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Pure alexia with intact perception of complex visual stimuli: a case study

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ABSTRACT

After a stroke involving the left occipitotemporal cortex our patient shows a word-length effect and has problems to identify letters or numbers in strings of symbols. But he is normal in identifying isolated letters and in non-verbally categorizing even complex images such as faces or natural scenes. His cortical lesion is stretching from the visual word form area (VWFA) anteriorly causing additional problems to name visual stimuli and to match acoustic stimuli with images. We conclude that our patient suffers from pure alexia without deficits to identify even complex visual stimuli. Our results directly contradict several explanations for letter-by-letter reading.

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Cortical specialization; lesion studies; stroke; visual perception; visual fields; pure alexia; letter-by-letter reader

Introduction

We adopt the definition of pure alexia proposed by Starrfelt and Shallice (2014) as an acquired reading disorder with intact writing and spelling, prolonged reaction times for reading, and a word-length effect, lesions in the posterior left hemisphere, but without aphasia, dementia, or visual agnosia. Please note that pure alexia denotes a specific syndrome while letter-by-letter reading can result from other disorders such as hemianopia or semantic dementia.

Early case studies of such an isolated reading disorder date back even to the end of the 19th century (Déjerine, 1891, 1892). Over the last century more than one hundred patients were described that suffered from more or less isolated reading disorders while only a few were tested so extensively that all of the above criteria could be verified (see Barton, Hanif, Eklinder Bjornstrom, & Hills, 2014 for a review). But virtually all cases showed the distinctive feature of (pure) alexia, the pronounced increase of reaction times with increasing word length (letter-by-letter reading; LBLR).

Only recently the cortical areas subserving word recognition in healthy individuals were identified by means of functional MRI studies. The area consistently activated in fMRI by strings of letters and words is localized in the left occipitotemporal cortex (Cohen et al., 2002; Devlin, Jamison, Gonnerman, & Matthews, 2006; Gaillard et al., 2006). Electrical cortical stimulation during brain surgery confirmed this anatomical location (Zemmoura, Herbet, Moritz-Gasser, & Duffau, 2015). The localization of this visual word form area (VWFA) should match the cortical areas defective in patients suffering from pure alexia and indeed this is the case.

In our view, the most important question still under debate seems to be how specific pure alexia is. Can the deficit be limited to words or is it necessarily a more general deficit? A longstanding debate exists regarding where in the hierarchy of visual processing to position letter-by-letter reading.

Standpoints vary between a deficit being highly specific for words at one extreme or at the other extreme being a general decrease of visual pattern recognition (Arguin, Fiset, & Bub, 2002; Behrmann, Nelson, & Sekuler, 1998).

The first extreme view, that of a purely “high level” disturbance postulates deficits of rather high-level pattern recognition specific only for letters and words, namely a damage to a specialized VWFA (Cohen et al., 2002; Starrfelt, Nielsen, Habekost, & Andersen, 2013; Warrington & Shallice, 1980). Of course, patient’s lesions do not have to be restricted to this VWFA but will often also involve areas specialized for example for digits, faces, or objects even if the VWFA itself would not be involved in the recognition of those objects. On the other “low level” extreme are authors who suppose that impairments only on a low or early level are the cause of the reading problems (Behrmann, Plaut, & Nelson, 1998; Chialant & Caramazza, 1998; Farah & Wallace, 1991). Deficits on a relatively low level as for example of general form discrimination would of course lead to more generalized impairments than higher level ones. One possible mechanism proposed by these authors is based on pathological lateral interactions between letters, as in the case of crowding (Crutch & Warrington, 2007), well known in many amblyopic patients who experience great problems in identifying letters within words while none for isolated letters. Another possible explanation would be a deficit in processing a range of high spatial frequencies (Fiset, Gosselin, Blais, & Arguin, 2006).

A dimension often overlooked in the literature is the visual field. About 90% of alexic patients whose visual fields were tested in the past suffered from an often substantial visual field defect which by itself may cause the letter-by-letter reading (Barton et al., 2014) due to an inability to simultaneously see the entire word. At most around a dozen patients described so far including the patient described in this study were reported to have an intact visual field. But patients were usually tested by different forms of perimetry with the

methods employed ranging from finger perimetry that will detect only very large field defects to Goldmann perimetry that is far more sensitive but also of very limited use for the central part of the visual field that is used for reading words. Hence, the claim that the patient's central visual field was completely intact often relied on too coarse measurements even in those patients whose fields were tested at all.

As indicated above, many of the so-called letter-by-letter reading patients are not pure letter-by-letter readers. But this does not imply that there is no highly specialized VWFA. It may well be that the blood supply of this cortical region is such that a stroke usually destroys not only the cortical tissue crucial for the parallel processing of several letters (hence the so-called VWFA) but also nearby areas that subserve different functions of visual pattern recognition such as digit processing (Grotheer, Ambrus, & Kovacs, 2016). Alternatively the VWFA might also be used to identify numbers. Hence, it is impossible to exclude the existence of such a pure VWFA or "parallel processor for over learned symbols" (such as letters and digits) on the basis of studies showing that a number of alexic patients suffer from additional deficits of visual pattern recognition such as face discrimination. In principle, a single patient suffering from pure alexia would be sufficient to reconcile the results of patient studies with those of imaging and ERP studies by demonstrating that, with a sufficiently small and adequately located lesion, a patient will suffer from a pure alexia.

Here, we present the data obtained on one such patient starting with the anatomical description of his cortical lesion, proceeding to clarify that he is a letter- by- letter reader without any relevant visual field defect, and then testing his abilities to recognize a number of different visual stimuli ranging from single letters to complex visual stimuli and natural scenes. Finally, we test the influence of crowding and present data on the spontaneous partial rehabilitation over an interval of ten years.

Methods and data

Case history and imaging results

KC suffered from an ischemic stroke in the territory of the left posterior cerebral artery at the age of 53 years and was healthy before the event. Heavy smoking was the only risk factor for cerebrovascular disease. KC is a right- handed man with 9 years of schooling and a vocational training as a plumber. He led his own business of pest control.

An MRI scan taken one week after stroke revealed a small ischemic lesion in the left occipitotemporal region involving the inferior temporal gyrus, the fusiform gyrus, and the lingual gyrus extending into parts of the parahippocampal gyrus without involvement of the optic radiation or striate cortex (Figure 1, Table 1).

KC subjectively only reported problems with reading. Clinical neurological examination did not reveal any motor or

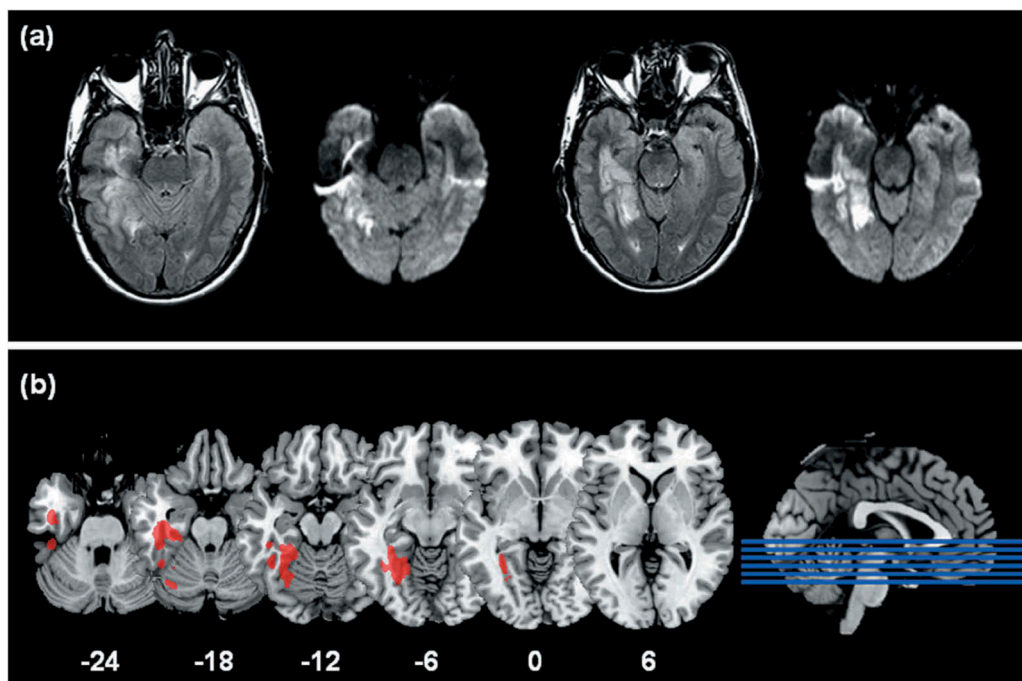


Figure 1. (a) MRI scan of KC's lesion (both dark fluid and diffusion weighted sequences). (b) Axial views of the volume of interest (VOI) of the left occipitotemporal lesion plotted on the Ch2 template of MRICron. The lesion was delineated manually on the T2 weighted MRI scan using the MRICron software package (Rorden et al., 2007). The original MRI scan was spatially coregistered and normalized to the FLAIR template ($n = 366$; Winkler AM, Kochunov P, Glahn DC; available at <http://brainder.org>) using the clinical toolbox of SPM (Rorden, Bonilha, Fridriksson, Bender, & Karnath, 2012). The patient's small lesion lies in the vicinity of the coordinates typically described as the peak location of the VWFA (McCandliss et al., 2003) as localized by functional MRI and involves roughly the anterior two thirds of the elongated fusiform gyrus. These authors describe the peak activation for letters in the left posterior occipitotemporal sulcus bordering the fusiform gyrus [$x = -43$, $y = -54$, $z = -12$] in Talairach coordinates corresponding [$x = -45$, $y = -57$, $z = -12$] in MNI coordinates (see Lancaster et al., 2007 for transformation). The center of mass of KC's lesion lies in the midportion of the fusiform gyrus [$x = -33$; $y = -42$; $z = -16$] in MNI coordinates therefore it lies slightly more medially, anteriorly and inferiorly to the peak activation of the VWFA but the lesion also partially overlaps with the VWFA.

Table 1. Statistics of the size and distribution of the volume of interest of KC's lesion.

Area number	Area name ^a	voxels
Total		9723 ($\approx 2.1 \text{ cm}^3$)
39	ParaHippocampal_L	559
47	Lingual_L	912
55	Fusiform_L	5139
89	Temporal_Inf_L	1847

^aAAL-VOIs atlas (Automated anatomical labelling) of MRICron (Rorden, Karnath, & Bonilha, 2007).

sensory deficits such as neglect. Demtect Test (https://bilder.buecher.de/zusatz/22/22508/22508264_lese_1.pdf), a screening test for cognitive abilities, suggested mild dementia due to memory deficits, which may be explained by the lesion's location near the hippocampus.

Formal testing took place one week as well as 2, 4, 7 months and finally 9 years post stroke. Five male subjects, age and education matched with KC, without any history of ophthalmological or neurological disease served as controls for all tests where no adequate data pools were available from our lab or from the literature.

KC and the control subjects gave informed written consent according to the Helsinki Declaration to participate in the study and approval was given by the ethics committee of the University of Bremen.

Low level visual perception: intact visual fields, color, stereo and form vision

To assess the exact extend of KC's deficits, we started with testing different aspects of low- and mid- level vision. Static computerized 30°-perimetry and Goldmann automated kinetic perimetry (Oculus Twinfield®) showed no visual field defect. KC's visual acuity, color vision and stereoacuity were normal as

tested with letter-charts, Ishihara plates and Lang-Stereotest® according to standard procedures and norms.

In a computerized psychophysical test on form localization either by means of simple detection or by form discrimination (Kraft et al., 2010) the patient showed no hidden visual field defect in different visual submodalities.

Method

The stimulus array was varied to test four visual submodalities: luminance, texture, motion, and color (Figure 2) in a detection task or else in a discrimination task. In both conditions the subject's task was to indicate the location of the circle via a button while fixating the central dot. A software program developed in-house was used to present the stimuli and to determine thresholds by separate staircase procedures for each quadrant and to measure performance. In our patient we defined the upper right quadrant of the visual field as the one to expect disturbances ("target quadrant"). This is the contra-lesional quadrant because his lesion was in the **left** occipitotemporal cortex and **below** the calcarine fissure. Norm data for this test are to be found in Spang et al. (2019).

Results

None of KC's thresholds in the target quadrant (and also in the other quadrants) deviated significantly from the age- matched control group (all deviations $< \pm 1.965 \sigma$; Table 2).

Reading: intact single letter identification versus disturbed word processing

A slow-down of word processing with increasing word length is the most important symptom of alexic patients usually without problems to identify isolated letters. We tested whether or not our patient suffered from a word-length effect.

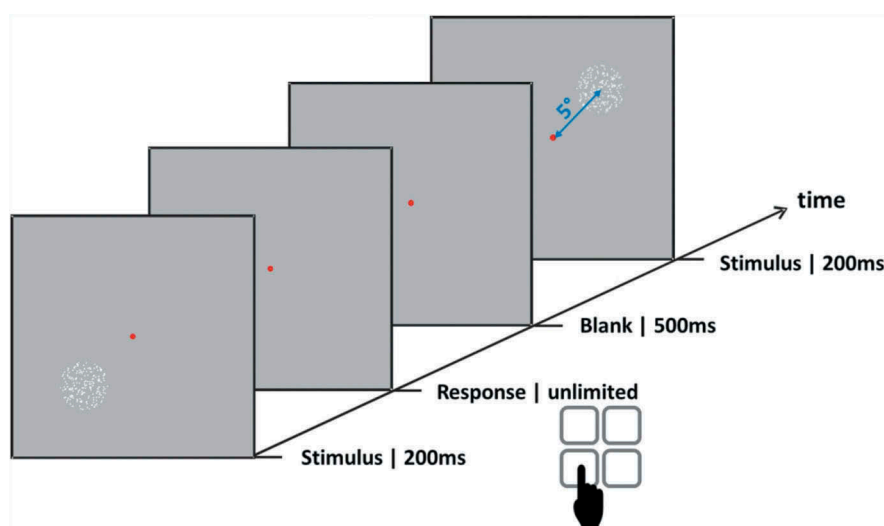


Figure 2. Stimulus array for quadrant specific luminance detection. Thresholds were determined by separate staircase procedures for each quadrant. Stimuli were displayed on a 21-in. monitor controlled by a PC with a spatial resolution of 1600 to 1200 pixels and a refresh rate of 75 Hz. Subjects were seated 60 cm from the screen and their head was stabilized by a chin rest. The stimulus array was presented for only 200 msec on the computer monitor. For the detection task a single circle appeared in one of the four visual field quadrants; for the form discrimination task the one circle had to be localized while three squares were simultaneously presented in the remaining visual field quadrants. In both conditions the subject's task was to indicate the location of the circle via a button press (4-alternative-forced-choice task; 4 AFC) while fixating the central dot.

Table 2. Results of the psychophysical tests on form localization.

Measure	Detection	Discrimination
Lum	-1.85	-0.86
Tex	-1.23	-0.7
Mot	0.92	0.54
Col	1.10	-0.33

Notes: Thresholds of KC in the right upper quadrant of the visual field (target quadrant) for the four submodalities (luminance, texture, motion, color) and two tasks, expressed as the difference in standard deviations between KC's results and those of the means of the controls ($n = 20$) of his age group (50–59 years) averaged for all quadrants of their visual field. Negative numbers are thresholds of our patient that are better than those of controls. Differences below 1.965σ are not significant on the 5% level.

Method

Words (Arial black, font height 52 arcmin = 9 mm) were displayed on a laptop computer (resolution 1280×1024), refresh rate 60 Hz, on a grey background, and were visible until an oral answer was given. We used words of 4, 6, and 9–11 letters (summarized as 9 letters) from the CELEX database, controlled for frequency of occurrence. Both common (between 65 and 2181 cases per million written words) and uncommon words (between 14 and 21 cases per million written words) were presented. Four sets of 60 words (4, 6, and 9 letter words, common and uncommon) were each tested in two sessions, in total encompassing 240 words. Two sets of the words used in 2008 were retested in 2017.

The 24 single letters (Arial black, font height 57 arcmin = 9.9 mm) of the alphabet were presented in pseudorandom order centrally on the setup for form vision (see above) on a grey background, followed by a set of 7 different masks, displayed for 91 msec in total. Masks consisted of sets of straight and bent lines shown in random orientation that sufficiently masked the letter. We used three presentation times for the letters: 65, 52, and 39 msec which were tested in three separate runs. Both KC and the 5 age-matched controls were instructed to name the letter shown as fast as possible and to guess letters not consciously identified.

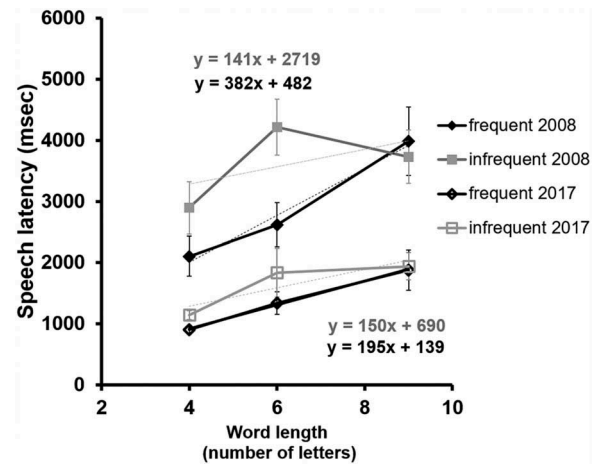


Figure 3. Mean naming latencies of KC as a function of word length separately for frequent and infrequent words. The intercepts and the slopes of the regression lines are indicated; error bars symbolize SEs. A software program developed in-house displayed stimuli and recorded verbal responses and reaction times via a commercial microphone. All stimuli were presented centrally at a distance of 60 cm from the screen following a central fixation point displayed for 500 msec. Voice responses and reaction times were subsequently evaluated by the experimenter.

Results

Word-length effect. KC showed the typical pattern of WLE with longer latencies for longer words and more errors for longer and infrequent words (Figure 3). Mean reading latency was strongly elevated (3477 msec when the 25% errors were excluded). WLE was 382 msec per letter for frequent words (calculated by setting string length against reaction time in a regression analysis) while the value for normal readers is about 30 msec per letter. When we retested KC nine years later, he had improved to a mean reading latency of 1497 msec and a WLE of 195 msec for frequent words. This is a “spontaneous recovery” based on everyday activities since the patient had declined any rehabilitation measures.

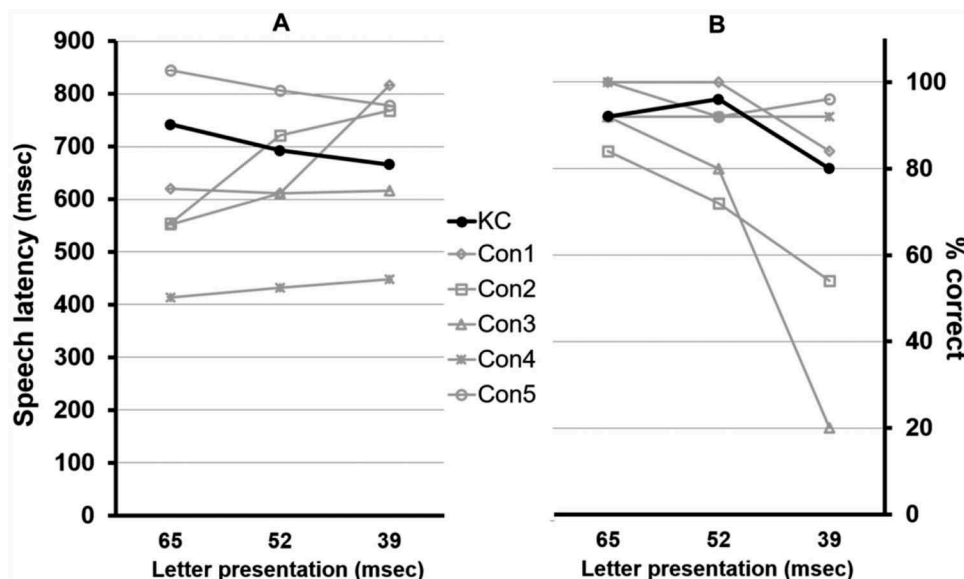


Figure 4. Mean (a) letter naming latencies and (b) percent correct results of KC and 5 matched control subjects as a function of the three presentation times. KC's results are within those of his age group.

Single letter identification. As Figure 4 shows, KC identifies single letters somewhat slower at the longest presentation time (65 msec) than most of our five control subjects but reacts within the group range for both shorter presentation times. The mean latency over all presentation times of KC of 722 msec ($SD = 74$ msec) did not differ significantly from that of the controls ($n = 5$; $M = 640$ msec; $SD = 140$ msec; $t = 0.535$, $p = 0.310$, one-tailed). His performance, at 89.3% correct, was even better than that of the controls at 83.5%. Significance was tested according to the methods proposed by Crawford and Howell (1998); Crawford & Garthwaite (2002) for comparison of single subject results with small groups (modified t-statistics. T-statistics in this paper will follow their algorithm (SINGLIMS.EXE) if not stated otherwise.

Perceptual speed: slowed down identification of letters and numbers in strings versus intact picture identification

A decreased reading speed could, in principle, be caused either by a general slowing down of cognitive capacities or else a general deficit of processing visual stimuli or else by a deficit to process visual inputs more complex than single letters (such as strings of letters and numbers). To discriminate between these possibilities, we tested KC regarding identification of strings of letters and numbers as well as (complex) visual stimuli.

Method

We used three “perceptual speed” subtests (P1, P2, P3) from the Ekstrom, French, and Harman (1976) kit of factor-referenced-cognitive tests.

Finding “a’s” test. In two consecutive sessions of each 2 minutes in total 1,640 English words were presented to the subjects printed on a sheet of paper. The task was to mark the five words containing the letter “a” in each of the in total 40 columns of 41 words. The score equals the number of “a’s” marked correctly. In our variation of this test we increased the distance between the letters (“a’s with gaps”) to rule out the “foveal crowding phenomenon” (Crutch & Warrington, 2007) as the cause for the decreased performance of KC. If crowding would be the root of the problem, finding “a’s” would be easier for KC in the modified test with larger distances between letters.

Number comparison test. The subjects inspected overall 96 pairs of multi-digit numbers (three to nine digits) in two consecutive sessions. In each of the two parts of the test they had to indicate whether or not the two numbers of each pair were different. Subjects had 1 ½ minutes for each of both parts. Their score equals the number of items marked correctly minus the items marked wrongly.

Identical pictures test. The test consisted of two times 48 rows of line drawings of geometrical figures or pictures arranged in two columns. The subject had to check which one of five similar geometrical figures or pictures in each row was identical to the prototype displayed as the leftmost

item of the row. Subjects had 1 1/2 minutes for each part. Their score equals the number of items marked correctly minus the items marked wrongly.

To test statistical significance we again used the methods proposed by Crawford and Howell (1998); Crawford & Garthwaite (2002) and compared KC to the norm scores given in the test manual and to the means of our four matched control subjects for all three subtests (one subject had to be excluded because of a history of dyslexia).

Results

The scores (and standard deviations) of the controls and the norm group are reported in Table 3.

KC was significantly slower in finding an “a” embedded in words as compared to the norm group ($t = -1.94$, $p = 0.027$, one-tailed). Moreover, KC’s results differed from those of our four controls by around two standard deviations. But these differences failed to reach significance both in the original test ($t = -1.72$, $p = 0.092$, one-tailed) and in the test with gaps ($t = -2.23$, $p = 0.056$, one-tailed) due to the high variance of control’s results.

KC’s ability to compare strings of numbers was significantly worse than the norm group ($t = -3.44$, $p < 0.001$, one-tailed) and that of our four controls ($t = -17.53$, $p < 0.001$, one-tailed).

In judging whether or not two complex pictures are identical, KC’s score of 51 was better than the mean of the controls ($M = 47.8$). There was no significant difference from both the four controls ($t = 0.21$, $p = 0.423$, one-tailed) and the norm group ($t = -0.19$, $p = 0.422$, one-tailed). Hence, his deficit was restricted to overlearned symbols, i.e. letters and numbers while not applying to (even more complex) visual forms.

Intact non-verbal categorisation of complex stimuli: objects, gender, scenes, and checkerboards

To further test KC’s ability in nonverbal visual object identification, we performed tests that do not require verbal responses but just categorisation via button press.

Manmade or natural?

Method. 100 black and white drawings of objects (300 × 300 pixels, sized around 9 arcdeg) from the database of the International Picture Naming Project (Szekely et al., 2005) were chosen and divided in two categories, namely man-made objects (62 pictures) on one hand and humans,

Table 3. Results of perceptual speed subtests.

Subtest	KC	Con1	Con2	Con3	Con4	M_{con}	SD_{con}	M_{norm}	SD_{norm}
A Test	18	86	42	47	51	56.5	20.0	47.0 ^a	14.9 ^a
A with gap	10	81	43	47	47	54.5	17.8	-	-
Number Test	10	20	20	19	20	19.8	0.5	26.6 ^b	4.8 ^b
Picture Test	51	68	40	43	40	47.8	13.6	53.2 ^a	11.2 ^a

Notes: Scores of KC, our control subjects (Con1-Con4), their means (M_{con}) and standard deviations (SD_{con}) and provided norm values (M_{norm} ; SD_{norm} ;) of the three “perceptual speed” subtests (P1, P2, P3) from the Ekstrom et al. (1976) kit of factor-referenced-cognitive tests: finding “a’s” in words, finding “a’s” in words with gaps, comparing numbers and comparing pictures. Each test comprised two parts and presentation was timed. There was a short pre-test for each test proper to familiarize KC and the age matched controls to the method. For details see the test manual.

^anorm = 288–300 males, suburban 11th and 12th graders ^b145 college males

animals, plants, and natural phenomenon (38 pictures) on the other hand. The task was to decide whether the object was manmade or natural. The pictures were presented centrally until the button press. As a control one female technician from our lab, aged 57 (MH), was tested. The aim of this test was to compare KC's ability to categorize with his ability to name the same pictures, as discussed below.

Results. KC was slightly faster than the control (MH) with a mean RT of 1,049 msec ($SD = 336$ msec) as compared to 1,332 msec ($SD = 548$) of the control for correct answers.

Man or woman?

Method. Two sets of 50 black and white female and male faces without visible hair were presented. In a two alternative forced choice task subjects had to decide on which side was the male face. The same task was presented to a norm group of 100 healthy control subjects (Schlede, 2009) in different age groups, with 20 in KC's age group (50–59 years), who also served as controls for the animal in the scene test.

Results. The median reaction time of our patient, at 861 msec, was above the mean of the medians of the age-matched control group ($M = 797$ msec) but within the confidence interval of $\pm 1.965 \sigma$ (Table 4; upper line). The same is true of the precision of his choices at 75% correct, as compared to the norm group (Hit $M = 80.9\%$).

Animal in the scene?

Method. In the same setting as for the categorisation of sex, pairs of photographs containing a range of animals (targets) and images of natural environments as well as buildings and statues (distractors) were chosen out of a set of a 1,000 coloured photographs kindly provided by Simon Thorpe (Kirchner & Thorpe, 2006) and presented for only 14 msec each.

Results. KC's median reaction time at 528 msec was below the mean of the medians of the age-matched control group ($M = 620$ msec). Our patient reached a level of 96% correct responses which corresponds to his age group. Reaction time and precision of KC did not differ significantly from the age-matched control group (Table 4, lower line).

Checkerboard matching

Method. We chose checkerboard stimuli based on a design by Mycroft, Behrmann, and Kay (2009). Forty-eight pairs of

checkerboards, 24 "same" and 24 "different" pairs, with grid sizes of 3×3 , 4×4 , 5×5 , and 6×6 checks were presented until the button press. KC and the five controls were encouraged to look around and indicate as fast as possible whether the pairs were same or different without receiving feedback. Only data from four controls could be analysed due to a technical defect.

Results. As expected, response times increased linearly with grid size and differed between "same" versus "different" presentations with longer latencies for "same" pairs for both KC and the controls (Figure 6). Slopes of the regression lines revealed shorter latencies for KC for "same" pairs (647 msec/item) than for the mean of controls (1.243 msec/item) and only slightly longer latencies for "different" pairs than controls (909 versus 714 msec/item). T-Tests between the reaction time means of the controls versus KC did not yield any significant differences. In addition, the increase of response times for the "different" pairs of KC was much lower than the example presented in the paper of Mycroft et al. (2009) indicating no deficit of KC for this test.

In summary, KC's results for these non-verbal categorisation tests did not differ significantly from our controls.

Visual-semantic interaction: disturbance to name visual objects

We tested possible involvements of language-related capabilities by evaluating KC's ability to name pictures of common objects with two established tests and with established norm ranges.

Method

In the first naming test we presented 247 black and white drawings of objects including the 100 drawings of the categorisation test mentioned above from the database of the International Picture Naming Project (Szekely et al., 2005).

For the second naming test we used the Category Specific Names Test of McKenna and Warrington (2007, 1978). The test encompasses 10 colored pictures of 4 semantic categories namely: body parts, colors, animals, and objects, each with the two levels I and II. Level II was similar but more difficult than level I. The pictures were scanned and presented on the computer screen. The task was to **name** the ten pictures of each category. The reaction times for naming the 10 pictures of each category were measured with a stopwatch. For this test norms exist from a large sample of healthy persons (n

Table 4. Results of categorization (gender and scenes).

Category	Hits				Reaction Time			
	KC	Age-matched norm ($n = 20$)			KC	Age-matched norm ($n = 20$)		
	%	M %	SD %	$CI \pm 1.965 \sigma$	median	M (Mdn) ^a	SD	$CI \pm 1.965 \sigma$
Man or Woman	75	80.9	6.2	68.7 – 93.1	861	797	112	575.8–1017.6
Animal or Scene	96	97.2	1.4	60.2–100	528	620	78	467.2–772.2

Notes: Percent correct responses and reaction times (msec) of KC and an age – matched control group (originating from a study of 100 healthy control subjects of different age groups of our lab; (Schlede, 2009) in discriminating between pictures of man versus women or else between scenes with or without an animal. For the discrimination of man versus woman a pair of faces (one male and one female) was presented lateralized, 5° right and left from the central fixation point for 150 msec. Each face was presented one time on the right side and one time on the left, resulting in 100 trials for each session. With the same setting, pairs of photographs were presented for only 14 msec with one photograph containing the animal. Two sessions of 50 trials were accomplished.

^amean of the medians

= 120; 50–74 years) with data on their cumulative scores (max = 10) for each category however without reaction times (Crutch, Randlesome, & Warrington, 2007).

Results

KC's mean naming latency for the black and white drawings was 3,195 msec ($SD = 2,723$) as compared to an expected latency of 1,057 msec ($SD = 207.3$; norms given in the database of the International Picture Naming Project = IPNP; $N = 100$ college students; data from English speakers). We excluded invalid answers and errors from the results; hence the latencies given are for 177 words out of 247. KC's naming latency was highly significantly longer as compared to the norm sample ($t = 10.262$, $p < 0.001$, one-tailed), indicating a distinct disturbance of visual access to the names of objects (Figure 7). He was also highly significantly slower ($t = 6.815$, $p < 0.001$, one-tailed) than the control subject MH ($M = 1,200$ msec, $SD = 544$ for 169 words that were correct) as calculated according to the proposal by Crawford et al. (Crawford, Garthwaite, & Wood, 2010). This result is in sharp contrast to the good performance of KC in the categorisation task (compare Figure 7 to Figure 5).

KC's naming performance in the Category-Specific Names Test was significantly below the scores of the norm population for body parts and objects of level I and below norm ranges of all categories (body parts, objects, fruits & vegetables, and animals) for the more difficult level II. He made more errors in level II than in level I. Summing up the time he needed to name the 4×10 items of all categories results in a cumulative time of 78 seconds for level I and 139 seconds for level II; compare results on visual acoustic matching below.

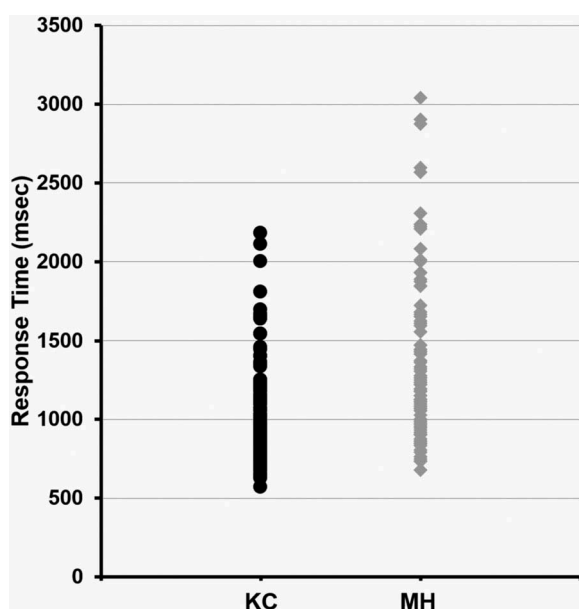


Figure 5. All response times for KC and one control subject (MH) to discriminate between man-made versus naturally occurring objects. Stimuli appeared on a 20-inch raster monitor (resolution 1280×1024 Pixel; 37.0×29.6 cm; refresh rate 72.0 Hz) at a viewing distance of 110 cm. Stimulus presentation and data collection via button press without feedback were developed with in-house software.

KC's highly increased latencies for naming objects are not due to a general deficit in visual pattern recognition – since he yielded normal results in non-verbal categorizations – but rather are due to an impaired ability to find the names of objects that he readily categorizes.

Acoustic-visual matching

To clarify why the patient was completely normal in categorizing images as long as his response did not require verbal responses we tested his ability to associate acoustic inputs with pictures.

Method

We again used the Category-Specific Names Test of McKenna and Warrington (2007, 1978) described above. This time the task was to match an auditory input (spoken word) with the image of one of the ten pictures of objects within each category by pointing at it. This task was accomplished by KC and our five male controls. The time between the end of the spoken word and the finger touch on the screen was measured with a stopwatch.

Results

KC was 100% correct for all categories of **acoustic-visual matching**; he did not differ from the norm sample and our controls. Surprisingly he took significantly longer (cumulative time all categories level I 75 sec; level II 122 sec) than our five controls to point at the 4×10 items in both levels (M_{controls} level I = 42 sec; $SD = 8.5$; $t = 3.544$, $p = 0.012$, one-tailed; M_{controls} level II = 47 sec; $SD = 4.4$; $t = 15.560$, $p < 0.001$). This result is in the same time range as naming these items.

Handwriting

It has been reported that some alexic patients also suffer from agraphia (Sheldon, Malcolm, & Barton, 2008). To check whether KC's problems are limited to analyzing written words or else involve also their production, we examined his ability to write.

Method

Few standardized tests on writing are available. One way of analyzing the ability to handwrite and to compare different individuals is to measure the time course of writing. We chose a text based on a paper by Groffmann and Fahrenberg (1960) that supplies norm data and moreover collected data from our five controls. The quality and speed of handwriting was checked with a text extracted from the beginning of the tale of the Grimm Brothers "The valiant little tailor". To become familiar with the text (39 words, 203 letters) the controls were encouraged to read it twice before the test. For KC the text was read out to him twice before the test. During the test the text was read out matched to individual writing speed and the subjects were instructed to write it down at normal speed. In a second test they were asked to write readable but as fast as possible. Statistical significance was tested according to the method proposed by Crawford and Garthwaite (2002) we compared KC to the norm values given by Groffmann and Fahrenberg and to the mean of the five control subjects.

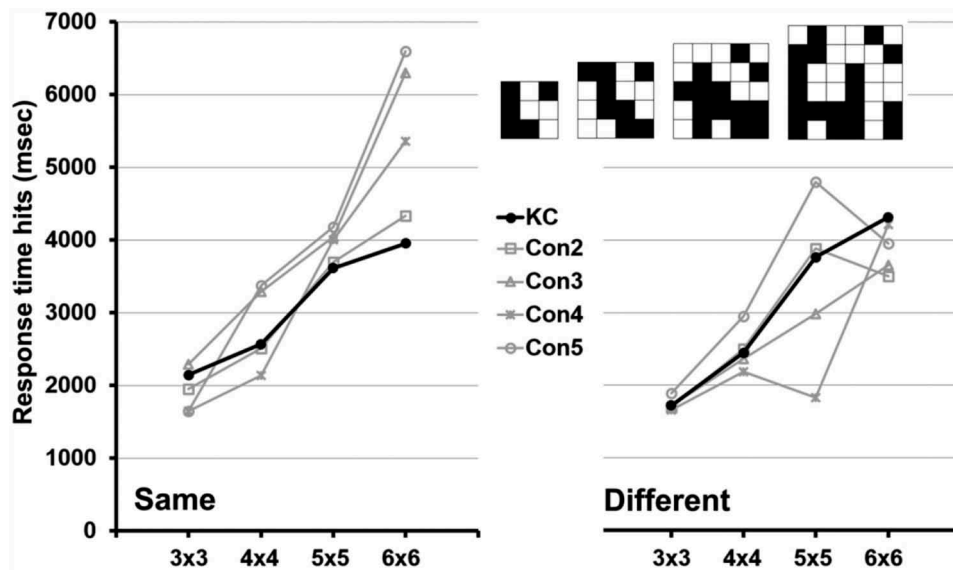


Figure 6. Response times for “same” (left part) and “different” trials of KC and the controls as a function of grid size. Examples of the stimuli used for the checkerboard matching test are shown. A set of 48 checkerboards was generated with grid sizes of 3×3 , 4×4 , 5×5 and 6×6 checks. The size of one square was 60 arcmin. Twelve sets of checkerboards were constructed for each grid size and six counterparts differing only in one square. Obvious patterns were avoided. Pairs were presented in pseudo randomized order at a viewing distance of 60 cm, 4 degrees right and left from the central fixation point on a black background, until the button press.

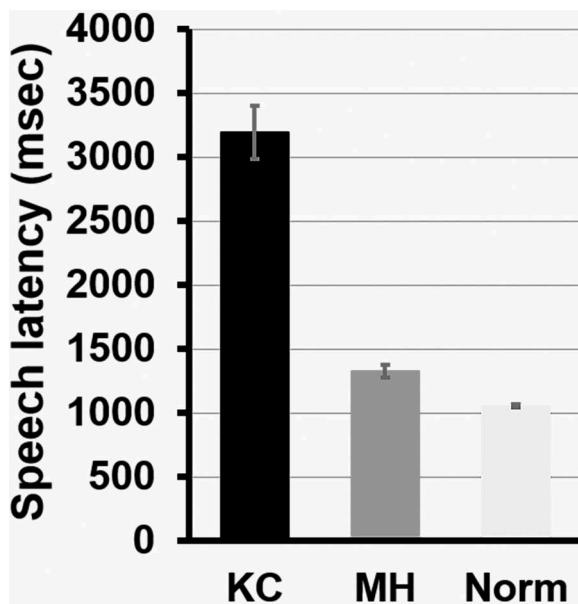


Figure 7. Mean latencies and standard errors of KC, one control subject (MH) and norm values from the International Picture Naming Project for naming visually presented common objects. The drawings on a black and white background were presented on the same laptop computer and setting as the word presentation and were visible until an oral answer was given. A software program developed in-house displayed stimuli and recorded verbal responses and reaction times via a commercial microphone (the t bone, EM 9900).

Results

KC required 181 seconds to write the text at normal speed and 162 seconds for speedy writing. This is somewhat but not significantly slower than the mean of the five matched controls for both normal ($M_{\text{normal}} = 137.4$ s; $SD = 38.5$ s; $t = 1.034$, $p = 0.18$, one-tailed) and speedy writing ($M_{\text{speed}} = 119.2$ s; $SD = 33.9$ s; $t = 1.153$, $p = 0.157$, one-tailed). The student norm times given by Groffmann and Fahrenberg ($n = 30$) were

slower than those of our controls ($M_{\text{normal}} = 167.3$ s; $M_{\text{speed}} = 137$ s) but still faster than KC and moreover did not differ significantly from KC's results.

Discussion

We extensively tested an alexic patient to clearly characterize his perceptual deficits from low level to high level visual perception while most existing studies concentrated on only a few tests.

We found that patient KC is a typical case of pure alexia with a lesion involving the VWFA (Figure 1, Table 1), a distinct word-length effect, and with difficulties to process not only words but also strings of letters and of numbers. While reading was strongly impaired, his handwriting appeared normal, and he wrote at normal speed.

The patient suffers from fewer symptoms after ten years than shortly after the stroke demonstrating the possibility of partly spontaneous recovery. He has normal central fields and hence the fact that he reads words in a letter-by-letter way is not caused by “holes” in his visual field. The patient has normal visual acuity, color and stereo vision which underlines the fact that his basic visual functions are fully intact. Even the segregation between figure and ground is fully functional in KC. Normal figure ground and form discrimination correspond to the fact that he is normal at identifying pictures of isolated objects as long as objects have to be classified but not named. The patient achieves fully normal identification of complex visual stimuli such as faces, complex checkerboards and discriminates between man-made versus natural objects or animals versus landscapes and man versus woman- as long as output is non-verbal, for example by comparing two visual stimuli. Closely related, the patient achieves normal speed when identifying *single* letters.

On the other hand KC has problems identifying digits and letters in words or strings of symbols. These problems indicate, in our view, that KC not only suffers from a deficit to identify words but from a general inability to simultaneously process strings of “overlearned” symbols namely letters and digits. It should be noted that McCandliss, Cohen, and Dehaene (2003) found an area directly neighboring the VWFA that was specifically activated by numbers.

KC’s reaction times slow down dramatically when he has to *name* objects (e.g. objects shown as line drawings) and not just name written words. This deficit obviously goes beyond visual problems related to written text but moreover involves relations between acoustic and visual input that are most probably language-related while not becoming apparent in everyday interactions. This is in marked contrast to his results when categorizing the same line drawings or other pictures nonverbally, for example by pointing as mentioned above.

The involvement of language may suggest that our patient’s lesion involves not only the VWFA but in addition a more anterior area involved in language processing (Büchel, Price, & Friston, 1998). But even the VWFA might link letter shapes to phonology (Striem-Amit, Cohen, Dehaene, & Amedi, 2012). Evidence for a more general visual deficit in letter- by- letter readers including *naming* of line drawings has been reported before (Behrmann et al., 1998; Starrfelt et al., 2013) while other alexic patients are normal in naming objects. This naming deficit may have caused some researchers to diagnose a deficit of the processing of the wider class of visual objects in pure alexia, hypothesizing a deficit of *low level* vision (Roberts et al., 2015), while in reality, these patients were able to identify the objects but unable to name them.

Behrmann et al. (1998) related the letter- by- letter reading deficit to the visual *complexity* of the stimulus. This assumption cannot, however, explain the results of our patient. For example, our results with the checkerboard test (Mycroft et al., 2009) clearly indicate that it is not *complexity* of the stimuli as such that causes letter- by- letter reading. This is in line with the results of Bormann, Frings, Dressing, Glauche, and Weiller (2018) who describe a double dissociation between visual processing and word reading and by Johnson and Raphail (2015) who find that letter confusability is not a significant predictor of reading time in pure alexia. In agreement with Sand, Robotham, Martelli, and Starrfelt (2018) we find that the reading problems are not alleviated when inter-digit distance is enlarged thus decreasing the possible influence of crowding and arguing against the suggestion by Crutch and Warrington (2007) that letter- by- letter reading is caused by crowding.

Conclusions

We tested a patient who is, after a stroke in his left hemisphere, a clear letter-by-letter reader without any visual field defect. His deficit also involves digits but no other less overlearned symbols and neither other complex visual stimuli-such as faces or natural scenes. KC demonstrates the existence, in humans, of a cortical area whose destruction removes the ability of the patient to read words while not individual letters. On the other hand, detection, discrimination, and categorization of even complex visual stimuli were intact. The quite

specific disorder of alexia in our patient is an example of the sometimes astonishingly narrow specialization of some cortical areas. Their contribution to the neuronal network apparently cannot be substituted sufficiently by other areas, even after extended time. Together, our results thus indicate a lesion of a highly specified cortical area and are incompatible with several other explanations for letter-by- letter reading such as crowding, a general deficit of low level vision, or a deficit of processing complex visual stimuli in general.

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No potential conflict of interest was reported by the authors.

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