstein, Sroka, & Munitz, 1969; Damasio, Damasio, & Tranel, 1986; de Renzi, 1986; Renzi, Faglioni, Grossi, & Nichelli, 1991; Gomori & Hawryluk, 1984; Henke, Schweinberger, Grigo, Klos, & Sommer, 1998; Newcombe, 1979). It remains unclear whether these are intrinsic to the deficit underlying prosopagnosia or reflect damage to adjacent object-processing mechanisms in structures like the fusiform gyri, particularly given

occasional reports of spared discrimination for such objects (Cole & Perez-Cruet, 1964; de Renzi, 1986; Henke et al., 1998; McNeil & Warrington, 1993; Riddoch, Johnston, Bracewell, Boutsen, & Humphreys, 2008). It is of interest that, in our own prior study, all three of the prosopagnosic subjects in this report also had impaired car recognition, despite the fact that their verbal semantic knowledge indicated considerable pre-morbid expertise with this category (Barton, Hanif, & Ashraf, 2009). Since R-AT2 showed normal perceptual discrimination of font and handwriting, consistent with her own subjective experience, one might be tempted to conclude that this is evidence of a dissociation between car and font/handwriting processing. However, this difference may be better attributed to the fact that the car recognition test probed long-term memories as well as perception, while the current test of text processing involved only perceptual discrimination. Indeed, R-AT2 performed well on our other experimental tests of perception of facial configuration, consistent with the proposal that anterior temporal damage that spares the FFA may result in more associative than apperceptive forms of prosopagnosia (Barton, 2008; Barton & Cherkasova, 2003; Barton, Press, Keenan, & O'Connor, 2002).

In conclusion, the fact that R-AT2, with sparing of the right FFA and probably of the right VWFA, has good perception of the structural properties of faces and textual style, while R-IOT3 and R-IOT4, with loss of these areas, have impairments of face and font/handwriting perception, argues that the right lateral fusiform gyri contains regions that make significant contributions to both of these perceptual functions. Despite the long-established dominance of the left hemisphere for reading text (which is also supported by the long completion times of subject L-IOT1 in word sorting as opposed to script sorting), the fact that the right hemisphere is involved in representations of font and handwriting style underlines an important point, that it is not the stimulus that is lateralized, but the type of information processing one performs upon it.

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