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DOI

[10.1093/brain/awaf009](https://doi.org/10.1093/brain/awaf009)

Publication date

2025

Document Version

Final published version

Published in

Brain

License

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[Link to publication](#)

Citation for published version (APA):

Lugtmeijer, S., Sobolewska, A. M., The Visual Brain Group, de Haan, E. H. F., & Scholte, H. S. (2025). Visual feature processing in a large stroke cohort: evidence against modular organization. *Brain*, 148(4), 1144-1154. <https://doi.org/10.1093/brain/awaf009>

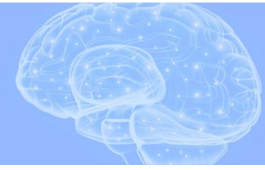
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Visual feature processing in a large stroke cohort: evidence against modular organization

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See Hebart (<https://doi.org/10.1093/brain/awaf100>) for a scientific commentary on this article.

Mid-level visual processing represents a crucial stage between basic sensory input and higher-level object recognition. The conventional model posits that fundamental visual qualities, such as colour and motion, are processed in specialized, retinotopic brain regions (e.g. V4 for colour, MT/V5 for motion). Using atlas-based lesion–symptom mapping and disconnectome maps in a cohort of 307 ischaemic stroke patients, we examined the neuroanatomical correlates underlying the processing of eight mid-level visual qualities.

Contrary to the predictions of the standard model, our results did not reveal consistent relationships between processing impairments and damage to traditionally associated brain regions. Although we validated our methodology by confirming the established relationship between visual field defects and damage to primary visual areas (V1, V2 and V3), we found no reliable evidence linking processing deficits to specific regions in the posterior brain.

These findings challenge the traditional modular view of visual processing and suggest that mid-level visual processing might be more distributed across neural networks than previously thought. This supports alternative models where visual maps represent constellations of co-occurring information rather than specific qualities.

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Keywords: vision; retinotopic maps; stroke; half-field defects; symptom–lesion mapping

Received September 11, 2024. Revised November 27, 2024. Accepted December 20, 2024. Advance access publication January 13, 2025

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Introduction

Visual perception is one of the most remarkable achievements of the human brain, transforming patterns of light hitting our retinas into rich, meaningful experiences of the world around us.¹ Mid-level vision is seen as a crucial stage in visual processing that bridges the gap between basic sensory input and higher-level (object) perception. Traditionally, scientists viewed this processing stage as a collection of specialized retinotopic modules in the brain, each dedicated to handling specific visual features, such as colour, motion, shape, orientation and texture, in separate dedicated retinotopic maps. This modular perspective was supported by influential studies showing that damage to specific brain regions could selectively impair the perception of individual features; for instance, damage to area MT could affect motion perception while leaving colour perception intact. This conceptualization culminated in the identification of >40 functionally dedicated visual areas in the posterior brain, based on electrophysiology, staining and lesion studies in animals,^{2,3} with the most famous connections linking cortical area V4 with colour perception and cortical area MT with motion perception.⁴ The functional selectivity of the visual brain is supported by multiple lines of evidence. Functional neuroimaging studies have revealed multiple specialized processing regions.^{5,6} The crucial role of area MT in motion perception has been demonstrated through several experimental approaches: temporary disruption using transcranial magnetic stimulation impairs motion direction discrimination,^{7–9} and MT stimulation can induce the perception of moving phosphenes in subjects with closed eyes.^{10–13} Causal evidence also comes from lesion studies in rhesus monkeys, where selective damage to area MT resulted in specific deficits in motion perception.¹⁴ Perhaps the most compelling evidence comes from neurological case studies. The seminal case of patient LM demonstrated selective motion blindness,^{15–17} and Vaina¹⁸ documented a double dissociation between two patients: one showed impaired colour and form discrimination with preserved motion perception, whereas the other exhibited the opposite pattern.

This modular organization aligns with our intuitive understanding of vision, where different aspects of the visual world seem to be processed separately. However, it subsequently introduces a significant challenge known as the property binding problem.^{19,20} For instance, when perceiving two red apples and one green apple, the brain must integrate separately processed information about shape and colour to form a coherent perception and somehow figure out which colours belong to which apple.

Accumulating evidence has challenged this modular perspective. Neurons in V4²¹ and area MT²² have been found to respond to both colour and motion, contradicting the notion of strict functional segregation. Studies have revealed distributed colour-processing and motion-processing networks,^{23–25} questioning the concept of single neurons being selectively tuned for specific visual features. Furthermore, optical imaging in ferrets²⁶ demonstrated that the same neural population in the visual cortex can respond to multiple combinations of orientation, length, motion axis and speed. These and other findings have led to extended versions of the dual pathway models of visual processing, such as those proposed by Kravitz *et al.*,^{27,28} which emphasize the existence of multiple recurrent systems within the pathways, each dedicated to a specific task.

In response to these challenges, an alternative model has been proposed that suggests the structure of the visual system emerges through learning to encode the visual world as efficiently as possible.^{29,30} This perspective posits a more fluid, interactive organization of the early visual system, where retinotopic maps reflect the covariances of information types in the external world, rather

than *a priori* categories, such as motion, colour and shape. In this view, maps represent correlations between visual primitives that co-occur in our surroundings. This model potentially resolves the property binding problem by eliminating the need for hyperspecialized processing pathways that do not share common information.

A central prediction, which has not been evaluated systematically, from the standard model is that there should be a relationship between deficits in mid-level vision (such as motion and colour processing) and specific anatomical locations. Given the evidence of significant processing occurring both downstream and upstream of feature-specialized regions, such as V4 and MT, feature processing deficits might arise not only from lesions confined to these specialized regions but also from lesions situated either upstream or downstream. Here, we investigate the neuroanatomical correlates of colour, shape, location, orientation, contrast, glossiness, texture and coherent motion processing in a large cohort of ischaemic stroke patients. We evaluated deficits in these mid-level features in the patients per hemifield and we used atlas-based lesion–symptom mapping and a disconnectome approach to identify brain areas contributing to performance in these eight different visual tasks. To validate our methods, we included an assessment of visual field deficits, which have been strongly linked to early visual cortex regions.

This study aims to provide crucial insights into the functional organization of the visual brain and to inform our understanding of visual deficits following brain injury. By examining a large patient cohort with diverse lesion locations, assessing a range of mid-level features per hemifield and using advanced analytical techniques, we seek to determine whether visual processing adheres more closely to a modular, feature-specific organization or a distributed, covariance-based architecture.

Materials and methods

Study design

The present study is part of a prospective, multi-centre cohort study, ‘A Functional Architecture of the Brain for Vision’ (FAB4V^{31–33}). The study involved patients admitted to one of the following hospitals in The Netherlands: University Medical Center Groningen (UMCG), Amsterdam University Medical Center (Amsterdam UMC), Radboud University Medical Center (Radboudumc), University Medical Center Utrecht (UMCU), Onze Lieve Vrouwe Gasthuis (OLVG), Maasziekenhuis Pantein, Rijnstate, Ommelander Ziekenhuis Groep and St. Antonius Ziekenhuis and Diaconessenhuis. Neuroimaging and neuropsychological assessment took place at the UMCG, Amsterdam UMC, Radboud UMC or the UMCU between September 2015 and December 2019. The Medical Review Ethics Committee Utrecht approved the study (METC-nr 2015.372).

Participants

Inclusion criteria for the FAB4V study consisted of a diagnosis of ischaemic stroke made by an expert neurologist, age between 18 and 90 years, and sufficient command of the Dutch language. Patients with cortical and subcortical lesions were included irrespective of location in order to see whether areas outside the posterior brain might be involved in low- to mid-level visual processing. Exclusion criteria consisted of serious neurological disorders (other than ischaemic stroke), psychiatric disorders, history of substance abuse, pre-existing visual impairment, pre-existing cognitive decline [score ≥ 3.6 on the Informant Questionnaire on Cognitive Decline

in the Elderly (IQCODE³⁴) or severe aphasia. Assessments were conducted between 2 weeks and 6 months post-stroke. All participants signed a written informed consent before participation, and procedures were performed in accordance with the Declaration of Helsinki.

Visual assessment

Visual field deficits

Prior to all tasks, patients were screened to detect visual field deficits. During the screening, participants were asked to fixate on a red dot in the centre of a black screen. The dot remained visible throughout the trial. A total of 45 stimuli (grey dots) were displayed sequentially, for 100 ms each. Nine dots were presented in each quadrant of the visual field (upper left, upper right, lower left and lower right); additionally, nine dots were presented in the centre of the screen. The location within each quadrant was chosen randomly. Participants were instructed to indicate when they saw a stimulus dot by pressing space bar, and they had 1200 ms to respond. The time intervals between stimuli varied across trials, ranging between 100 and 300 ms, uniformly distributed. An eye-tracker (Eyelink 1000; SR Research Ltd.) was used to monitor eye movements. If a patient made an eye movement while a stimulus was being presented, that respective stimulus trial was substituted with another one at a later stage during the task. Visual field deficits were defined as a failure to detect at least half of the stimuli in at least one quadrant. All scores were converted into binary format, indicating either impairment or non-impairment. Deficits were then categorized into left visual field deficits (lower and/or upper left quadrants) and right visual field deficits (lower and/or upper right quadrants). Patients with other visual field deficits were not included in the analyses.

Perception of visual features

Eight experimental tasks assessed perception of visual features: colour (red–green isoluminant stimuli), shape (Efron shapes),

location (dots in circles), orientation (angled lines), contrast (varying grey bars), glossiness (surface shine differences), texture (Brodatz greyscale album³⁵) and correlated motion (varying percentages of coherently moving dots). Figure 1 illustrates these stimuli. Given that the visual system is duplicated in the human brain, the left visual field is processed in the right posterior brain and vice versa, patients with unilateral lesions will compensate for visual disturbances by making eye or head movements in free-view tasks. Therefore, we developed a gaze-contingent presentation test set-up using an eye-tracker, with which we are able to diagnose half-field deficits.³¹

All tasks except motion followed a standard format (Fig. 2). Trials began with a central fixation dot. After 1 s, a target appeared 5° left or right for 1.5 s, allowing for the evaluation of function per hemifield. Two response stimuli then appeared 5° above and below fixation for 3 s, one matching the target. Participants had to indicate which of the two response stimuli was identical to the target stimulus within 4 s after the response stimuli appeared. If the response was not made within 4 s, the trial was coded as incorrect. In the motion task, participants were presented with only a target stimulus containing moving dots. The coherence percentage of these dots changed adaptively across trials, and participants had to indicate whether the dots were moving upwards or downwards. Participants responded to targets by pulling a joystick towards or away from them. In the case of motoric limitations, participants could respond verbally. This made the task appropriate for patients with aphasia or motoric difficulties.

To control for eye fixations and movements, an eye-tracker was used. The target presentation was controlled in a gaze-contingent manner such that the target always remained in the same retinal position, independent of eye movements. This allowed for separate hemifield testing. If participants were not able to inhibit eye movements, a short presentation procedure without an eye-tracker was used. In the short presentation procedure, the target stimulus was presented for 200 ms, meaning that the participant could not make an eye movement in time to fixate on it.

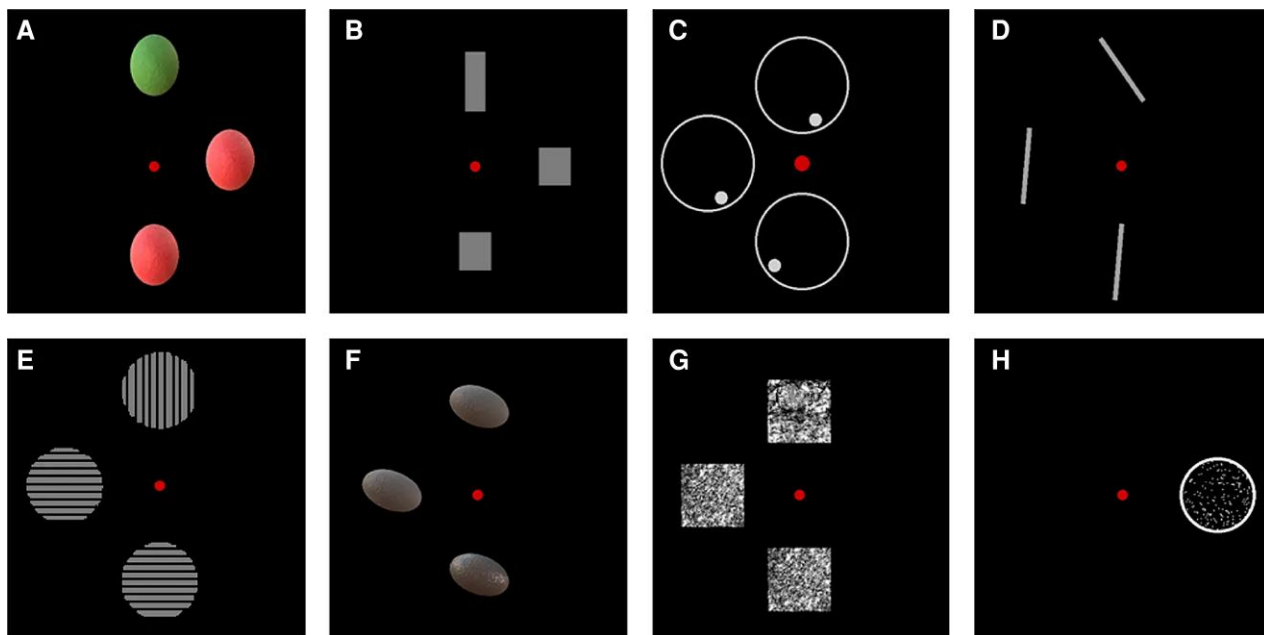


Figure 1 Examples of stimulus pictures. The pictures were used to assess the perception of colour (A), shape (B), location (C), orientation (D), contrast (E), glossiness (F), texture (G) and coherent motion (H). Adapted from Lammers et al.³¹

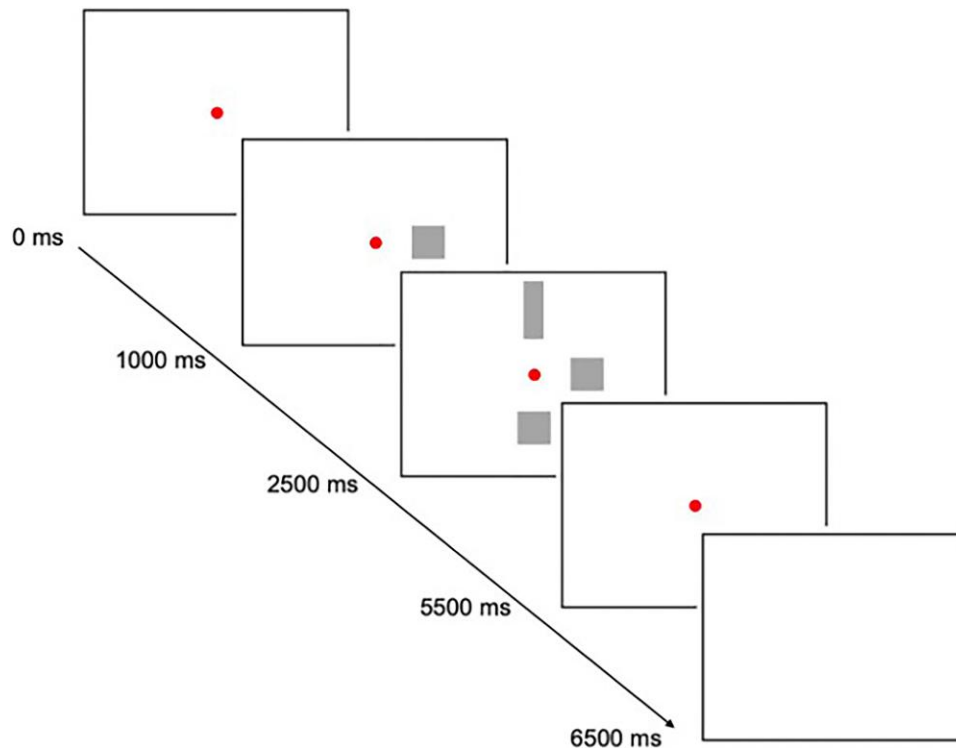


Figure 2 Schematic overview of the task protocol for the assessment of shape perception with the cumulative time (in milliseconds). Adapted from Lammers *et al.*³¹

All tasks, except the motion task, consisted of 12 practice trials (6 per hemifield) and 24 test trials (12 per hemifield). The lowest score (fewest correct identifications of identical stimuli) of two hemifields was used in the analyses. The motion task consisted of 24 practice trials (12 per hemifield) and 48 test trials (24 per hemifield). The highest score (indicating a higher percentage of coherence of the moving dots needed to identify direction) of two hemifields was used in the analyses. Subsequently, all task scores were converted into binary format, indicating either impairment or non-impairment. For completeness, analyses were also performed using the continuous task scores (see [Supplementary material, 'Results' Section I](#)). For patients with a score on all tasks, the number of deficits was determined. For a detailed description of the procedure and materials, including the impairment cut-offs for each task, see Lammers *et al.*³¹

Imaging data acquisition

MRI data were collected on a Philips R5 3 T MR scanner at the Amsterdam UMC and the UMCU, and on a Siemens Magnetom Prisma 3 T MR Scanner at the UMCG and Radboud UMC. For each patient, a 3D-fluid-attenuated inversion recovery (FLAIR) image was acquired. The sequence details of the Philips were as follows: T2 FLAIR [inversion time (TI) = 1650 ms, repetition time (TR) = 4800 ms, echo time (TE) = 253 ms, field of view (FOV) = 250 mm, voxel size = 1.12 mm × 1.12 mm × 0.56 mm]. The sequence details of the Siemens were as follows: T2 FLAIR (TI = 1650 ms, TR = 4800 ms, TE = 484 ms, FOV = 280 mm, voxel size = 0.9 mm × 0.9 mm × 0.9 mm).

Lesion segmentation and normalization

Lesions were delineated semi-automatically in native space using ITK-snap software.³⁶ Hyper-intensities around the lesion that showed further degeneration of white matter and gliosis were

considered as part of the lesion. Four researchers identified and marked the lesions. To check for inter-rater reliability, a random sample of eight scans (10% of the total scans) was selected, and each researcher identified the lesions independently. The mean inter-rater agreement was 81.3%. If there was uncertainty about specific scans, a neurologist or radiologist was consulted.

The MRIs and the corresponding lesion maps were normalized using a unified segmentation/normalization approach in Statistical Parametric Mapping software (SPM12^{37,38}). To correct for the presence of lesions during the normalization, enantiomorphic normalization was used for unilateral lesions.³⁹ For symmetrical, bilateral lesions, cost function masking was applied. Each individual normalization was examined by visually comparing the normalized lesion mask overlaid on the FLAIR in the Montreal Neurological Institute (MNI) space with the lesion mask and FLAIR image in the native space. If necessary, manual corrections were made to the segmentations in the MNI space.

Atlas-based lesion–symptom mapping

To relate the presence or absence of visual field and feature deficits to lesion locations, we used lesion–symptom mapping. Atlas-based lesion–symptom mapping was conducted using the statistical lesion analysis software NiiStat (<https://github.com/neurolabus/NiiStat>). To delineate grey matter regions of interest (ROIs) we used the Glasser atlas (https://figshare.com/articles/dataset/HCP-MMP1_0_projected_on_MNI2009a_GM_volumetric_in_NIFTI_format/3501911).⁴⁰ The Glasser atlas is based on architecture, function, connectivity and topography and identifies 180 parcels per hemisphere. We opted to investigate the entire brain, even though our specific assumptions focused on the posterior regions, because lesions upstream or downstream of these visual areas could also result in deficits in visual processing.

Table 1 Numbers of patients included in all subgroups

	Total n	Non-impaired	Impaired	Percentage impaired
Visual features				
Colour	153	115	38	25
Coherent motion	113	88	25	22
Orientation	178	146	32	18
Location	179	148	31	17
Texture	153	122	31	20
Shape	188	163	25	13
Contrast	153	134	19	12
Glossiness	137	119	18	13
Visual field defects				
Right side	134	125	9	7
Left side	135	125	10	7

This atlas provides a good balance between granularity and statistical utility. Its parcellation is fine grained enough to capture meaningful functional organization of the brain, while maintaining parcels large enough to leverage the advantages of atlas-based analyses. These larger parcels enhance statistical power in two ways: they reduce the familywise error rate and effectively increase the number of areas with sufficient coverage across participants. Importantly, this approach relaxes the requirement for perfect lesion overlap, because damage affecting the same ROI can be analysed collectively even when individual lesions do not coincide completely.

The lesion status of an ROI is represented by a binary score, determined by the number of lesions affecting that ROI exceeding a preset threshold. Because lesion volume is an important confound, given that larger lesions tend to cause more severe deficits regardless of location,⁴¹ and in line with recommendations by DeMarco and Turkeltaub,⁴² we regressed lesion volume on both the behavioural scores and lesion data.^{42,43} We analysed only ROIs that were included in the lesion masks of $\geq 5\%$ of the patients.⁴⁴ Setting a minimum overlap threshold reduces a bias in the results by voxels that are only rarely affected. It also prevents invalid statistical tests by comparing data from a group against one person.⁴⁵ To correct for multiple testing, we used permutation testing with 10 000 permutations and a significance threshold of $P < 0.05$.⁴⁴⁻⁴⁷ Tests are one-sided because we expect decreased performance only as a consequence of a lesion. For all lesion–symptom mapping analyses, we controlled for the effects of age, education level (scored on a range from one to seven, low to highly educated), interval between stroke and assessment, scanner type and lesion volume. Participants with missing data in any of these control variables were excluded from the analyses.

Setting threshold values for lesion–symptom mapping is guided by recent publications but remain to some degree arbitrary.⁴⁴⁻⁴⁷ Therefore, to demonstrate that our results are robust, we ran extra analyses that are presented as supplementary results. First, we addressed the choice in α -threshold for correction for multiple testing. Controlling for familywise error rate using permutation thresholding and a corrected α -level of 0.05 is often considered to be a gold standard for lesion symptom mapping.⁴⁵⁻⁴⁷ Given that we aimed to investigate evidence, or lack thereof, for a modular visual system, we included analyses with a more lenient α -level of 0.1 in the [Supplementary material, 'Results' Section I](#). To test for the robustness of our results we also included a stricter α -level of 0.001.

Second, setting the threshold for the sufficient lesion affection influences how many ROIs are included in the analyses. Setting a high threshold results in low coverage of the brain, whereas too

low a threshold results in more displacement of lesion–symptom relationships.⁴⁴ In the analyses in the main manuscript, we applied the commonly used threshold of 5% of the patients.⁴⁴ [Supplementary material, 'Results' Section II](#) includes the results with a lower threshold of four patients.⁴⁵

Finally, advantages of atlas-based analyses include the increase of statistical power by reducing the number of tests and leveraging accumulative lesion burden in each ROI. However, for functions that are highly localized, an atlas-based approach might add noise, making it harder to detect a real effect. To address this, we ran our analyses voxel-wise ([Supplementary material, 'Results' Section III](#)).

Disconnectome maps

Lesions cause local disruptions in function but also disconnections between distant regions. For each lesion, a disconnectome map of white matter pathway disconnection probabilities was calculated using *BCBtoolkit*.⁴⁸ In this approach, a set of 10 healthy control diffusion-weighted imaging datasets⁴⁹ is used to track fibres passing through the lesions in patients. The lesions in the MNI space are registered to each control native space using affine and diffeomorphic deformations^{50,51} and are subsequently used as seed for the tractography (<https://trackvis.org/>).⁵² Tractographies from the lesions are transformed in visitation maps,⁵³ binarized and transformed back to MNI space using the inverse of precedent deformations. Next, a percentage overlap map is created by summing, at each point in MNI space, the normalized visitation map of each healthy subject. The resulting disconnectome map takes into account the interindividual variability of tract reconstructions in controls and indicates a probability of disconnection from 0 to 100% for a given lesion. Finally, the disconnectome maps are binarized with a cut-off at the default value of 50%. These binarized disconnectome maps are subsequently used for the same atlas-based analyses as those of the original binary lesion maps. In this case, a probability of $>50\%$ of disconnection of Glasser grey matter areas is related to visual deficits.

Statistical analyses

Associations between the performance on the visual tasks (behavioural measures) and lesion volumes were tested with partial correlations (Pearson's r), adjusting for age, education level, interval between stroke and assessment, and scanner type. Given that the lesion volumes were not normally distributed, the significance of the correlations was assessed by permutation testing with 10 000 permutations, in line with the lesion–symptom mapping analyses.

Results

Participant selection

From our initial cohort of 307 stroke patients, we obtained varying sample sizes for each visual task. The colour task included 224 patients, orientation 263, motion 172, location 261, texture 222, shape 273, contrast 226 and glossiness 194. Missing data on single tasks were attributable to fatigue or time constraints. We excluded 104 patients from all visual feature analyses for various reasons: 91 had no available lesion data, 7 presented with hemianopia, 2 experienced technical errors during task execution, and 4 had missing demographic control variables.

We were also able to assess the visual field deficits of 198 patients. Of these, 54 patients were excluded from analyses owing to no lesion data available ($n = 47$), technical error when executing the task ($n = 1$), no visual field abnormality specification ($n = 1$), or abnormality other than left or right visual field abnormality ($n = 5$).

Table 1 presents the final sample sizes for all subgroups, including the number of impaired patients for each visual feature and visual field deficit assessment. Table 2 summarizes the clinical and demographic characteristics of all included patients. It is important to note that sample sizes vary across tasks owing to differences in data availability. Consequently, some patients might be included in certain analyses but not in others.

Pairwise correlations between lesion volumes and task scores

Given that lesion volume is often correlated with symptom severity, it is recommended to control for lesion volume in lesion–symptom analyses.⁴² As an initial step, we investigated the relationship between lesion volume and behavioural measures for all participant subgroups (groups based on availability of data) using partial correlations. These analyses accounted for the effects of age, education, interval between stroke and assessment, and scanner type. The significance of these correlations was assessed using permutation tests with 10 000 permutations. We found no significant associations between lesion volumes and task scores after applying false discovery rate correction for multiple comparisons.

The lack of correlations suggests that the overall size of the lesion might not be a significant predictor of performance on our visual processing tasks. Instead, the specific location of the lesion might be more crucial, highlighting the importance of our subsequent lesion–symptom mapping analyses.

Atlas-based lesion–symptom mapping

Visual field deficits

Given that it is well documented that visual field deficits are strongly related to lesions in early visual areas in the contralateral hemisphere, we initially aimed to confirm this relationship in our sample. Demonstrating this association shows the validity of our analysis method. Our analysis of visual field deficits indeed aligned with existing literature,^{54,55} mapping these deficits to the early visual cortex. For left field visual deficits, we analysed 123 of 360 grey-matter ROIs from the Glasser atlas, which had sufficient lesion coverage (>5%, corresponding to at least seven lesions; for a complete list, see Supplementary Table 1). Given that a score of zero indicates non-impaired performance and one impaired, only z -scores

Table 2 Clinical characteristics of all included patients

Parameter	Value
All patients, n	200
Age (years), mean (SD) [range]	59.4 (13.2) [19–83]
Male/female, n (%)	140/60 (70/30)
Education level ^a , mean (SD)	5.3 (1.28)
NIHSS ^b , mean (SD)	6.4 (5.83)
Time since stroke ^b , mean (SD)	8.3 (4.89)
Stroke laterality r:l:b (%)	82 (44.3%):74 (40%):29 (15.7%)
Median lesion volume (cm ³) [range]	6.43 [<0.01 –357.47]
Median lesion volume (cm ³), r:l:b	7.59:4.74:6.97

NIHSS = National Institutes of Health Stroke Scale; r:l:b = right:left:bilateral; SD = standard deviation.

^aEducation on a seven-point scale, ranging from one (primary education) to seven (university education).

^bInterval between stroke and assessment (in weeks).

exceeding the positive z -threshold are meaningful. After controlling for age, education, interval between stroke and assessment, scanner type and lesion volume, we found significant correlations with lesion status in six right hemisphere regions (threshold $z > 4.76$; Fig. 3): primary visual cortex (V1; $z = 7.74$), second visual area (V2; $z = 7.50$), third visual area (V3; $z = 5.76$), prestriate area ($z = 7.07$), parahippocampal area 3 ($z = 6.56$) and ventral visual complex ($z = 4.80$) (see Fig. 3).

For right field visual deficits, 111 ROIs had sufficient lesion coverage (Supplementary Table 2). Significant correlations emerged in three left hemisphere regions (threshold $z > 4.93$): primary visual cortex (V1; $z = 6.43$), second visual area (V2; $z = 6.53$) and third visual area (V3; $z = 5.83$) (see Fig. 3).

Visual features

Our results regarding the relationship between visual field deficits and early visual areas showed that using atlas-based lesion–symptom mapping, we can detect localized functions in the visual system. Our main aim was to investigate whether those localized associations can also be found for mid-level visual features and whether these map onto areas in the visual cortex as described in the literature. Figure 4 illustrates the distribution of lesions for all included patients, and Fig. 5 illustrates the distribution of lesions in patients with impairments for each visual feature. The number of ROIs with sufficient lesion coverage (>5% of the sample) varied across visual features owing to differences in task completion (mean = 121.9, standard deviation = 11.6; for complete lists, see Supplementary Tables 3–10). All analyses controlled for age, education, interval between stroke and assessment, scanner type and lesion volume.

The lesion–symptom mapping results indicate minimal relationship between lesions in specific brain areas and the processing of the eight mid-level visual features. Higher scores denote deficits, hence only values below the negative z -threshold are significant.

Atlas-based lesion–symptom mapping revealed no significant associations between lesion status and performance on any of the visual feature tasks or the total number of feature deficits.

To test the reliability of our results, we repeated our analyses in four different ways: (i) with continuous instead of binarized scores for performance on visual features (Supplementary material, 'Results' Section 1); (ii) with a more lenient (0.1) and stricter (0.001) corrected α -level for permutation testing for family-wise error

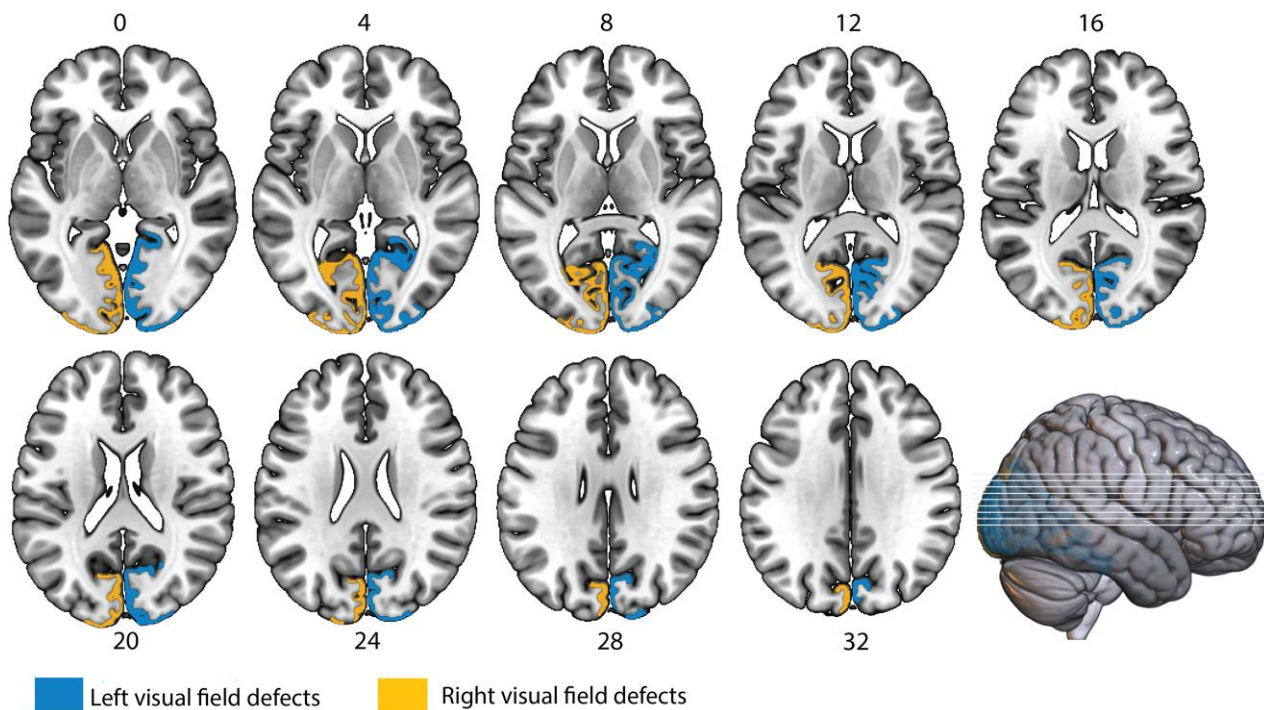


Figure 3 Significant associations from the atlas-based lesion–symptom mapping analyses. All results are controlled for age, education, interval between stroke and assessment, scanner and lesion volume and are corrected for multiple testing, using permutation testing (10 000 permutations, corrected $P < 0.05$). Numbers refer to Montreal Neurological Institute coordinates. The left hemisphere is depicted on the left.

rate (Supplementary material, ‘Results’ Section II); (iii) with a lower threshold for sufficient lesion affection (Supplementary material, ‘Results’ Section III); and (iv) using voxel-wise instead of atlas-based analyses (Supplementary material, ‘Results’ Section III). Taken together, the results of these analyses align with those of the primary analyses, reinforcing the robustness of our findings.

Disconnectome maps

Lesions not only cause local disruptions but also disconnect brain areas. White matter disconnection might lead to impaired functioning in regions distant from the lesion itself. Disconnectome maps estimate, for every voxel, the probability of being disconnected based on the binary lesion. Applying the same atlas-based lesion–symptom mapping analyses to these disconnectome maps provides insight into the distant effects of lesions. For three patients, the disconnectome map could not be determined owing to small focal grey matter lesions.

Visual field defects

For left field visual defects, of the 360 grey-matter ROIs included in the Glasser atlas, 267 had sufficient lesion coverage (>5% corresponded to at least seven lesions; for a list of included ROIs, see Supplementary Table 11) to be included in the analysis. Significant correlations were found with disconnectome maps after controlling for age, education, interval between stroke and assessment, scanner, and lesion volume in 19 regions (threshold $z > 4.95$). All ROIs were in the right hemisphere, predominantly in the visual cortex, extending into the medial temporal cortex.

For right field visual defects, of the 360 grey-matter ROIs included in the Glasser atlas, 263 had sufficient lesion coverage (at

least seven lesions; Supplementary Table 12). Significant correlations were found with disconnectome maps after controlling for age, education, interval between stroke and assessment, scanner, and lesion volume in 14 areas (threshold $z > 5.12$) in the left hemisphere in the visual and medial temporal cortex.

Visual features

The lesion–symptom mapping results indicate that there is no relationship or minimal relationship between lesions in specific brain areas and their corresponding disconnectome maps and the processing of the eight mid-level visual features and total number of feature deficits.

Only for motion, a significant correlation was found in the right temporo-parietal junction ($z = 3.87$) and an area in the lateral occipital cortex in the right hemisphere (LO3, $z = 3.70$, threshold $z > 3.67$). The temporo-parietal junction has been associated with many cognitive functions, mainly related to integration of information and contextual updating,⁵⁶ but not specifically to processing of motion. In contrast, LO3 is thought to integrate motion and shape information.⁵⁷ Our study suggests that disconnection of these areas, instead of direct tissue loss, results in deficits in motion perception.

Previous studies have shown that directly disconnected regions correspond more strongly to task-related fMRI meta-analytical maps than lesions alone.^{48,58} Furthermore, white matter disconnections are a strong predictor of neuropsychological test scores 1 year after stroke.⁵⁹ Our results do show a strong association between disconnection of visual regions and visual field defects but not for most mid-level visual features. This could be related to indirect effects of stroke lesions in distant regions that are functionally but not structurally connected. However, like task-fMRI studies

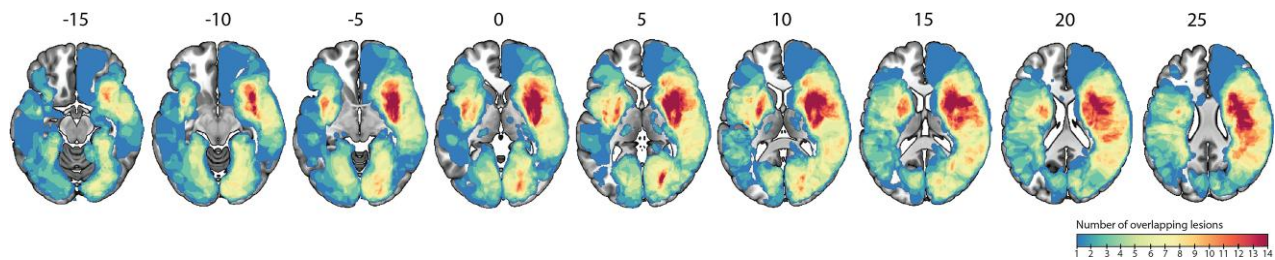


Figure 4 Lesion prevalence map for all included patients ($n = 200$). Numbers refer to Montreal Neurological Institute coordinates. The left hemisphere is depicted on the left. The colour bar indicates the number of patients with a lesion for each voxel.

in healthy subjects, investigating the relationship between lesions and functional networks related to visual feature perception would identify networks involved in rather than required for feature perception.⁴⁶ In sum, our disconnection analyses, in line with our lesion location analyses, provide evidence for localization of visual field defects but only very limited for mid-level feature defects.

Discussion

This study represents the first large-scale investigation into the neural foundations of mid-level visual feature processing in ischaemic stroke patients. We examined eight key visual features: colour, shape, contrast, location, orientation, glossiness, coherent motion and texture. Contrary to expectations, we did not observe consistent associations between behavioural impairments in these visual features and specific brain regions. This lack of clear localization is particularly striking given the well-established literature on the topic. Our findings challenge the prevailing conventional model of visual processing and offer new insights into the visual architecture of the brain.

For decades, neuroscientific research has posited strong links between certain brain areas and specific visual functions. Area V4, for instance, has been widely regarded as a critical hub for colour processing, whereas area MT/V5 has been similarly associated with motion perception.^{4,60} Our results, however, suggest a more complex and perhaps distributed pattern of visual processing that does not align neatly with these traditional demarcations.

Moreover, our findings could have implications for the long-standing ‘binding problem’ in visual neuroscience. This problem arises from the notion of strong separation in mid-level feature processing, where different visual attributes are supposedly processed in distinct brain regions and must later be integrated to form coherent percepts. The absence of clear regional specificity in our results could suggest that this binding problem might be less pronounced than previously thought, or perhaps has been conceptualized incorrectly.

The absence of significant associations between behavioural impairments and specific brain regions is unlikely to stem from limitations in the sensitivity of our visual tasks. Our testing approach incorporated several methodological strengths that enhanced our ability to detect subtle deficits. First, our innovative gaze-contingent testing set-up allowed precise control over stimulus presentation and enabled separate testing of each hemifield. The effectiveness of this approach is demonstrated by its high completion rate across our patient population, including those with aphasia or motor difficulties.³¹ Second, our tasks were carefully calibrated based on established research. For example, the red–green range in our colour perception task was specifically chosen based on seminal studies of colour perception in stroke patients.^{61,62} Third, the pattern of results itself supports the sensitivity of tasks:

we observed a rich and differentiated set of deficits across patients, with varying degrees of impairment across different visual features. This variability in performance indicates that our tasks successfully captured meaningful differences in visual processing capabilities, rather than producing ceiling or floor effects that would suggest limited sensitivity.

An inherent limitation in stroke lesion studies stems from the vascular architecture of the brain. As documented by Sperber and Karnath,⁴⁴ the distribution of stroke lesions is not uniform across the brain, with some regions being less susceptible to stroke damage. This anatomical constraint affects our ability to study certain regions that previous research has linked to specific visual processing functions. For instance, despite our large sample size, we found limited coverage of area MT (labelled as MST in the Glasser atlas). Nevertheless, our patient sample exhibited impairments across all visual features examined, even in cases where the putative critical regions showed limited lesion coverage. This dissociation is particularly striking in the case of colour and shape processing: traditional models would predict deficits in these domains to emerge from right V4 damage, whereas our patients exhibiting colour and shape deficits showed no consistent pattern of V4 lesions. This finding challenges the straightforward mapping between V4 damage and specific visual processing impairments. Our results are weaker with regard to area MT and deficits in motion processing. Although we observe a substantial number of deficits in motion perception, we have few patients with lesions in area MT. Those patients that we have do not have a clear deficit in motion processing, but there are not enough of them to draw reliable conclusions, and the observation that deficits in motion processing occur without damage to area MT does not discount the importance of this area. Damage to other areas, relaying information from MT, or connections between area MT and other areas could also explain this pattern.

To ensure the reliability of our methodology, we included an assessment of visual field defects. Our results clearly demonstrated a link between contralesional damage in primary visual areas V1, V2 and V3 and visual field deficits. This finding, consistent with previous research,^{55,63} validates the robustness of our approach and lends credibility to our unexpected findings regarding mid-level visual features.

Our findings raise an important methodological consideration in understanding the organization of visual processing: the fundamental distinction between an area showing functional responsiveness to specific stimuli and the behavioural consequences of damage to that area. This apparent discrepancy highlights a crucial principle in cognitive neuroscience: functional activation of a brain region during a task does not necessarily indicate that this region is essential for performing that task. Areas can be part of broader processing networks without being critical nodes whose damage would result in specific deficits. The neural processing of mid-level

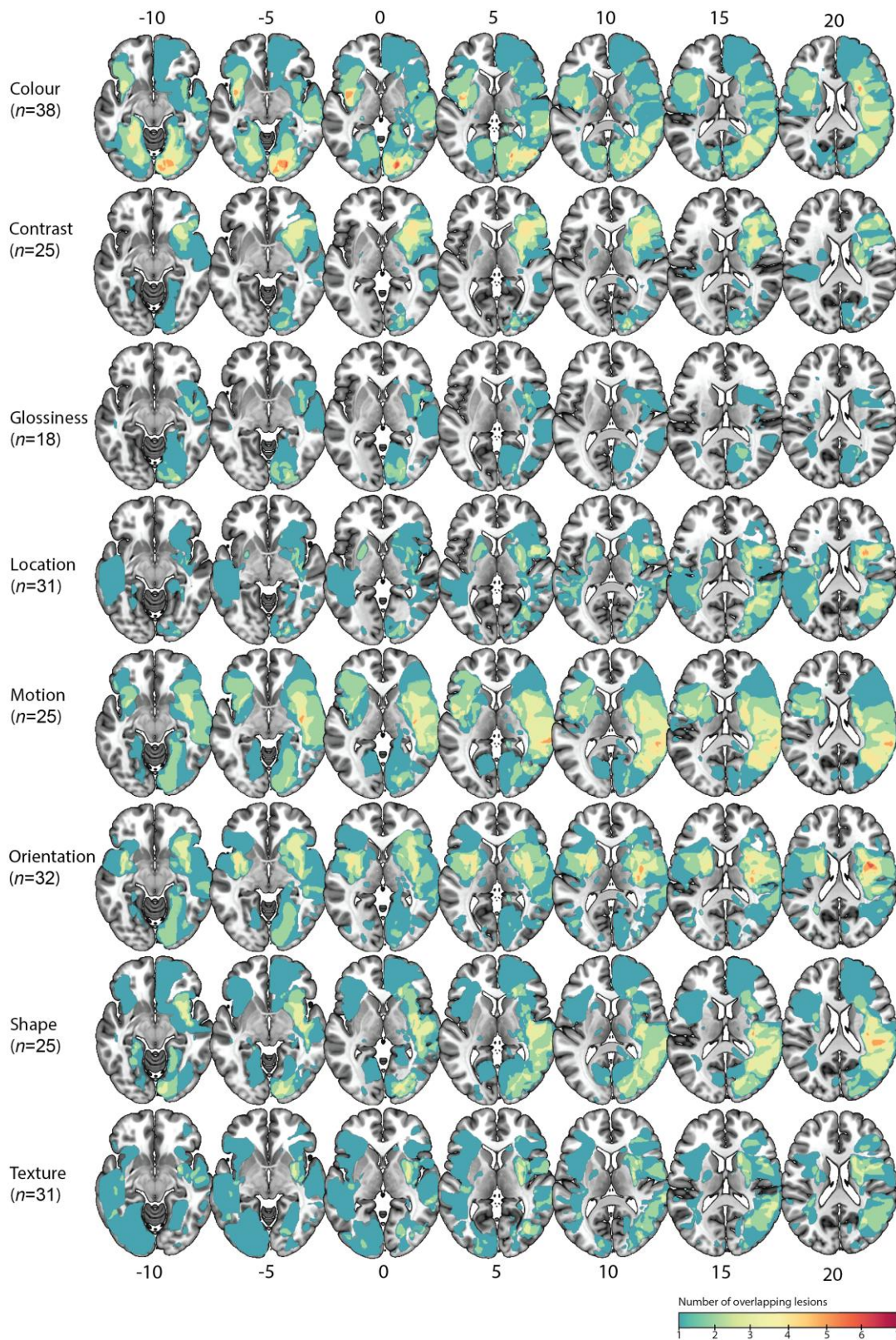


Figure 5 Lesion prevalence maps for patients impaired on the visual feature tasks. Numbers refer to Montreal Neurological Institute coordinates. The left hemisphere is depicted on the left. The colour bar indicates the number of patients with a lesion for each voxel.

visual qualities appears to be more resilient to focal damage than would be predicted by a strictly modular model where specific regions are essential for processing particular qualities.^{64,65}

Our findings therefore do not support the traditional localizationist view of the human visual brain but suggest instead that the processing of these fundamental visual qualities involves

more distributed networks rather than being confined to specific cortical regions. This interpretation aligns with more recent network-based models of visual processing, where multiple regions can support fundamental visual functions through distributed processing mechanisms. The results indirectly support the alternative, patchwork model of the visual brain, which proposes that visual maps represent constellations of co-occurring information in the external world rather than being tuned to specific visual categories.^{29,30} Although the absence of evidence is not evidence of absence, our data align with a large number of recent imaging studies²³ and perspectives,^{27,28} suggesting that although certain areas might preferentially process specific visual qualities, this processing is not dependent exclusively on these regions.

Our study advances theoretical understanding of mid-level visual feature processing across the human visual brain. It suggests that the organization of the brain for visual processing might be more flexible and interconnected than previously thought, potentially resolving longstanding issues, such as the 'binding problem' in visual perception.

The clinical implications of our findings are significant. Understanding how the location of an infarct relates to neurological outcomes is crucial for both understanding stroke pathogenesis and guiding recovery processes. Our results suggest that recovery and rehabilitation strategies might benefit from targeting broader networks rather than focusing solely on traditionally defined 'specialized' regions.

Data availability

The data that support the findings of this study are openly available on Open Science Framework (OSF) at osf.io/yq93s.

Acknowledgements

The Visual Brain Group is Anouk R. Smits, Ben A. Schmand, Edward H. F. de Haan, Frank Erik de Leeuw, Gert Jan Luijckx, H. Steven Scholte, Joke M. Spikman, L. Jaap Kappelle, Linda Geerligs, Martine J. E. van Zandvoort, Matthan W. A. Caan, Matthijs A. H. L. L. Raemaekers, Mathias Prokop, Nick F. Ramsey, Nikki A. Lammers, Nils S. van den Berg, Noor Seijdel, Paul J. Nederkoorn, Rients B. Huitema, Bob Kentridge, Roy P. C. Kessels, Selma Lugtmeijer and Yair Pinto.

Funding

This study was supported by a European Research Council Advanced (ERC Advanced) Grant (#339374) awarded to E.H.F.d.H.

Competing interests

The authors report no competing interests.

Supplementary material

[Supplementary material](#) is available at *Brain* online.

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