Research Report

Midlevel visual deficits after strokes involving area human V4

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Abstract
We present the results of 51 stroke patients with free central visual fields of which about half suffer from clear deficits of midlevel vision undetected by standard clinical tests. These patients yield significantly elevated thresholds for detection and/or discrimination between forms defined by motion, colour, or line orientation (‘texture’). As demonstrated by voxel-based lesion-symptom mapping (VLSM) the underlying lesions involve mainly area human V4 (hV4) located in the posterior third of the fusiform gyrus and extending into the lingual gyrus.

Patient’s detection thresholds correlate only very weakly between the submodalities tested, indicating partly separate neural networks on mid-level vision for colour, motion, and texture detection. Correlations are far stronger for form discrimination tasks, indicating partly shared mechanisms for even simple form discrimination of distinct visual submodalities. We conclude that deficits of visual perception are far more common after strokes in visual brain areas than is apparent in clinical practice. Our results further clarify the functional organization of midlevel visual cortical areas.

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1. Introduction: specificity of cortex?
Animal and single cell studies have demonstrated that around 50% of primate neocortex is concerned with visual perception (Kandel & Wurtz, 2000) and that visual cortex contains more than 30 modules with differing specialization for visual submodalities such as contrast, colour, or motion perception (Van Essen, Anderson, & Felleman, 1992). Common sense tells us that brain tissue is there for a purpose, and loss of chunks of this tissue should have negative consequences. Lesions in
different areas should therefore cause a large variety of deficits of visual perception. The most frequently reported deficits are visual field defects that are easily detected using perimetry. But only relatively few mostly single-case studies reported deficits of midlevel vision following lesions of visual brain areas in patients with intact visual fields, hence the exact contribution of the more than 30 modules of primate visual cortex is far from clear (Van Essen & Gallant, 1994).

The deficits we investigated are on a level below object recognition but above luminance discrimination, the so-called midlevel vision including discrimination of simple forms. Deficits on this level between agnosias and visual field defects have been termed ‘indiscriminations’ (Fahle, 2003). For example, Troscianko et al. (1996) and Ruttinger et al. (1999) reported patients suffering from an isolated loss of colour discrimination without visual field loss or apparent deficits in any other visual submodality. Similarly, Zihl et al. and others (Vaina, Lemay, Bienfang, Choi, & Nakayama, 1990; Zihl, von Cramon, & Mai, 1983) described rare cases of an isolated strong deficit in motion perception though a later test of the ‘Zihl’ patient indicated additional simultanagnosia (Gruesser & Landis, 1991). The relative specificity of these isolated deficits of colour or motion perception fits in very well with the traditional view of cortical specificity as put forward, e.g., by Zeki’s ‘colour area’ (V4) or VS/MT’s description as the ‘motion area’ (Britten, Shadlen, Newsome, & Movshon, 1993; Zeki, 1978).

But this view of highly specialized and unitary cortical areas that (almost) exclusively perform one type of task – a bit like the older view of highly specialized sensory and motor speech areas – has lost part of its appeal due to both imaging and single-cell studies (Baizer, Ungerleider, & Desimone, 1991; Freiwald & Tsao, 2010; Moeller, Freiwald, & Tsao, 2008; Van Essen et al., 1992; Van Essen & Gallant, 1994). Especially, the scarcity of clinical reports on specific visual deficits argues against this view of a single ‘motion’ or ‘colour’ area. If such specific areas would exist, quite a number of strokes should destroy such an area leading to specific deficits of perception. Patients do not usually show such isolated deficits. Rather their symptoms are compatible with the existence of small networks of even more specialized areas subserving different aspects of, for example face recognition. The same may be true, we hypothesize, for the perception of colour, motion, and other elementary features. One reason that even these highly specific deficits of post-stroke vision usually remain undetected in the clinic (and by the patients themselves) may be their specificity and the lack of appropriate clinical tests to detect relatively specific losses and that are missed by using qualitative tests presented only centrally.

To further clarify whether or not cortical specificity goes beyond specialization for all aspects of ‘colour’ or ‘motion’, we investigated the specificity of functional loss following stroke regarding both the detection and discrimination of stimuli defined by contrasts in luminance, wavelength, line orientation, or motion direction. Having tested more than one hundred patients (Kraft et al., 2014) with anatomical lesions after occipital, occipitotemporal, or occipito-parietal infarction, we found 51 patients whose central ten degrees of their visual fields were intact. Analysis of their behavioural (psychophysical) results collected at least two months after stroke is presented here. We correlated behavioural results of subgroups of patients with pathological scores in one or several modalities with their anatomical lesion locations by means of voxel-based lesion-symptom mapping (VLSM) to allocate these visual deficits to specific brain regions. The method of VLSM (Bates et al., 2003) has been used before to correlate stroke lesions to clinical deficits such a neglect (Beume et al., 2017; Karnath, Rennig, Johannsen, & Rorden, 2011), somatosensory deficits (Meyer et al., 2015) and reading and writing (Baldo et al., 2018) but there was no attempt of correlating visual subsystems systematically to anatomical locations.

We hypothesize that a relatively high percentage of patients after strokes of visual areas suffer from (highly) specific disturbances of visual perception that are not detected by clinical tests. Given the high number of distinct visual cortical areas, we suppose that submodalities such as colour or motion are perceived and processed at several distinct functional and anatomical levels. Hence, detection and discrimination of simple forms defined by different submodalities may be defective relatively isolated from each other. It may be too simple to ask whether or not e.g., colour vision is normal since colour perception can be disturbed on different levels, represented by separated elements of a neuronal network incorporating both bottom up and top down elements (Rumelhart, McClelland, & the PDPResearchGroup, 1986; Van Essen et al., 1992; Herzog & Fahle, 1998; Tsotsos, Rodrı´guez-Sánchez, Rothenstein, & Simine, 2008; Bartolomeo, Bachoud-Levi, & Thiebaut de Schotten, 2014). This hypothesis would explain why so few patients show a complete defect of e.g., colour or motion perception.

2. Methods

2.1. Ethics statement

The study was conducted in conformity with the declaration of Helsinki and was approved by the local ethics committees in Bremen and Berlin. Written informed consent was obtained from all participants. They were free to withdraw from the study at any time. All subjects were unaware of the purpose of the experiments. Participants of the control group were paid for their participation. Patients were reimbursed for their travelling costs. No part of the study analyses was pre-registered prior to the research being conducted. The data have been collected over a period of more than 10 years. In the informed consent there was approval of the patients to publish anonymized data. Anonymized psychophysical study data, presentation and analysis codes are published in https://doi.org/10.5281/zenodo.3479558. As the imaging data cannot be fully anonymized for ethical reasons these data cannot be publicly archived. Data can be accessed through contact of the corresponding author (mfahle@uni-bremen.de). Data will be released subsequent to requestors meeting the following conditions: approval of an ethics committee; pledge of secrecy. Participants.

In this study psychophysical data of 51 patients are presented, a subgroup of the 128 patients included in the paper of Kraft et al. (2014). We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria,
whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study. Patients were chosen based on the site of lesion according to the following criteria: unilateral lesion of the occipital and/or temporal and/or parietal cortex; lesion onset older than two months; no aphasia; no neglect (tested by three paper and pencil tests); no dementia; no visual field defects within the central 10° in standard perimetry; no psychiatric or ophthalmological disorders. In addition, luminance contrast detection in the target quadrant had to be within normal limits. Patients were tested between 2 and 12 months after the stroke, i.e., in a ‘chronic’ state after visual reorganization processes had time to restore function (Thiel & Kolmel, 1991). Controls (N = 61) were included if they reported no neurological, psychiatric, or ophthalmological disturbances. All subjects had normal or corrected to normal visual acuity. For demographical data of patients and controls see Table 1.

2.2 Stimuli, task and procedure

The stimuli, task, and procedure are illustrated in Fig. 1. Stimulus details were already described in Kraft et al. (2010). Stimuli were displayed on a 21” CRT monitor with a spatial resolution of 1600 × 1200 pixels and a refresh rate of 75 Hz controlled by a PC. A software programme developed in-house served to present stimulus displays and to collect performance data. Subjects were seated 60 cm from the screen. To minimize head movements and to ensure a constant viewing distance the head was stabilized by a chin rest and brow bar. Participants were instructed to fixate a central fixation point with a diameter of 12 arcmin presented during all experiments.

All experimental tasks were performed binocularly. During each trial the stimulus array was presented for only 200 msec (Fig. 1). The short presentation time prevented artefacts from scanning eye movements. For the detection task a single circle with a diameter of 210 arcmin was presented in one of the four visual field quadrants in pseudorandom order. For the discrimination task based on form discrimination between circle and square, three squares with a side length of 186 arcmin were presented additionally in the remaining visual field quadrants. The midpoints of stimuli were placed at an eccentricity of 5° (deg) from the central fixation point. 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). The subject’s response initiated the next trial after a delay of 500 msec.

For both conditions (localisation based on detection or else (form) discrimination) perceptual thresholds (62.5% correct responses) were defined in each experimental run for each visual field quadrant using the adaptive staircase procedure QUEST (Quick Estimation by Sequential Testing; Watson & Pelli, 1983) yielding separate threshold values for each quadrant. After a short training with some clearly suprathreshold presentations the sequence of the four independent staircases was organized in randomized order within each experimental run. Subjects completed 30 trials per visual field quadrant, i.e., 120 trials per run. Each visual submodality (luminance, texture, motion, and colour) and task (shape localisation based on detection vs form discrimination) was tested in a separate run resulting in 8 experimental runs. The sequence of tasks was held constant across subjects. Subjects first performed the shape localisation tasks based on detection in the order luminance, texture, motion, and colour. Subsequently the shape localisation tasks based on form discrimination were conducted in the same order.

In a 4AFC task the theoretical probability of guessing for each response is 25%. A response bias in favour of one visual field quadrant could mimic a lower threshold. Therefore, we controlled the distribution of button presses over the four quadrants for each subject in every testing run eliminating strong response biases.

2.3 Submodality-specific stimuli

For the submodality luminance 20 000 white dots (maximal luminance, 108 cd/m²) with a diameter of 5.6 arcmin each were presented against a grey background (54 cd/m²). The difference between white dots and background was defined as 100% luminance contrast and served as the starting point for the adaptive staircase procedure. QUEST modulated the difference between target and background in percent luminance difference.

For the submodality texture 20 arcmin long and 1.4 arcmin wide lines were presented on a virtual grid with an inter-line distance of 14 arcmin, randomly jittered by up to 2 arcmin. Background rotation of line elements was 45 deg. Starting orientation of target lines was 135 deg, resulting in a target-background difference of 90 deg. QUEST modulated the orientation difference between target lines versus background lines.

For the submodality motion 20 000 black dots (5.6 arcmin, ≈ 3 cd/m²) moving at a velocity of 3 deg/s were presented on a grey background (54 cd/m²). Background dots moved continuously to the right whereas the target dots moved to the left, hence motion direction difference was 180 at the beginning of the staircase procedure. QUEST modulated the difference between target and background motion directions.

For the submodality colour an Ishihara-like setup was created. Dots were presented on a virtual grid with an inter-
Fig. 1 – A Temporal sequence of task. B Stimuli used. They were defined by differences in luminance, colour, orientation, or motion. In the detection task a circle was presented in one of the four visual field quadrants. For the discrimination task three squares were presented additionally to the circle in the remaining visual field quadrants. Subject’s task was to indicate the location of the circle via a button press (4-alternative-forced-choice task; 4 AFC). The subject’s response initiated the next trial after a delay of 500 msec.
dot distance of 14 arcmin jittered with a Gaussian distribution of 1.5 arcmin resulting in a dot radius between 4 and 10 arcmin (on average around 7 arcmin) and starting point for QUEST was 650 nm (corresponding to red; Minolta Color Analyzer CA-100RT). To avoid discrimination between target and background on the basis of luminance differences random luminance noise (between 0% and 40% of maximum luminance) was introduced to each stimulus dot. QUEST modulated the difference between target and background colour hues.

2.4. Data analysis

Controls were divided into three age groups: 20–39 yrs, 40–59 yrs., and 60+ yrs. of about equal size. Individual patient’s results were compared to the corresponding age group.

2.5. Logarithmization, normalization, and statistics

As the expected psychophysical response distributions especially for contrast and motion vision follow a logarithmic characteristic, we logarithmized all results of controls and patients.

In addition, in order to correct for age we normalized each individual threshold by the following equation:

\[ \text{Threshold}_\text{norm} = \frac{\text{Threshold}_{\text{individual}} - \text{mean} \text{ Threshold}_{{\text{age}-\text{matched \ controls}}}}{\text{SD}_{{\text{age}-\text{matched \ controls}}}} \]

The mean thresholds of the age matched controls are defined as the mean of the four quadrants of the visual field. An individual normalized threshold represents the number of standard deviations (SD) from the age mean. We define more than three SD’s above the mean of controls as pathological.

All statistical data analyses were carried out with SPSS software (Version 23). For each visual submodality correlation analyses (Spearman Rho rank order) were conducted between shape localisation based on detection and form discrimination noise (between 0% and 40% of maximum luminance) was introduced to each stimulus dot. QUEST modulated the difference between target and background colour hues.

2.6. Topographical sequencing

We first defined for each patient the visual field quadrant expected to be most affected based on the position of the lesion in the MRI/CT scan. Depending on the side and whether the lesion was above or below the calcarine fissure, we chose the contra-lesional visual field and either the lower or else upper (contra-lesional) quadrant of the visual field. This quadrant was considered the target quadrant (Q). Its companion on the same (contra-lesional) side was QII since we expected deficits to spread on the same cortical hemisphere more than to the opposite side. The quadrant mirror-symmetrical to QI was defined as QII since it is connected to QI via callosal fibres. The quadrant least expected to show deficits in visual performance was defined as QV. In cases where the lesion extended both above and below the calcarine sulcus, we chose the more lesioned portion of the hemisphere.

All four visual quadrants of the healthy controls yielded roughly similar results. We chose the bottom right quadrant (QIV) which represented the ‘average’ quadrant for comparisons between healthy controls and the patient group.

2.7. Lesion mapping

Details of image acquisition are described in the paper of Kraft et al. (2014). Patients’ T2 weighted images served as the basis for lesion delineation because they offered the best contrast for subacute brain lesions. Only in one patient CT scans were used because MRI’s were not available. Lesions were manually drawn onto the 24 slices of the T2-weighted MRI scan using MRicron (http://www.cabiatl.com/mricro/mricron/stats.html). Accuracy of lesion delineation was inspected visually at each slice by comparing the lesion to the corresponding diffusion weighted images. Each lesion 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 SPM5 (Rorden, Bonilha, Fridriksson, Bender, & Karnath, 2012) resulting in 51 lesion volumes (Voi-volume of interest). Lesions in the right hemisphere were flipped to the left to increase statistical power. In a first step maps individual ROIs were combined to generate lesion overlap maps and subtraction maps. To further relate lesions and behavioural data we used the voxel-based lesion-symp-tom mapping (VLSM) approach of the MRICron Software package (Rorden et al., 2007). The binarized psychophysical scores of the target quadrant QI of all 51 patients were used for calculation separately for each modality (detection and discrimination of texture, motion, and colour as well as discrimination of luminance, each as a single predictor). By means of the Liebermeister test, uncorrected z values for each submodality resulted in seven statistical maps. Voxels damaged in less than 15% of patients were ignored. The critical cut-off z values for \( p = .05 \) were calculated after correction for multiple comparisons by using false discovery thresholding as implemented in the software package. Statistical maps of significant voxels (\( p < .05 \)) were overlaid onto the AAL atlas brain (Tzourio-Mazoyer et al., 2002) for visualization and descriptive statistics calculated to indicate the number of significant voxels in the different anatomical areas. Please note, that all the lesions were restricted to the posterior part of the brain because of our selection criteria including only lesions in “visual areas”. In addition we did not control for lesion size. This means that the results are to be judged with care.

3. Results

3.1. Behavioral data

We tested the perception ability of both stroke patients and controls for four submodalities of vision, both for detection and form discrimination, based on a) luminance contrast; b) differences in texture; c) differences in motion direction; d) differences in wave length composition (‘colour’).

3.2. General effects

Mean thresholds for the form discrimination tasks are highly significantly lower than discrimination thresholds (values are
listed in Supplementary Table 1). Thresholds in controls increase as a function of age, except for colour. We find that 7 of our 61 controls yield performance three SD’s above the mean for one submodality in the right lower quadrant (Fig. 2, left side; the other quadrants yield similar results, not shown). Results more than three SD’s above the mean of controls are defined as pathological both in controls and patients.

The individual results of the 51 patients included in our study are presented as deviations from the results of the corresponding task of normal observers for the target quadrant I in Fig. 2 right side (see Supplementary Fig. 1-3 for the results of the other quadrants). Fig. 2 shows that we did choose relevant tests: Almost half of patients yield pathological results in at least one test and no patient fails all subtests indicating that all patients understood the task. Except for luminance detection (caused by ‘elimination’ of pathological results as outlined above), we find at least one patient with pathological results for each of our subtests.

The total number of pathological results is clearly higher for the patients as compared to the normal controls. This is also true for the other quadrants QII- IV (see Supplementary Fig. 1-3). There are no pathological results for the luminance detection in this quadrant because this was one of our exclusion criteria (see 2.2). Form discrimination yields more pathological results than detection. For example concerning discrimination, 41% of patients are disturbed in one or more submodalities as compared to 8% of controls, hence 92% of controls have “0” pathological result in any submodality (Fig. 3 right part “Discrimination”).

Figs. 2 and 3 demonstrate that deficits of visual perception even without visual field defects are a common symptom after strokes in visual cortical areas. While around 90% of controls have normal performance in all tests, in patients 22% (detection) and 28% (discrimination) yield pathological results in one subtest and further 6% (detection) and almost 14% of patients (discrimination) show deficits in more than one subtest.

![Fig. 2](image)

Fig. 2 – Individual results of controls (N = 61) and patients (N = 51). Left two columns: Normalized data of all controls in the right lower quadrant for detection (left column) and discrimination tasks (right column) Right two columns: Normalized data of all patients in the contralesional quadrant (= target quadrant I), for the other quadrants see Supplementary Fig. 1-3; green: normal range, red: normalized threshold more than three standard deviations above the means of controls, grey: data missing.
3.3. Detection versus discrimination

Fig. 2 shows a double dissociation between detection and discrimination in each submodality, with several patients yielding pathological results for discrimination while normal results for detection or, more important, the other way round.

The average results of the 51 patients with free visual fields for all four submodalities, both for detection and discrimination in all four visual field quadrants are shown in Fig. 4. Results are expressed as standard deviations above (or rarely below) those of the age matched controls. As expected, the means are always lower, i.e., better in the ipsilesional quadrants (QIII, QIV) except for luminance. Except for luminance all discrimination results in QI and II differ significantly from zero, which is the mean level of the controls. Detection in QI and II deviate significantly from zero only for texture and colour, not for motion (see Supplementary Fig. 4-7 for distributions of patients and controls).

3.3.1. Luminance (luminance contrast)

Testing of the visual field in static and kinetic perimetry is based on detection of luminance differences in the visual field. This task is similar to the detection of luminance contrast in our test. We excluded all patients showing deficits in either perimetry or luminance detection to ensure intact visual fields (Fig. 4A).

We were less sure what to expect for the results on form discrimination, i.e., finding the circle among squares. Performance is slightly below the mean of healthy observers in the contralesional quadrants, but not significantly changed (Fig. 4E).

3.3.2. Texture (orientation contrast)

The significant decrease of patient’s detection of orientation differences in QI is accompanied by a decrease of performance in the remaining (even ipsilesional) quadrants (Fig. 4B). Still, the loss of performance is significant only in the contralesional hemifield. The results on form discrimination based on orientation differences follow a very similar pattern, with a highly significant loss in QI and less pronounced losses in QII and non-significant losses in the ipsilesional quadrants (Fig. 4F).

3.3.3. Motion (motion direction)

As in the previous submodalities, results in the expected quadrant QI are decreased more so for discrimination than for detection (Fig. 4C, G). This is true in comparison with both the controls and the ipsilesional quadrants – with the latter showing almost normal performance. Performance is significantly impaired only for the discrimination task.

3.3.4. Colour (‘wavelength contrast’)

In colour–based contour detection and form discrimination patients show a significant decrease of performance expressed as an increase in thresholds in the expected quadrant (QI), and, surprisingly, in the second contralesional quadrant (QII). This holds true both in comparison to the ipsilesional quadrants and in comparison, to the results of healthy controls. The deficits are comparable for detection and discrimination (Fig. 4D, H).

3.4. Correlations between submodalities

The rank orders obtained for each control subject between results for the different submodalities show only weak correlations (with two exceptions) for detection and discrimination (Fig. 5 A, B, grey colour). This is to say that there exists only a relatively low tendency in normal subjects to be a gifted ‘viewer’ in general but that good results in one submodality are not a very good indicator for good performance in other submodalities except for motion-based tests. In patients the correlations between detection modules are even weaker. Correlation coefficients are-with one exception-far more random than in controls indicating further ‘disintegration’ between submodalities caused by the lesion (Fig. 5A, orange colour). For discrimination, however (Fig. 5B, orange colour), the opposite holds true, meaning that a deficit in any of the submodalities of form discrimination indicates a tendency for discrimination in another submodality to be impaired with three out of six possible correlations being significant on the .01% level.

3.5. Correlations between hemispheres and between detection and discrimination tasks

Mean correlations between target QI from the visual field of the lesioned hemisphere and its mirror-symmetrical QIII representing the ‘healthy’ visual field are highly significant both for patients and for controls (Fig. 5C, D). We find significant correlations between both quadrants for each and every of the tests for controls and with one exception for patients. This is to say that while both patients and controls show weak correlations between the results in different submodules (see Fig. 5A, B), they do have stable correlations.

Fig. 3 – Percentage of pathological results of patients (red) and controls (grey). Percentage of results in the contralesional quadrant (I, patients) or right lower quadrant (controls). Abscissa indicates the number of submodalities with pathological results (>3SD), in either no, one, or else more than one submodality. Hence, more than 90% of controls have no pathological result (“0”) in any of the Submodalities and none has pathological results in more than 1 submodality.

Fig. 4 – Percentages of patients showing pathological results in the expected quadrants (QI, QII) except for luminance. Performance is slightly below the mean of healthy observers in the contralesional quadrants, but not significantly changed (Fig. 4E).
within each submodule between the right and left hemisphere represented by the quadrants QI and QIII and therefore between the lesioned and intact hemispheres (of patients). Correlations for the entire hemifields conform to the results of the quadrants mentioned above (data not shown). You may be good at motion detection and discrimination while not for wavelengths, but if you are good at motion detection in your right visual field, you are also good in your left visual field weaker in the patients while still significant except for colour.

Correlations between the results for detection and discrimination within the same submodality exist in controls for luminance and to a lesser degree for colour (Fig. 5 E). In patients the correlation between the results for detection and discrimination is significant only for texture and less so for luminance. It is important here that stimuli for discrimination are presented far above thresholds for detection; hence even an impaired detection system might detect the stimuli and hence allow discrimination.

Scatter plots of the data used for correlation analysis including linear regression lines are presented in the Supplementary Figs. 8A and B and 9 to illustrate the distribution of individual results and to enable the comparison of thresholds of patients and controls.

3.6 Imaging results

Stroke lesions of the 51 patients included in this study are distributed over a wide range of temporal, parietal, and occipital regions (Fig. 6). In 26 of the 51 patients the left hemisphere is affected but to increase statistical power right lesions are flipped to the other side. Patients with bilateral lesions were a priori excluded from the study except for one patient with a very small lesion on the opposite side or in unrelated portions of the opposite cortex (n = 2) and especially the cerebellum (4 patients). Twenty-six patients (15 have an original left lesion) have a pathological score (+3 SDs) in at least one submodality in the target quadrant I (Fig. 2) and are in the following labelled “PS patients”. We first compared the anatomical distribution of lesions of the 26 PS patients with those of the 25 patients with normal scores, called “NS patients”. The lesion overlap of the normalized imaging results of 25 patients without any pathological scores in the visual tests as displayed in Fig. 6A and Fig. 6B shows the lesion overlap of the remaining 26 patients with pathological scores irrespective of submodality (a subtraction plot is presented in the Supplementary Fig. 10). While there is hardly any overlap in the NS patients, we find an area of substantial overlap in the PS patients located in the posterior third of the fusiform gyrus extending into the lingual gyrus.

To better characterize this area of overlap we performed a binary voxel-based lesion-symptom mapping analysis (VLSM) of each submodality as a single predictor, resulting in seven statistical maps (three for detection; four for discrimination). Three out of the seven maps revealed a significant link between lesioned voxels and pathological perception, namely for detection and discrimination of texture as well as the detection of colour (Table 2). This is to say that we find voxels...
Fig. 5 – A–E Spearman Rho rank order correlations in patients (red) and controls (grey). A, B Correlations between submodalities for detection (A) or discrimination (B) in the contralesional quadrant for patients and the right lower quadrant for controls; numbers in the right upper part indicate the corresponding absolute p-values; C,D Correlations between the ipsilesional quadrant and the contralesional quadrant for patients and left lower quadrant versus right lower quadrant in controls of each submodality for detection (C) and discrimination (D); E Correlations between detection and discrimination tasks of the same submodality in the ipsilesional quadrant for patients and the right lower quadrant for controls. Numbers in bold font indicate significant results (p < .01).
whose lesion is significantly correlated with a specific visual deficit.

The overlay of significant voxels of these three maps is shown in Fig. 7. There is only one patch of significant voxels in these three modalities plotted for texture detection in the first row, for texture discrimination in the second row, and colour detection in the last row. The location of this patch does not vary much between these three modalities. Colour detection has the greatest number of significant voxel (ColDet 3561), texture detection fewer (TexDet 1734), and texture discrimination the least (TexDis 829). The distribution and extend of significant voxels (based on the AAL Atlas of MRcron) for these three maps is listed in Table 3. All three maps reveal significant voxels in the border area between the lingual and fusiform gyrus.

Since pathological scores for both texture detection and discrimination yield significant voxels, we further evaluated lesion locations for the subgroup of patients with any deficit in texture processing by overlaying lesions. Four patients score...
pathologically in both texture detection and discrimination and their summary overlay is shown in the upper panel of Fig. 8. The subtraction analysis of patients with isolated pathological scores in either texture detection ($n = 6$) or discrimination ($n = 7$) is plotted in the lower panel of Fig. 8. It is striking that the lesions of the four patients with a more general deficit in texture processing are strongly overlapping. On the other hand, the subtraction plot in the lower panel indicates that the processing of texture detection lies more posteriorly and therefore nearer to the primary visual cortex while the discrimination task is processed more anteriorly as expected from the known hierarchy of processing visual objects in vision.

Finally (in contrast to the topographical sequencing used so far for the previous analysis of the data depending on lesion location), we sorted the 26 patients with pathological scores (PS patients) according to their perceptual deficit by summing up individual thresholds (three for detection and four for discrimination in the target quadrant (QI) compared to the individual companion contralesional quadrant (QII). (The sum of the 26 deficit scores was 321.3 in Q I, 183.2 in Q II, 132.8 in Q III and 90.4 in Q IV for the sorting based on lesion site indicating that elevated perceptual thresholds were often not restricted to a single quadrant and even affected the ipsilesional side. We cannot exclude a small influence of neglect here in spite of the fact that we had excluded all patients with pathological results in paper and pencil tests). Eight of the 26 patients (in contrast to expectation) performed worse in QII than QI. Half of the 26 patients had their lesion above, the other half below the calcarine fissure. Irrespective of lesion site, nine patients performed worse in the upper contralesional hemifield and 17 patients in the lower contralesional hemifield. To that end, we calculated summary overlay plots of patient’s lesions based on whether the upper or else the

![Fig. 7](image-url) Plots of the significant voxels ($p < .05$) of the voxel based statistical analysis for modalities texture detection, texture discrimination, and colour detection from top to bottom. Colours code the z-values corrected for multiple comparisons using the false discovery rate. Significant voxels do not differ much in location between these modalities.

| Area          | TexDet | TexDis | ColDet |
|---------------|--------|--------|--------|
|               | N voxel | X  | Y  | Z  | z  | N voxel | X  | Y  | Z  | z  | N voxel | X  | Y  | Z  | z  |
| Total         | 1734    |     |    |    |    | 829     |     |    |    |    | 3561     |     |    |    |    |
| Lingual       | 865     | −25 | −77 | −12 | 4.1| 504     | −29 | −65 | −3  | 3  | 2013     | −20 | −80 | −12 | 3.8|
| Fusiform      | 788     | −25 | −75 | −13 | 4.1| 279     | −27 | −74 | −6  | 3  | 1356     | −24 | −74 | −13 | 3.8|
lower quadrant of their contralesional hemifield yielded most elevated perceptual thresholds. As can be seen in Fig. 9, lesion

Fig. 8 — Upper panel: Overlay summary plots of the four patients with pathological scores in both texture detection and discrimination (n = 4). Colour code represents the number of overlapping lesions from pink (n = 1) to red (n = 4). Lower panel: Subtraction plot Texture Detection (n = 6) minus Texture Discrimination (n = 7). Colour coding indicates the percentage of overlapping lesions, increasing from yellow to red (1–35%). These voxels are damaged more frequently in patients with a pathological score in texture detection than in patients with a pathological score in texture discrimination. Colour codes from green to blue (−1 to −35%) indicate regions damaged more frequently in Texture Discrimination than in Texture Detection. MNI Z-coordinates are indicated below each of the nine transverse sections.

Fig. 9 — Overlay plot of lesions of patients (PS patients; n = 26) sorted according to their perceptual thresholds summed over all tests. Lesions of patients with thresholds more strongly elevated in the upper contralesional hemifield (n = 9) are shown in the upper row, those of patients with dominant deficits in the lower hemifield (n = 17) are overlaid in the lower row. The lesions of the patients in the upper row tend to be more medially and in lower slices that the ones in the lower row. Colour code represents the number of overlapping lesions from pink (n = 1) to red (n = 6).
positions differed between those two groups of patients indicating a topographical organization of “midlevel” visual cortical areas.

4. Discussion

We investigated the effects of strokes involving the occipital, occipito-temporal and occipito-parietal parts of the brain on detection and discrimination of visual forms defined by luminance, colour, motion, and texture and tested correlations with the underlying cortical lesions. The results show that almost half of patients suffer from specific deficits undetected by clinical tests in spite of free visual fields. The cortical lesions underlying these perceptual deficits involve predominantly area hV4 and its surroundings.

4.1. Correlations between deficits of different submodalities of vision

The highly selective and varied pattern of pathological results (Fig. 2) indicates that patients did indeed understand the tasks and were able to perform within the normal range for those submodalities not disturbed (Fahle, 2003; Kraft et al., 2014). The fact that they had normal visual fields assures that the optic tract and visual areas V1, V2, V3 were intact since lesions there produce scotoma (Horton & Hoyt, 1991; Inouye, 1909). Deficits we found do not produce very pronounced symptoms subjectively since they involve the contralesional hemifield and not all submodalities. Moreover, our tests primarily concern the ventral stream (Merigan & Maunsell, 1993).

Deficits appear in all four submodalities tested most often for texture and colour and various types of combinations between the deficits in detection and discrimination exist. There are patients with elevated thresholds in just one submodality and others with two and more indicating the existence of (partly) separated neuronal networks.

We find patients suffering exclusively from problems in detecting forms while there are others who demonstrate only elevated thresholds for discriminating forms demonstrating a double dissociation between form detection and discrimination (Fig. 2). (Of course there are also patients who suffer from problems with both detection and discrimination). Please note that the stimulus intensities for the detection task are much higher than those for the discrimination task, obviously allowing discrimination even with deficits of the detection mechanism.

Detection thresholds in healthy controls correlate significantly on the $p < .01$ level only between those for luminance and motion (Fig. 5A). Detection thresholds for patients are worse and correlate hardly at all between submodalities with $p$-values (far) less significant than those for controls (in five out of six cases). This finding points to at least partly separate neural mechanisms underlying the detection of differences in luminance, wavelength, motion, and line orientation that can be individually ‘disturbed’ thereby decreasing correlations below the levels found in controls. It is hardly surprising that deficits in the detection of luminance contrast bear consequences for the detection of motion, colour and texture boundaries ($p < .05$) but these correlations are completely lost in the patient group. This finding indicates that there is no significant “spill-over” of deficits in one submodality to other submodalities-since otherwise correlations should increase rather than decrease in patients.

Discrimination thresholds, on the other hand, are far closer correlated in patients than in controls with (far) higher significance levels in all cases (Fig. 5B). The increased correlations we find in patients indicate that the mechanisms for discrimination are incorporated at more closely related neural networks in the visual cortices than those for detection are. If this common system of form discrimination suffers a defect, form discrimination based on several submodalities is impaired, introducing a correlation between the results for different submodalities.

4.2. Correlations between hemispheres and between detection and discrimination

Normal subjects yield high correlations between results in both hemifields for each individual submodality for both detection and discrimination but show only minor correlations between performances for different submodalities (Fig. 5C, D). In other words, good results in one hemifield for any given submodality are usually associated with good results in the other hemifield for the same submodality (but not necessarily for others). The results of patients show somewhat lower correlations between the two hemifields, especially for colour discrimination (Fig. 5C, D). This finding reflects the impact of the lesion that slightly decreases the correlation between hemispheres present in normal controls.

Finally, correlations between the results for detection and discrimination within each submodality reach significance in normal controls only for luminance (and almost for colour) differences while for line orientation (texture) in patients (Fig. 5E). We have argued above that discrimination and detection rely indeed on partly different neuronal mechanisms, with clearly differing thresholds, so one does not have to expect the same high correlations between detection and discrimination as between hemispheres, and this is what we find. Still, given the fact that we test correlations between two types of thresholds of the same submodality, a certain amount of correlation is not surprising.

Our suggestion of ‘early’ detection systems that are more separated from each other than the ‘later’ systems’ discriminating between forms makes a testable prediction. Namely, the number of ‘defective’ results should be higher for discrimination than for detection tasks (Fig. 2). This is indeed what we find and while a number of explanations are possible, it is reassuring that the data are compatible with our suggestion (Baizer et al., 1991; Tsotsos et al., 2008). We will discuss this further in the section on imaging data.

4.3. Interpretation of imaging results

We complemented our perceptual tests with a correlation between the deficits and the location of patients’ cortical lesions as detected by (MRT) imaging. The underlying hypothesis was that there would be differences in lesions’ locations between deficits in different submodalities and between deficits in detection versus discrimination.
An area located in the posterior third of the elongated fusiform gyrus and extending into the lingual gyrus is predominantly lesioned in patients that score pathologically in any submodality-specific test as compared to patients scoring within the normal range (overlay plot Fig. 6 and subtraction plot Suppl. Fig. 10). Maximally eight of the 26 lesions of patients with a pathological score overlap. From these lesions extend mainly along the course of the gyrus well in line with the assumption of neighboring but partly separate networks for different submodalities and discrimination versus detection.

The voxel-based statistical analysis (VLSM) of each submodality as a single predictor yields significant voxels in this region of maximal overlap for patients with pathological perception in texture detection, texture discrimination, and colour detection. The other correlations between perceptual and structural deficits (luminance discrimination, motion detection and discrimination, colour discrimination) fail to reach significance as well as an exploratory analysis using continuous data. One reason for the lack of significance could be the small number of patients showing a perceptual deficit in a single submodality as there was just one patient scoring pathologically in motion detection. The significant voxel areas of the groups with impaired texture detection and texture discrimination do not differ much. In contrast to healthy controls patients show a significant correlation between deficits of texture discrimination and detection (Fig. 5 E). This indicates neighboring neuronal networks for texture processing, in line with the behavioral results.

The coordinates in MNI space of the center of the significant three maps mentioned above, namely texture detection, texture discrimination and colour detection, conform to the location of human visual cortex area V4 (hV4) (Arcaro, McMains, Singer, & Kastner, 2009; Brewer, Liu, Wade, & Wandell, 2005). This area lies medially to face selective areas and posteriorly to place selective areas. Area hV4 borders anteriorly to the ventral occipital area (VO1) which is part of the ventral temporal cortex (VTC). However the anatomical borders, and the retinotopical and functional organization of hV4 are still under debate (Winawer & Witthoft, 2015). According to the model of Brewer et al. (2005) it represents the entire contralateral visual hemifield.

While earlier functional MRI studies on humans considered V4 primarily to be a colour area (Zeki et al., 1991) newer studies indicate that hV4 is involved in the encoding of texture, form and surfaces (Dumoulin & Hess, 2007; Konen & Kastner, 2008). The role of visual area V4 in object perception is not fully understood. Based mainly on monkey studies it is considered as a mid-tier area of vision facilitating figure-ground segmentation (see Roe et al. (2012), for a review). Studies on human V4 systematically comparing responses to multiple feature spaces are still lacking. The finding that the functional organization for the attributes of colour, size, and orientation is not highly segregated in macaque V4 (Ghose & Ts’o, 2017) may explain our results of largely congruent significant areas of the VLSM analysis for texture detection, texture discrimination, and colour detection. In addition a few single case studies of strokes in V4 (Gallant, Shoup, & Mazer, 2000; Rizzo, Nawrot, Blake, & Damasio, 1992) support our view of V4 as an area important for colour vision and pattern processing.

The lack of a “significant” area of overlap for impaired motion discrimination may indicate a rather spread out network for form from motion (Gilai-Dotan et al., 2013).

Since impairments in texture detection and texture discrimination both provided maps of significant voxels it was possible to use subtraction analysis for these patients (Fig. 8 below). The results show that an impaired detection of orientation differences (texture) is associated with lesions located more posteriorly than lesions causing an impaired discrimination of form from texture. This difference in cortical lesion sites is the basis for the fact that some patients suffer from deficits of texture discrimination only while others from selective deficits of texture detection. This implies that in the patients with impaired discrimination of texture the cortical area responsible for the feature selection of texture detection was functional and lying nearer to the posterior pole. The lesions of the four patients affected in both detection and discrimination all overlapped at the border between the lingual and fusiform gyri mentioned above (Fig. 8 above).

4.4. Conclusions

We would like to stress that almost half of patients suffering from strokes of visual cortical areas show highly significant deficits of one or several visual submodalities (Fig. 2), even in the absence of visual field defects or other clinical symptoms. These deficits involve the part of the visual field expected on the basis of the lesions’ topography (Fig. 4) and may well impair everyday visual performance in subtle ways and that the patients are not fully aware of. Although we chose the behavioural results of the expected contralateral quadrant for the voxel-based lesion-symptom mapping (VLSM) approach it is obvious from our data that often patient’s results were affected even in the “intact” hemifield when compared to the controls. Two factors might contribute. First, a general deficit of visual processing; however, the fact that most of our patients were capable to solve even more complex tasks such as discriminating between male and female faces (results not shown) argues against this possibility. The second possible explanation is that on the level of hV4 a certain amount of bilateral processing takes place. Hence, a stroke involving one side may also affect processing of the ipsilesional visual field for pattern recognition while not for luminance detection (since the latter is achieved in the strictly contralaterally connected V1). It is interesting in this context, that indeed results for the mirror-symmetrical quadrant (Q III) are clearly worse than those for the other quadrant on the intact side (Q IV) see page 21.

Patient’s detection thresholds correlate very weakly between submodalities. Thresholds for (most) discriminations, on the other hand, are significantly correlated indicating partly shared mechanisms for even simple form discrimination. Moreover, we do find a double dissociation between deficits in detection versus discrimination in the same submodality in several patients indicating separate neural mechanisms for detection versus discrimination.

\(^{1}\) Coordinates given in Talairach space were transformed into MNI space based on the formula of Lancaster et al. (2007).

The coordinates in MNI space of the center of the significant three maps mentioned above, namely texture detection, texture discrimination and colour detection, conform to the location of human visual cortex area V4 (hV4) (Arcaro, McMains, Singer, & Kastner, 2009; Brewer, Liu, Wade, & Wandell, 2005). This area lies medially to face selective areas and posteriorly to place selective areas. Area hV4 borders anteriorly to the ventral occipital area (VO1) which is part of the ventral temporal cortex (VTC). However the anatomical borders, and the retinotopical and functional organization of hV4 are still under debate (Winawer & Witthoft, 2015). According to the model of Brewer et al. (2005) it represents the entire contralateral visual hemifield.
The imaging results are compatible with this view, showing different areas of overlap between the deficits of patients suffering from problems with texture detection versus texture discrimination.

We interpret these findings as indicating that visual perception relies on a multi-layered neuronal network with strong feedback connections (Herzog & Fahle, 1998). Hence, terms such as ’disturbance of colour vision’ are too vague. Given that processing of submodalities such as colour incorporates several separate levels, realized in different cortical networks, a more precise clarification would be desirable regarding the level on which processing in the network is disturbed.

The high variation between patient’s results may in part rely on the effects of compensatory effects in the neuronal networks “disturbed” by the cortical lesion. These compensatory mechanisms may involve both other regions of the ipsilesional network and (mirror-symmetrical) regions of the contralesional network. Especially the contralesional contributions may be of importance, given the fact, mentioned above, that we do find clear signs in our data that even a strictly unilateral cortical lesion of hV4 often reduces performance for the ipsilesional visual field, indicating a partial bilateral processing of both visual half fields on the level of hV4.

Open practices

The study in this article earned an Open Materials badge for transparent practices. Materials for the study are available at https://doi.org/10.5281/zenodo.3479558.

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Supplementary data

Supplementary data to this article can be found on line at https://doi.org/10.1016/j.cortex.2020.06.006.

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