Word and Text Processing in Acquired Prosopagnosia

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Objective: A novel hypothesis of object recognition asserts that multiple regions are engaged in processing an object type, and that cerebral regions participate in processing multiple types of objects. In particular, for high-level expert processing, it proposes shared rather than dedicated resources for word and face perception, and predicts that prosopagnosic subjects would have minor deficits in visual word processing, and alexic subjects would have subtle impairments in face perception. In this study, we evaluated whether prosopagnosic subjects had deficits in processing either the word content or the style of visual text.

Methods: Eleven prosopagnosic subjects, 6 with unilateral right lesions and 5 with bilateral lesions, participated. In the first study, we evaluated their word length effect in reading single words. In the second study, we assessed their time and accuracy for sorting text by word content independent of style, and for sorting text by handwriting or font style independent of word content.

Results: Only subjects with bilateral lesions showed mildly elevated word length effects. Subjects were not slowed in sorting text by word content, but were nearly uniformly impaired in accuracy for sorting text by style.

Interpretation: Our results show that prosopagnosic subjects are impaired not only in face recognition but also in perceiving stylistic aspects of text. This supports a modified version of the many-to-many hypothesis that incorporates hemispheric specialization for processing different aspects of visual text.

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Face and visual word recognition are highly expert visual processes that can be selectively impaired, resulting in prosopagnosia, the inability to recognize faces,[1] or pure alexia, the loss of reading proficiency.[2] Our knowledge of the neuroanatomic basis of these 2 functions has been advanced by functional neuroimaging, which reveals that faces and words activate similar bilateral networks,[3,4] with a key distinction that activation is greater in the right hemisphere for faces[5] and in the left for words.[6] Nevertheless, there is significant overlap between voxels activated by faces and those activated by words,[7] leading to the suggestion that hemispheric specialization for words and faces evolves through competition in these networks.[8–10]

These findings have implications for our concepts of visual object representation in the brain. A one-to-one view proposes that 1 type of object is processed by 1 region, which is dedicated to processing only that object type. The finding that words and faces activate multiple regions argues against this, and supports at least a many-to-one view, that multiple regions are involved in processing 1 object type. However, whether a region is devoted to a single object type[11–13] or participates in processing many object types[14,15] is contentious. A recent many-to-many hypothesis[8] argues that object processing involves networks whose individual regions participate in processing >1 object type. In this view, object specification is not located within a single region, but is an emergent property of the pattern of network activation.[16]

A key neuropsychological prediction of the many-to-many hypothesis is that selective agnosias such as prosopagnosia and pure alexia will show subtle deficits in processing other object types, a relative rather than absolute selectivity.[8] One longstanding controversy is whether

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prosopagnosia affects other forms of visual recognition; for example, recent evidence suggests that prosopagnosic subjects show poorer car recognition than predicted by their semantic knowledge about cars.[17] At least some alexic subjects have subtle deficits in other visual processing.[18,19] However, given the overlap between face and word networks,[7] the more intriguing question is whether prosopagnosia includes subtle word processing impairments, and conversely whether alexia includes subtle face perception deficits. Given that the lateralization of words and faces is only partial,[5,6] a more specific prediction is that minor deficits for the other stimulus type would be found even after unilateral lesions.[8] One recent study of 3 prosopagnosic subjects and 4 alexic subjects suggested that this was the case,[20] but a study of 5 prosopagnosic subjects found normal word processing in 4 subjects.[21]

We performed 2 studies of word perception in a prosopagnosic cohort. In the first, we examined single word reading for the word length effect. In the second, we contrasted word recognition versus recognition of font or handwriting style, extending the observations we had previously reported in 3 cases.[22] Our guiding hypothesis was that either word or textual style recognition (or both) would be impaired in prosopagnosic subjects.

Subjects and Methods

Subjects

The institutional review boards of the University of British Columbia and Vancouver Hospital approved the protocol, and all subjects gave informed consent in accordance with the principles of the Declaration of Helsinki.

Control subjects for study 1 were 13 healthy subjects, 6 male, with a mean age of 37.9 years (standard deviation = 9.2, range = 25–54). All were right-handed except for 1 ambidextrous participant, and all were fluent in spoken and written English. Control subjects for study 2 were 11 subjects, 4 male, of mean age 41.5 years (standard deviation = 15.0, range = 15–72), all right-handed. In addition, as a nonprosopagnosic occipital lesion control we tested a 53-year-old female subject who 3 years prior to testing had had a right medial occipital stroke causing persistent left hemianopia.

The 11 prosopagnosic subjects (7 male, 4 female) had a mean age of 48 years (standard deviation = 15.0, range = 23–70). All had a neuro-ophthalmologic examination, including Goldmann perimetry and Farnsworth–Munsell 100-hue testing, and had best-corrected visual acuity of 20/30 or better. All complained of impaired face recognition in daily life and were impaired on both a famous faces test of recognition[23] and on at least 1 of either the Cambridge Face Memory test[24] or the faces component of the Warrington Recognition Memory test,[25] while performing normally on the word component of the latter (Table 1). None had complaints of mistaking one type of object for another in daily life, and all were able to identify real objects and objects in line drawings during the neuro-ophthalmologic examination. They were also administered a battery of standard neuropsychological tests to exclude more general problems of attention, memory, and vision (Table 2).

All prosopagnosic subjects had structural (Figs 1 and 2) and functional magnetic resonance imaging (MRI) to localize the core components of the face processing network, using the HVEM (Human Vision and Eye Movement) dynamic face localizer protocol.[26] T2*-weighted functional scans were used to collect data from 36 interleaved axial slices (repetition time = 2,000 milliseconds, echo time = 30 milliseconds, field of view = 240 × 216mm, 3mm thickness with 1mm gap, voxel size = 3 × 3mm, 128 reconstruction matrix, reconstructed voxel size = 1.875 × 1.65mm). The functional slices were coregistered onto a T1-weighed anatomical image for each patient.

The HVEM dynamic face localizer scan consisted of grayscale video clips of faces and objects. Each stimulus block included 6 video clips lasting 1.5 seconds each, separated by a 500-millisecond blank screen. Stimulus blocks were separated by a 12-second fixation block. Each condition (faces or objects) was repeated 8 times per run. Attention was sustained by asking the patients to press a button on an MRI-compatible button box when the same video was presented twice in a row. Functional data were analyzed using BrainVoyager QX software (Brain Innovation, Maastricht, the Netherlands). Preprocessing steps included slice time correction (cubic spline interpolation), 3-dimensional motion correction (trilinear/sinc interpolation), and high-pass temporal filtering (general linear model–Fourier, 2 sines/cosines). Using a false-discovery rate of $q < 0.05$ (corrected for multiple comparisons), we identified the core regions of face perception, bilaterally, within each participant.[3] Contiguous clusters of at least 5 face-selective voxels located on the lateral temporal portion of the fusiform gyrus were designated as the fusiform face area, whereas clusters located on the lateral surface of the inferior occipital gyrus were designated as the occipital face area. Face-selective clusters located on the posterior segment of the superior temporal sulcus were designated as the superior temporal sulcus.

The nomenclature for our prosopagnosic subjects follows the evidence for tissue loss or hypointensity on T1-weighted images. The anterior tip of the middle fusiform sulcus,[27] at the approximate midpoint between the anterior temporal and occipital poles, served as a boundary (Talairach y = −30). Lesions mainly anterior to this line were designated as anterior temporal (AT) and those posterior to it as inferior occipitotemporal (IOT). Some subjects had additional complexities to their lesions. Fluid-attenuated inversion recovery (FLAIR) sequences in R-AT3 revealed additional left medial temporal lobe and insula hyperintensities (see Fig 1). B-ATOT2 had bilateral fusiform lesions and a right anterior temporal lesion, as well as posterior periventricular hyperintensities on FLAIR sequences. L-IOT2, who had resection of the left fusiform gyrus for epilepsy, also had atrophy of the right fusiform gyrus and failed to show activation of the right fusiform face area; hence he is grouped with the subjects with bilateral lesions (see Fig 2).

TABLE 1. Patient Data

Subject	Age at Testing, yr	Onset Age, yr	Etiology	Field	Face Recognition Tests			
					Famous Faces (d′) > 2.19[a]	CFMT	WRMT Faces/50	WRMT Words/50
Unilateral lesions								
R-IOT1	54	37	Vascular malformation	LUQ	1.96[b]	44	33[b]	41
R-IOT3	70	68	Stroke	LHH	0.29[b]	38[b]	33[b]	47
R-IOT4	62	57	Stroke	LUQ	1.29[b]	27[b]	39	50
R-AT2	34	25	Herpes encephalitis	Full	0.65[b]	33[b]	27[b]	47
R-AT3	37	30	Herpes encephalitis	Full	0.90[b]	31[b]	31[b]	47
R-AT5	60	32	Tumor resection	Full	1.52[b]	35[b]	28[b]	46
Bilateral lesions								
L-IOT2	59	39	Resection, epilepsy	Full	0.00[b]	21[b]	27[b]	42
B-IOT2	60	27	Hemorrhage	BHH	1.31[b]	24[b]	21[b]	42
B-ATOT2	23	10	Herpes encephalitis	Full	−0.15[b]	24[b]	19[b]	39
B-AT1	25	21	Herpes encephalitis	Full	−0.36[b]	30[b]	27[b]	45
B-AT2	47	24	Trauma	Full	0.68[b]	31[b]	31[b]	46

BHH = bilateral hemianopia; CFMT = Cambridge Face Memory Test; LHH = left hemianopia; LUQ = left upper quadrantanopia; WRMT = Warrington Recognition Memory Test.
[a]Lower limit of d′ for control subjects.
[b]Abnormal results.

The functional imaging data aligned with the T1-weighted structural nomenclature. Subjects with an IOT designation did not show activation by faces of the right fusiform face area, whereas those with an AT designation alone showed activation of all 3 core areas in each hemisphere, with the exception of R-AT5, who did not show activation of the right superior temporal sulcus (Table 3).

Finally, clinical computed tomographic imaging was available for the occipital lesion control subject (Fig 3).

Study 1: Word Length Effect

An elevated word length effect is a key diagnostic feature of alexia.[28] Although prolonged reading times may stem from a variety of impairments, ranging from the perceptual to the linguistic, the number of letters in a word may index the amount of perceptual processing involved, and an elevated word length effect may be more characteristic of perceptual than linguistic deficits in word processing.[28]

STIMULI AND PROTOCOL. We followed a method used in a prior study of alexia.[29] Subjects viewed the stimuli on a cathode ray tube display monitor with the screen positioned 57cm away, and their heads stabilized with chin and forehead rests. A LabTec (Vancouver, WA) C-315 microphone recorded verbal responses. The experiment was programmed in Experiment Builder 1.5.1 (www.sr-research.com). Words were displayed in black 24-point mono-spaced Courier font on a white background, and centered on the screen. Each character in this font occupies the same amount of horizontal space, about 1.5°. We chose 140 words from the Medical Research Council Psycholinguistic database (websites.psychology.uwa.edu.au/school/MRCDatabase/uwa_mrc.htm),[30] 20 each for 7 different word lengths ranging from 3 to 9 letters. The mean Kucera–Francis written frequency of these words were 380 ± 3,553 occurrences per million words read.

A trial began with a fixation cross of 0.7° width at screen center, which was replaced after 2,000 milliseconds by a single word at the center. The participant triggered the start of a trial with a key press, causing a central dot to replace the fixation cross. The single word display appeared after fixation and stayed within 1° of the central dot for 200 milliseconds. The subject's task was to read the word out loud as soon as they had identified the whole word. The microphone recorded the verbal response. The word remained visible until the subject then pressed a key to terminate the trial and begin the next one, with the fixation cross again.

TABLE 2. Neuropsychological Test Results

Test	Maximum	R-IOT1	R-IOT3	R-IOT4	R-AT2	R-AT3	R-AT5	L-IOT2	B-IOT2	B-ATOT2	B-AT1	B-AT2
Attention												
Trails A	—	39	59[a]	48[a]	21	22	43	54[a]	80[b]	30	18	30
Trails B	—	61	151	102[a]	44	37	78	117[a]	142[b]	93[a]	25	40
Star cancellation	54	54	54	54	54	54	54	53	53	54	54	54
Visual search	60	54	—	n/a	59	59	52	60	56	59	59	56
Memory												
Digit span–forward	16	12	7[a]	8	13	16	10	10	14	7[b]	12	9
Spatial span–forward	16	9	6[a]	10	9	12	6[b]	10	8	8[a]	10	9
Word list, immediate recall	48	28	31	37	35	31	24	27	35	27[b]	27[b]	23[a]
Visuoperceptual												
Hooper Visual Organization	30	27	27	22	28	27.5	22	9	22.5	12[b]	20	28
Benton Judgment of Line Orientation	30	29	20	24	28	30	21	23	29	22	28	28
Visual Object and Spatial Perception												
Object												
Screening	20	20	20	18	20	20	17	20	20	20	20	20
Incomplete letters	20	19	19	19	20	19	20	17	19	19	19	19
Silhouettes	30	21	22	18	18	22	19	3[b]	12[b]	4.5[b]	10[b]	25
Object decision	20	16	19	19	20	17	14	13[b]	14	10[b]	16	18
Progressive silhouettes	20	9	16	13	10	11	17[b]	10	15	4	17[b]	8
Spatial												
Dot counting	10	10	9	9	10	10	10	10	10	9	10	10
Position discrimination	20	20	18	19	20	19	18	19	19	15[b]	19	20
Number location	10	10	9	10	9	10	10	10	10	8	10	10
Cube analysis	10	10	9	10	10	10	8	10	10	9	10	9
Imagery												
Mental rotation	10	10	10	10	9	10	10	7	10	10	10	5

[a]Denotes borderline performance.
[b]Impaired.

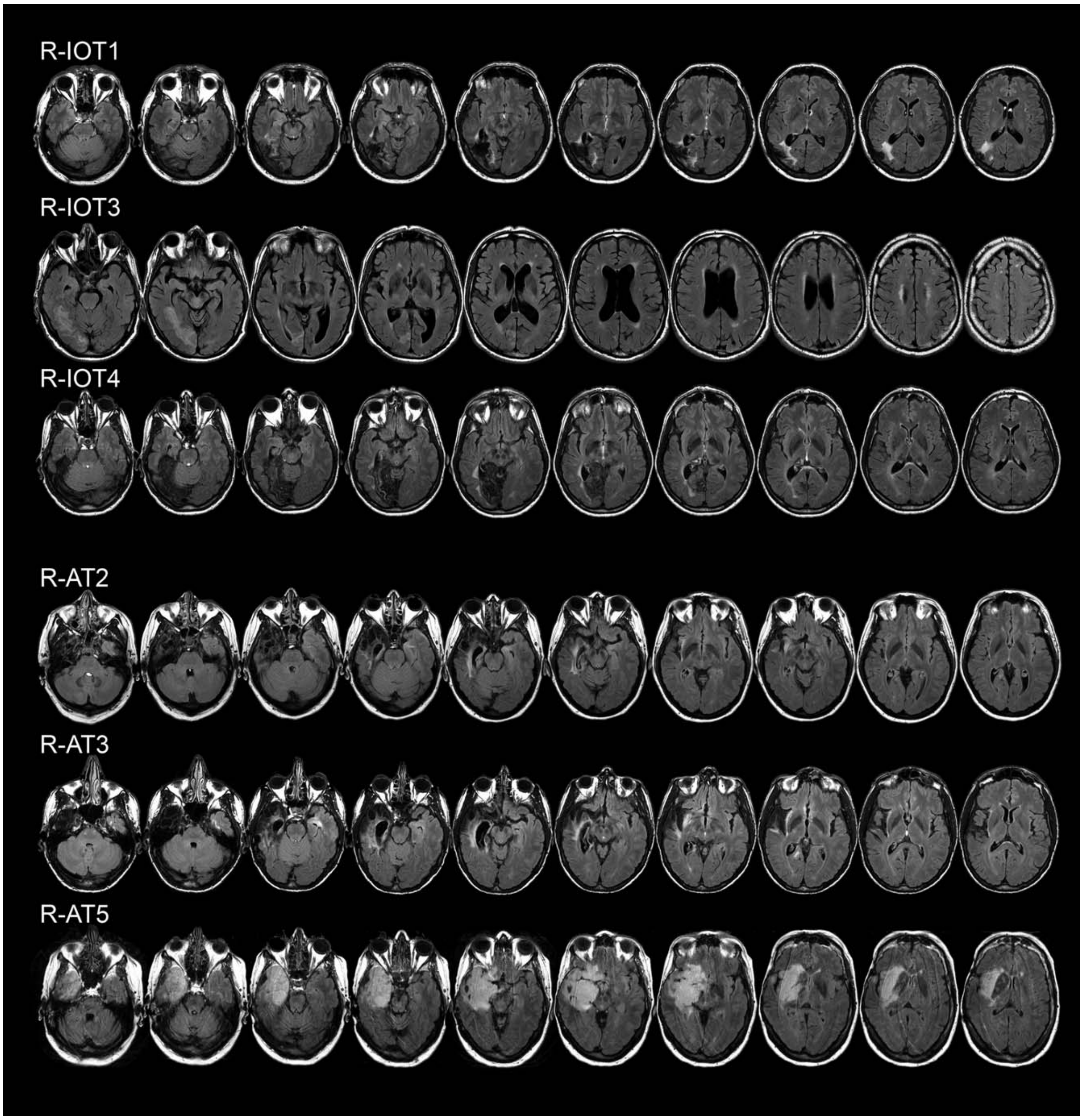

FIGURE 1: Fluid-attenuated inversion recovery magnetic resonance axial images of the lesions of the 6 prosopagnosic subjects with unilateral (right) lesions. The top 3 rows are for the 3 subjects with occipitotemporal lesions; the bottom 3 rows are for the 3 subjects with anterior temporal lesions.

Data from control subjects included 3 conditions from separate blocks: full visual field, and simulated right and simulated left homonymous hemianopia, as previously reported.[29] We created the simulations with a gaze-contingent paradigm. The current fixation location was sent to the computer controlling the display, which caused the entire screen to the left or right of the current point of fixation to be set to the same luminance and color as the background. Screen updates occurred within a single frame (maximum lag of 7 milliseconds). If the subject's gaze was directed outside of the monitor or if the eye tracker lost track of the pupil, as could occur if the subject pulled their head away from the eye tracker or closed their eyes, the entire screen assumed the color of the background. This simulation creates effects similar to those reported for real hemianopia in line bisection,[31,32] visual search,[33] and word reading.[29]

The verbal record was reviewed to exclude trials in which the latency was triggered by a nonverbal sound. We also excluded incorrect trials, on which subjects uttered the wrong word. From the remaining correct trials we plotted the mean

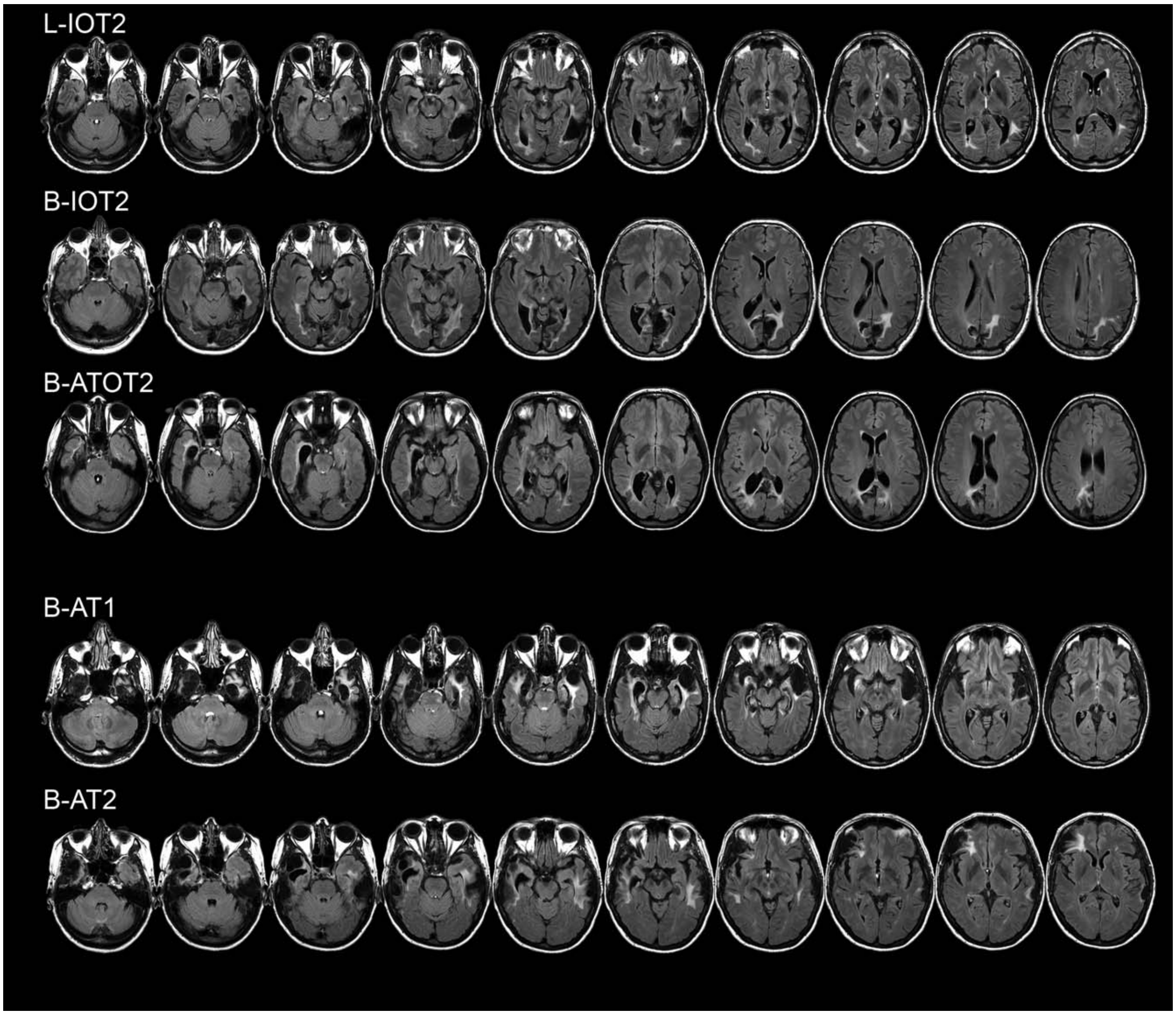

FIGURE 2: Fluid-attenuated inversion recovery magnetic resonance axial images of the lesions of the 5 prosopagnosic subjects with bilateral lesions. The top 3 rows are for the 3 subjects with occipitotemporal lesions; the bottom 2 rows are for the 2 subjects with anterior temporal lesions.

response time as a function of number of letters, the slope of which is the word length effect, defined as the increase in time needed to process a word with each additional letter. From control subject data we calculated 95% prediction upper limits for full field viewing as well as simulated right or left hemianopia. Subjects were compared to the appropriate condition, based on whether they had a hemifield defect affecting the central 5°.

Study 2: Sorting by Word versus Text Style

Recent reports on word perception in prosopagnosia focused solely on processing text for word content.[20,21] However, previous small studies and anecdotal reports[22,34] suggested that prosopagnosic subjects with right-sided lesions may be impaired not in word recognition but in font or handwriting recognition, a frequently neglected aspect of visual text processing, whereas the opposite may be true of alexic patients with left-sided lesions.[35] Thus, although text processing is often assumed to be synonymous with word recognition, we would argue that the many-to-many hypothesis is actually agnostic as to whether it is the processing of the words or the stylistic content of text that is affected in prosopagnosia.

STIMULI AND PROTOCOL. We used the method and stimuli from a prior report of 1 alexic subject and 3 of the prosopagnosic subjects in the current study[22] to examine this issue in a larger prosopagnosic cohort.

Our handwriting stimulus set consisted of 10 words ranging from 2 to 11 letters, each written by 10 different subjects, yielding 100 stimuli. Stimuli were printed in black on white paper and fixed to 102 × 63mm cards. The main bodies of these lowercase words were 3 to 5mm in height. Our computer font stimulus set consisted of 7 four-letter words, each printed in upper case in 8 different styles, yielding 56 stimuli. Font size varied between 16, 18, and 20 point to minimize size cues. All

TABLE 3. Functional Magnetic Resonance Imaging Results

Patient	Region	Peak *t* Value	Cluster Size	Coordinates		
				X	Y	Z
R-IOT1	rOFA	Lesion				
	rFFA	Lesion				
	rpSTS	5.52	146	57	−40	13
	lOFA	4.98	51	−36	−79	−14
	lFFA	6.71	281	−33	−68	−23
	lpSTS	6.32	785	−57	−28	−2
R-IOT3	rOFA	Lesion				
	rFFA	Lesion				
	rpSTS	4.76	259	56	−44	2
	lOFA	3.87	31	−40	−65	−19
	lFFA	8.43	325	−41	−42	−17
	lpSTS	6.37	551	−56	−42	5
R-IOT4	rOFA	4.54	88	27	−89	−5
	rFFA	Lesion				
	rpSTS	4.34	194	51	−36	3
	lOFA	9.01	786	−32	−83	−13
	lFFA	7.34	169	−33	−43	−20
	lpSTS	7.47	414	−57	−38	2
R-AT2	rOFA	3.48	51	29	−86	−9
	rFFA	8.34	626	38	−41	−22
	rpSTS	12.59	1,825	43	−38	3
	lOFA	8.10	184	−32	−79	−11
	lFFA	6.02	97	−43	−43	−22
	lpSTS	7.79	343	−58	−44	4
R-AT3	rOFA	8.76	187	45	−78	−11
	rFFA	8.11	289	40	−55	−20
	rpSTS	5.74	462	59	−44	12
	lOFA	3.78	84	−39	−72	−19
	lFFA	12.82	491	−41	−54	−17
	lpSTS	3.42	5	−58	−47	8
R-AT5	rOFA	4.63	7	26	−74	−15
	rFFA	4.13	7	35	−50	−18
	rpSTS	—				
	lOFA	5.88	49	−34	−76	−15
	lFFA	4.04	5	−34	−47	−19
B-IOT2	rOFA	5.45	45	26	−81	−14
	rFFA	Lesion				
	rpSTS	10.37	966	58	−42	1

TABLE 3: Continued

Patient	Region	Peak *t* Value	Cluster Size	Coordinates		
				X	Y	Z
	lOFA	Lesion				
	lFFA	Lesion				
	lpSTS	9.94	731	−50	−51	1
L-IOT2	rOFA	6.66	146	43	−65	−5
	rFFA	Atrophy				
	rpSTS	4.54	48	40	−32	−6
	lOFA	3.43	5	−28	−92	−15
	lFFA	Lesion				
	lpSTS	3.72	10	−57	−56	−8
B-ATOT2	rOFA	4.57	439	25	−88	−14
	rFFA	Lesion				
	rpSTS	3.82	93	47	−45	8
	lOFA	4.94	132	−29	−92	−23
	lFFA	4.25	123	−29	−55	−10
	lpSTS	7.08	252	−59	−51	2
B-AT1	rOFA	12.37	3,956	30	−88	−5
	rFFA	13.09	1,064	39	−52	−20
	rpSTS	9.67	329	46	−49	−2
	lOFA	9.43	1,543	−30	−85	−8
	lFFA	5.96	57	−39	−55	−26
	lpSTS	5.90	50	−60	−46	4
B-AT2	rOFA	6.77	359	43	−68	−13
	rFFA	12.76	679	39	−46	−19
	rpSTS	11.64	1,464	50	−29	3
	lOFA	8.32	738	−42	−76	−26
	lFFA	5.81	175	−44	−46	−30
	lpSTS	4.54	396	−55	−43	−7

words were printed in black on white paper and fixed to 50 × 60mm cards. Words were 4 to 5mm in height.

The cards for the handwritten set were shuffled and the deck was handed to the subject with instructions to sort the cards accurately and quickly into piles of different words, regardless of handwriting. They were timed with a stopwatch. Following this, the 10 cards with the word "maintenance" were placed on the table as exemplars of the 10 different handwriting styles. The subject was now told to sort the remaining cards into piles by handwriting style, rather than word. They were to place each card underneath the "maintenance" exemplar card whose handwriting it most resembled. After placing the card they were not allowed to review it again. Subjects were timed by a stopwatch. After completing the handwritten set, a similar protocol was used for the computer font set. Although the prior study showed that sorting by words is more accurate and rapid than sorting by style,[22] this asymmetry in task performance is offset by the value of using the exact same stimulus set for both tasks; any difference in subject performance compared to controls cannot be attributed to stimulus differences.

Font and handwriting tests were analyzed similarly. We calculated a per-item completion time by dividing the time to complete sorting by the number of items in the set.

There were no errors when sorting by word. For sorting by style, we measured 2 indices of accuracy. The first was a

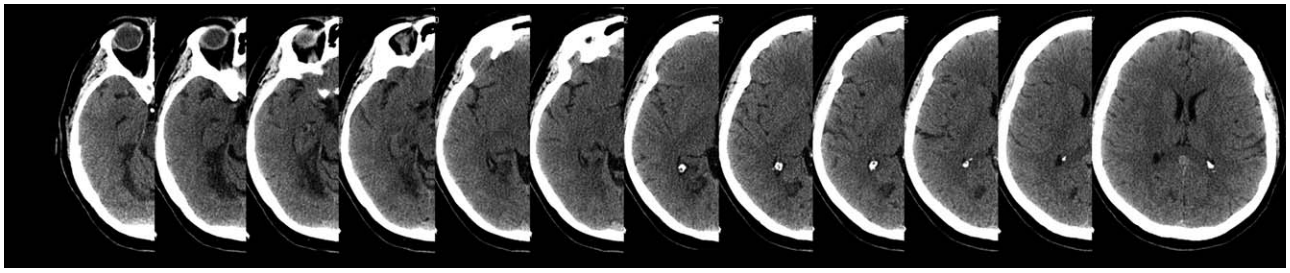

FIGURE 3: Axial computed tomographic images of the affected right hemisphere of the occipital lesion control subject.

simple "fraction correct" measure. Second, to capture the randomness of the assignments made by the subject, we computed a "cluster index."[22] We generated contingency tables in which the rows represented the handwriting classification given by the subjects to each card and the columns represented the actual handwriting style of the card. 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, which is then divided by the number of items in the test to give a final cluster index. Inability to perceive style would be characterized by more random assignments of cards, resulting in a low value for the cluster index.

All completion time and accuracy scores for subjects were compared to 95% prediction limits of the control subjects.

Results

Study 1: Word Length Effect

Subject R-IOT3 was not available for this study. None of the remaining 5 subjects with unilateral right-sided lesions had an elevated word length effect (Table 4, Fig 4). However, this was found in 4 of the 5 subjects with bilateral lesions, 2 of whom also had elevated mean response times. In subject B-IOT2, the significance of his elevated word length effect has to be tempered by the finding that he has bilateral hemifield deficits. However, subjects L-IOT2, B-ATOT2, and B-AT2 all had increased word length effects despite full visual fields. The effects are modest, however, compared to alexic patients, whose word length effects exceed 500ms/letter in the majority, and are >100ms/letter in >90% of subjects.[28]

Study 2: Sorting of Word versus Style

None of the 11 subjects showed an elevated completion time for sorting printed type by word (see Table 4). Only 1 subject (R-IOT3) had a borderline elevated completion time for sorting handwritten text by word, but he was the oldest subject and his sorting time was similar to that of his wife (Subject C3, Fig 5).

Completion time for sorting by style was elevated for either font or handwriting in 4 of 6 subjects with inferior occipital lesions, 2 with unilateral and 2 with bilateral damage. In contrast, none of 5 subjects with lesions limited to the anterior temporal lobes showed elevated sorting times (see Fig 5).

Accuracy and cluster indices for sorting text by style were more frequently abnormal than completion time (see Table 4, Fig 6). All but 1 subject were impaired on accuracy for handwriting style, 7 of whom also had a reduced cluster index. Accuracy and cluster indices were frequently but less consistently abnormal for font style, either being abnormal in 2 of 6 subjects with unilateral lesions and in all 5 subjects with bilateral lesions. Only 1 subject (R-AT2) was normal on all indices of style sorting. Scores did not differ between patients with bilateral and those with unilateral lesions, for either font (accuracy $t_{[9]} = 1.79$, $p = 0.11$; cluster $t_{[9]} = 1.65$, $p = 0.16$) or handwriting processing (accuracy $t_{[9]} = 0.36$, $p = 0.73$; cluster $t_{[9]} = 0.48$, $p = 0.65$).

In contrast to our prosopagnosic subjects, the occipital control subject scored in the higher range of performance of healthy subjects on all accuracy and cluster indices. She was only slightly slow on sorting handwriting style, which might be due either to the known effect of hemianopia in prolonging search tasks[33] or a speed–accuracy tradeoff given her superior accuracy in this task.

Discussion

In the first study, we found that word reading showed elevated word length effects only in subjects with bilateral lesions, whereas sorting times in the second study did not provide convincing evidence of a defect in style-invariant word recognition in any subject. Conversely, deficits in processing the style of text, particularly for handwriting, were evident in nearly all subjects.

Our first study focused on the word length effect, which is increased in alexia.[28] The word length effect is a more effective measure of word expertise than mean reading time,[36] and an increased word length effect is more characteristic of perceptual than linguistic word-

TABLE 4. Experimental Results

Subject	Study 1		Study 2							
	Mean Reaction Time, ms	Word Length Effect, ms/Letter	Font				Handwriting			
			Word	Style			Word	Style		
			Time, s/item	Time, s/item	Accuracy	Cluster	Time, s/item	Time, s/item	Accuracy	Cluster
95% prediction limits, controls										
Full	859	53	4.63	15.35	0.65	134	6.32	20.15	0.44	190
Left HH	2,179	170								
Unilateral										
R-IOT1	899	36.1	1.45	5.73	0.73	155	1.86	10.21	0.38[a]	240
R-IOT3	—	—	4.46	36.25[a]	0.60[a]	135	6.80[a]	60.67[a]	0.39[a]	136[a]
R-IOT4	933	23.6	2.61	17.44[a]	0.75	150	3.16	19.17	0.39[a]	172[a]
R-AT2	529	4.8	1.52	6.60	0.81	187	1.85	8.64	0.50	257
R-AT3	572	14.4	2.05	7.75	0.67	183	1.95	13.83	0.29[a]	165[a]
R-AT5	822	49.8	2.93	6.77	0.46[a]	97[a]	3.06	11.39	0.22[a]	99[a]
Bilateral										
B-IOT2	1,373[a]	260.4[a]	2.82	19.35[a]	0.60[a]	119[a]	4.30	23.33[a]	0.36[a]	156[a]
L-IOT2	1,989	85.9[a]	3.30	20.06[a]	0.23[a]	60[a]	4.13	18.53	0.21[a]	126[a]
B-ATOT2	1,191[a]	92.1[a]	2.00	14.38	0.67	132[a]	2.01	9.44	0.40[a]	201
B-AT1	679	27.1	1.79	7.73	0.58[a]	116[a]	1.75	10.02	0.39[a]	198
B-AT2	837	96.4[a]	1.86	5.19	0.46[a]	164	2.39	10.27	0.36[a]	141[a]
Occipital lesion control										
CS			1.39	9.83	0.90	222	1.80	22.66[a]	0.73	407

[a]Abnormal results.
CS = control subject; HH = homonymous hemianopia.

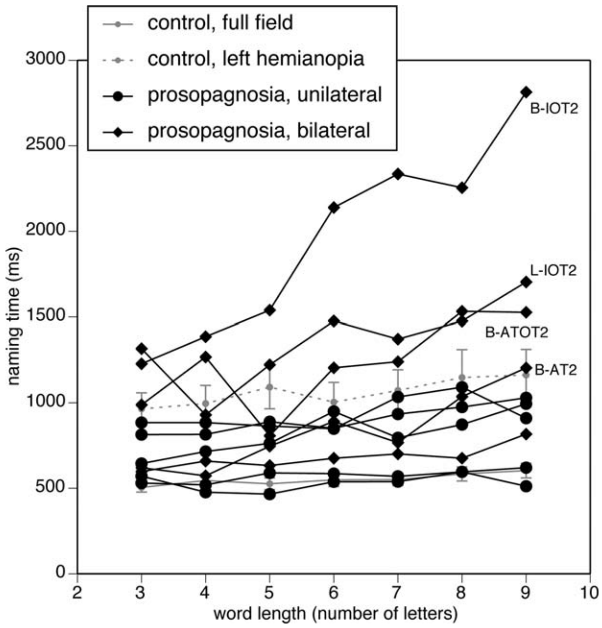

FIGURE 4: Results, study 1. Naming time plotted as a function of word length (number of letters) is shown for individual subjects and control group means. Named data are for individuals with a prolonged word length effect.

processing impairments[28]; hence we chose to focus on this measure in investigating perceptual problems in word processing in prosopagnosia. Nevertheless, this first study requires subjects to read words aloud and thus involves additional linguistic processes, such as accessing a mental lexicon or a grapheme-to-phoneme conversion process. In contrast, the word recognition probed in the second study may be a purer reflection of perceptual word processing, as it required discrimination of word content across variations in style, but does not require identification of the word, its meaning, or its pronunciation. In our prosopagnosic subjects with unilateral right-sided lesions, the results of both studies agree, indicating that perceptual processing of words is not impaired. However, in subjects with bilateral lesions, word-sorting was intact in the second study, whereas modest elevations in word length effects were found in most of these subjects in the first study. This suggests 1 of 2 possibilities. The first is that the word length effect is simply a more sensitive measure of the perceptual processing of words, which is impaired when there is additional left-sided damage. The second is that the elevated word length effect reflects mild damage to aspects of reading beyond the perceptual processing of single words, and that these are lateralized to the left hemisphere.

Our results do not support the prediction that right-sided lesions causing prosopagnosia would also impair reading.[8] Our finding of intact reading of single words is consistent with 1 prior study of 4 such subjects[21] but conflicts with another of 3 other subjects.[20] However, 2 of the patients with impaired face processing in the latter study were described previously as having visual object agnosia,[37] with perceptual problems that involved more than just faces. Hence it may not be surprising that a more general perceptual deficit would also affect the processing of visual words.

The above prediction, that reading would also be impaired in prosopagnosic subjects with unilateral right-sided lesions, is based first on a neuroimaging observation that visual text activates right fusiform regions that overlap those activated by faces,[7] and second on an assumption that the activation seen reflects processing of word content. However, neuroimaging data are inherently limited in that they cannot reveal the cognitive

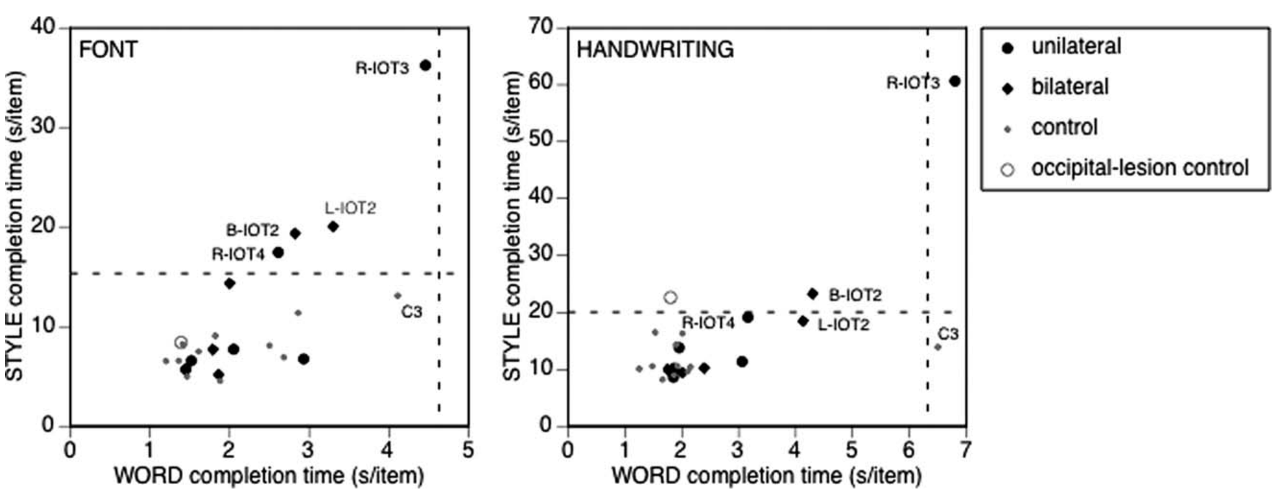

FIGURE 5: Results of study 2, completion times. Times for sorting by word content are shown on the x-axis, whereas the y-axis plots the sorting by style, left graph for computer font stimuli, right graph for handwritten stimuli. Horizontal and vertical dashed lines indicate 95% prediction limits of normal performance; subjects falling either right or above these lines are considered impaired. C3 is the wife of and age-matched control for patient R-IOT3.

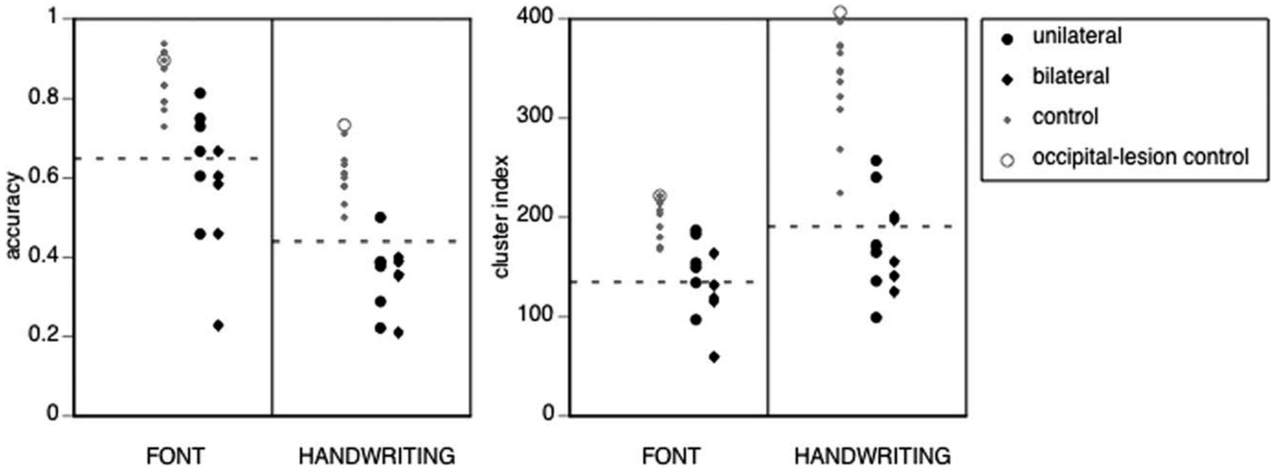

FIGURE 6: Results of study 2, accuracy and cluster index for sorting visual text by style of font or handwriting. The left graph is for accuracy; the right graph is for the cluster index. In each graph, the left half is for computer font stimuli, and the right half is for handwritten stimuli. The horizontal dashed lines indicate the lower 95% prediction limits of normal performance; subjects below these limits are considered abnormal.

operation being performed on the stimulus in the activated area. Even adaptation studies are not definitive; if changing a stimulus property results in release from adaptation in a region, that area could be either involved in processing that specific property or simply receiving neural inputs sensitive to that property, processing of which occurs elsewhere. Hence the observation that right fusiform regions are activated by visual text does not mean that they are processing words.

Rather, a key point in interpreting our results is that complex stimuli like faces and text have multiple dimensions. This is well recognized for faces, which convey not only identity but also expression, age, gender, and attractiveness, among others. This is reflected in concepts that regions of the face network contribute selectively to these properties[3]; whereas the fusiform face area may critically process facial identity, the superior temporal sulcus may be more involved in expression,[38] a proposal that is supported by observed dissociations in studies of patients with cerebral lesions.[39] Although there are fewer data for text processing, the available evidence suggests that there are hemispheric differences, with left-sided lesions impairing the extraction of word content and right-sided lesions impairing the processing of textual style.[22,34] Supporting this may be neuroimaging observations that, compared to printed text, handwritten text generates greater activation in bilateral ventral occipitotemporal cortex, but the effect is larger on the right.[40] Furthermore, there are lateralization parallels in the auditory modality; whereas the processing of spoken words and their linguistic aspects involve left temporal and frontal structures more than those on the right, the reverse is true when subjects are processing song, which can be considered a stylistic aspect of speech,[41–43] just as font is a stylistic aspect of writing. Also, just as handwriting may provide stylistic cues to the identity of the writer, the voice is a stylistic cue that can identify the speaker of a communication. Functional neuroimaging has revealed temporal voice areas in the middle and anterior superior temporal sulcus that are more active on the right,[44] and adaptation functional MRI studies show sensitivity to voice identity in the right anterior superior temporal sulcus.[45] Neuropsychological data supporting a right hemispheric dominance for voice recognition have also been reviewed elsewhere.[46]

The results of our second study add to this, by showing that right or bilateral lesions causing prosopagnosia almost invariably impair the discrimination of font or handwriting. In contrast to our prior report, which found such impairments in 2 prosopagnosic patients with right fusiform lesions but not in 1 with only a right anterior temporal lesion, the current study of a much larger sample of 11 patients found impaired processing of textual style after either fusiform or anterior temporal lesions, indicating that this form of perception involves an integrated perceptual network rather than a single occipital region.[22] Furthermore, we found that style processing was not more severely impaired in those with bilateral lesions, implying that the right hemisphere makes the critical contribution to its perception, an inference that is also supported by reports of preserved perception of handwriting or font style by alexic patients with unilateral left occipital lesions.[22,34,35,47]

What do our results mean for the many-to-many hypothesis[8] of visual processing, and the complementary lateralization of word and face processing? Although they do not support the more restrictive proposal that prosopagnosic subjects with unilateral right-sided lesions would show minor impairments in word processing, they do show that such subjects have a deficit in visual text processing, but for style rather than words. Hence they are compatible with this hypothesis if we consider the possibility that the cognitive operations performed on visual text are not homogenous across the entire network activated by words, but show regional and especially hemispheric specialization. Seeing style independent of word content likely relies on extracting different text properties than reading words independent of style; our results and prior ones[22,34] suggest that it is not the stimulus that is lateralized but the operation. Whether hemispheric specialization is true for the operations in face processing is not yet clear. One neuroimaging study suggested that part-based face processing activated the left hemisphere whereas holistic processing activated the right,[48] but neuropsychological evidence is lacking. Nevertheless, it would be intriguing in the future to explore the similarities between the contrasting hemispheric operations performed on text and faces, to advance our understanding of the lateralization of visual processes.

Two points are important to stress in closing. First, our finding of intact reading by prosopagnosic subjects with right-sided lesions does not prove that word processing does not occur in right visual areas; the dominant role of the left fusiform gyrus in reading may mask a redundant right-sided contribution in subjects with an intact left hemisphere. Some argue that the residual reading ability in patients with deep dyslexia following left brain damage reflects right hemispheric word processing.[49] Conversely, our finding of impaired processing of font and handwriting in these subjects does suggest that the right visual areas make a critical nonredundant contribution to the processing of stylistic aspects of visual text.

Second, given the size of natural human lesions, it is not possible to state in any particular subject whether coexisting defects in processing faces and textual style are due to damage to a single process or region, or to damage to separate processes involving adjacent regions. However, the high rate of co-occurrence of face and textual style processing deficits in our series of subjects with lesions of variable size and location suggests that the existence of a shared neural resource that processes both of these very different stimuli should not be discounted. If so, this provides support for a modified version of the many-to-many hypothesis that incorporates hemispheric specialization of operations for complex multidimensional stimuli.

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Authorship

C.H. collected and analyzed experimental data, and participated in writing. R.P. assisted in collecting and analyzing data, and performed neuroimaging assessments and neuropsychological testing. B.D. assisted in subject recruitment and review of the manuscript. J.J.S.B. was responsible for test design and wrote the first draft. C.H. and R.P. are co–first authors.

Potential Conflicts of Interest

Nothing to report.

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