Visual responses to targets and distracters by inferior temporal neurons after lesions of extrastriate areas V4 and TEO

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While lesions of visual areas V4 and TEO only modestly affect discrimination of isolated objects, they significantly impair the ability to selectively attend to an object surrounded by distracters. To test whether such deficits result from a loss of inputs to higher order areas, we recorded from area TE neurons after removing portions of V4 and TEO in a monkey. Responses to isolated targets in a lesion-affected visual quadrant were substantially preserved, indicating that TE still receives information even after removing a major source of input. Distracters increased or decreased the response to targets more in the lesion-affected than in the normal quadrant, supporting the idea that V4 and/or TEO are sites where top-down attentional inputs filter out distracting stimuli. *NeuroReport* 15:1611–1615 © 2004 Lippincott Williams & Wilkins.

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INTRODUCTION

When attention is focused on a behaviorally relevant stimulus in the visual field, the processing of that object is enhanced relative to that of any surrounding distracters. Several electrophysiological studies have suggested that this comes about by the filtering of distracting stimuli from the receptive fields of neurons along the ventral processing stream, an occipitotemporal cortical pathway that is critical for visual object recognition in primates [1–4].

The important role of ventral stream areas in attentional filtering is also supported by several lesion studies [5–11]. In particular, De Weerd *et al.* [9,11] found that lesions of extrastriate areas V4 and/or TEO produced a severe impairment in the discrimination of a variety of target stimuli when they were surrounded by salient luminance distracters, whereas the discrimination of the same stimuli posed little difficulty in the absence of distracters. Similar results have been found in a human patient with a V4 lesion [12].

Because areas V4 and TEO provide the main input to inferior temporal area TE, the next processing stage in the ventral stream [13,14], one possible explanation for the behavioral results is that V4 and TEO lesions simply deprive TE of visual input, essentially deafferenting the highest levels of the ventral stream. In that case, object discrimination might be mediated by alternative pathways that do not have the capacity to both process object features and filter out distracting stimuli from receptive fields. To test this, we recorded the responses of area TE neurons to target stimuli presented either in a visual quadrant affected by a combined V4 and TEO lesion, or in an unaffected quadrant.

If TE neurons did continue to respond to visual input in the absence of V4 and TEO, the next step would be to test whether the TE neurons would show reduced efficiency in filtering out distracting information from their receptive fields. We planned to test this by comparing neuronal responses in the normal and lesion-affected quadrants to stimuli presented either alone or surrounded by irrelevant distracters (Fig. 1d). We reasoned that if V4 and TEO were critical sites where top-down attentional inputs filtered distracters from receptive fields, then lesions of these areas would result in impaired attentional filtering by neurons in area TE, which receives inputs from these two areas.

MATERIALS AND METHODS

Lesions and recording procedure: One adult male monkey (*Macaca mulatta*, monkey M1 from ref. [9]), weighing ~9 kg, was used. All surgical and behavioral procedures were carried out in accordance with National Institutes of Health guidelines, under a protocol approved by the National Institute of Mental Health Institutional Animal Care and Use Committee, and have been described in detail

previously [9]. Briefly, the monkey was prepared with a lesion in the right hemisphere intended to remove all of area TEO and the dorsal portion of area V4, thereby differentially affecting the visual field quadrants (Fig. 1 a,b).

Neuronal activity was recorded from single area TE units in the right hemisphere while the monkey attended to target stimuli presented either at fixation or extrafoveally in either the upper-right, unaffected quadrant of the visual field (normal quadrant), or in the lower-left quadrant, which was missing input from both areas V4 and TEO (lesion-affected quadrant, Fig. 1b). Responses were averaged over a 200 ms time window, starting 75 ms after the stimulus onset, corresponding to the minimum response latency observed.

In each daily recording session, a tungsten electrode was advanced into area TE through a plastic recording chamber surgically implanted on the dorsal surface of the skull. Stereotaxic locations and depth of individual penetrations were reconstructed from previously obtained magnetic resonance imaging (MRI) scans. After isolation of a neuron, its responses were probed with a set of 10 stimuli presented at fixation. Stimuli were randomly drawn from a large library of images (photographs, artwork, etc.). Some of the images were clearly recognizable as objects (e.g., human faces, animals, fruits, etc.), whereas others appeared as abstract pictures and patterns. We selected as targets two stimuli, one which was the most effective in driving the cell and the other which was the least effective stimulus, in order to span a wide range of stimulus selectivity.

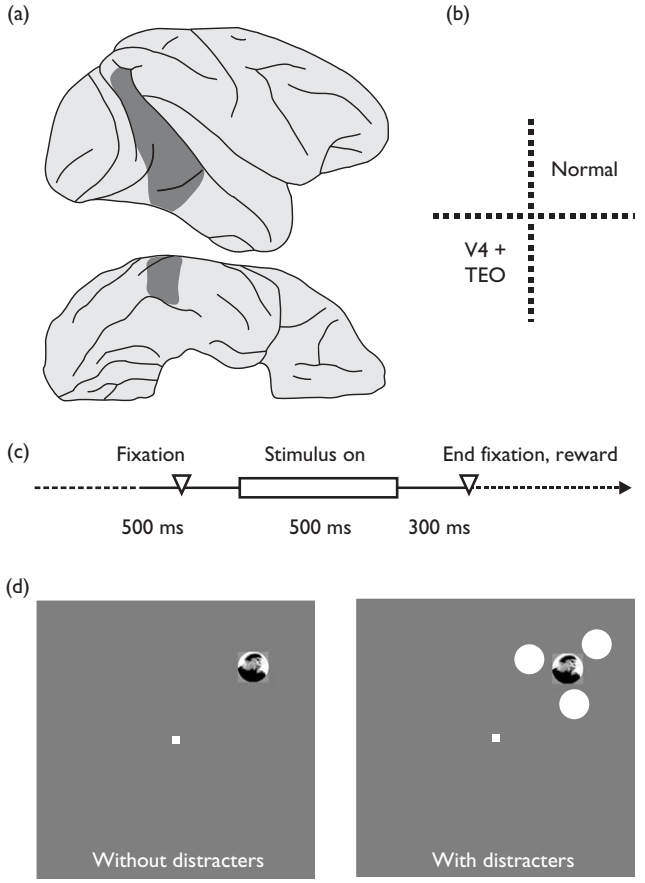

Fig. 1. Lesions and behavioral task. (**a**) Schematic representation of the combined lesion of dorsal area V4 and area TEO, projected on the lateral and ventral aspects of the right hemisphere on the basis of post-operative MRI scans (see [9] for details). (**b**) Illustration of normal and lesion-affected visual field quadrants. The monkey also had a V4 lesion in the lower visual field representation of the left hemisphere (not shown), which was not studied in the present study. (**c**) Trial timeline. At the beginning of each trial, the monkey was required to fixate a small spot (0.2°) that appeared at the center of a computer monitor. Five hundred ms after fixation was reached, a stimulus was presented in the periphery for a duration of 500 ms. After the stimulus was turned off, the monkey was required to maintain fixation for an additional 300 ms, until the fixation spot disappeared. Trials were aborted when eye movements, monitored with the scleral search coil technique, exceeded 1.5° from the fixation spot. (**d**) Target stimuli were 2.3° in diameter and consisted of either complex, colorful images (as in this example) or oriented gratings (see text). Targets were presented at ~5° of eccentricity on a uniform grey background (luminance 16.7 cd/m^2) either alone (left panel) or surrounded by an array of 3 distracters, represented by bright white circles of identical size (luminance 50.3 cd/m^2), randomly positioned at a center-to-center distance of 2.5° from the target stimulus (right panel).

Behavioral tasks: The chosen stimuli were presented in the context of two different behavioral tasks, both aimed at directing attention to the target stimulus. In both tasks (Fig. 1c,d), the monkey fixated a small spot at the center of the display and was rewarded with a drop of juice for releasing a response bar within 1000 ms from the presentation of a go target (see below) and for holding the bar until the end of the trial for no-go targets. For about two-thirds of the recorded neurons, the task was to discriminate the orientation of high-contrast, low spatial frequency monochrome sinusoidal gratings whose phase was randomized from trial to trial. Targets were oriented vertically in 50% of the trials (go targets), and were rotated anti-clockwise or clockwise in the remaining 50% (no-go targets). The orientation difference between vertical and non-vertical stimuli was kept near threshold according to a staircase procedure [9]. On a proportion of the no-go trials (10–30%), the oriented gratings were replaced, unpredictably, by one of the two complex stimuli that had been chosen beforehand. Since the monkey could not predict which stimulus to expect, the orientation discrimination task effectively served as a tool to maintain attention at the location of the colorful images.

For the remaining third of the neurons recorded, no oriented gratings were presented. Instead, the monkey was required to discriminate between the two targets selected for that session. Over the course of a few preliminary trials, the monkey learned to give a go response to one of the targets, and a no-go response to the other one.

For both orientation and object discrimination tasks, alternating blocks of trials were presented in the normal and lesion-affected quadrants. A block was completed when responses to 20–40 presentations of both complex stimuli were collected. This routine was repeated with and without distracters surrounding the target (Fig. 1d); the number of trials with and without distracters was equal within a block. Because no significant differences between the two tasks were found, the data obtained from the two were pooled together.

RESULTS

Neuronal response to single complex stimuli: A total of 72 TE neurons had visual responses to target stimuli presented at fixation. Area TE receptive fields are typically large, including the center of gaze and often extending into both the contralateral and ipsilateral visual fields [15–17].

Accordingly, the majority of the recorded neurons responded significantly to at least one of the stimuli presented in the extrafoveal region of both visual quadrants, allowing us to assess the effects of the lesions within each neuron. Thirteen cells, however, were poorly responsive to all extrafoveal stimuli and were excluded from the analyses, along with one neuron that was responsive in the normal but not in the lesion-affected quadrant, and one in which the reverse was true.

For the remaining 57 cells, there was little overall difference in responsiveness between quadrants (Fig. 2). Across the population, firing rates for stimuli presented in the normal (15.8 s/s) and lesion-affected quadrant (14.3 s/s), were not significantly different (paired *t*-test, $p > 0.05$). These data indicate that TE neurons can be driven by stimuli presented in the visual field quadrant affected by the combined lesion of V4 and TEO.

We then asked whether removal of areas V4 and TEO impaired the ability of TE neurons to respond differentially to the different stimuli. First, we observed that stimulus preference, as qualitatively determined at the fovea, was in several cases different in the normal and lesion-affected quadrants. Indeed, 30 (52%) cells showed significantly different tuning across quadrants, based on a significant interaction between stimulus and location in the computed 2-way analysis of variance (ANOVA, $p < 0.05$). In order to quantify each neuron's ability to discriminate between the two target stimuli, while taking into account the variability of stimulus preference across quadrants, we computed in each quadrant a normalized index of stimulus selectivity according to the formula $(S1-S2)/(S1+S2)$, where S1 and S2 were the average firing rates to the more effective and to the less effective stimulus at that location, respectively. The difference between normalized indices in the normal quadrant (mean 0.35) and in the lesion-affected quadrant (mean 0.28) was not significant (paired *t*-test, $p > 0.05$). Thus, lesions of V4 + TEO did not substantially alter either the magnitude of responses or the degree of selectivity of TE neurons, for stimuli presented in isolation.

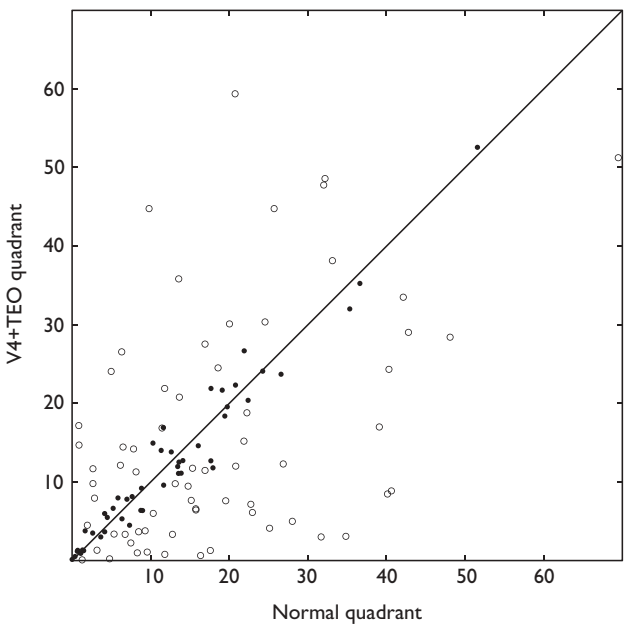

Fig. 2. Responsiveness of neurons to individual stimuli. Each data point in the chart represents the average firing rate (spikes/second) in response to a target stimulus presented in the normal quadrant, plotted against the responses in the lesion-affected quadrant. Open circles represent stimuli for which the responses in the two quadrants were significantly different (2-independent-sample *t*-test, $p < 0.05$).

Effect of distracters on neuronal responses to complex objects: Physiological studies have shown that when an animal attends to a stimulus in the receptive field of a V4 cell, responses to simultaneously presented distracter stimuli within the receptive field are filtered out, i.e., they have little influence on the cell's response. In this case, the message communicated from V4 to TE is restricted to the properties of the attended stimulus [4]. Given the behavioral finding that distracters impair the processing of an attended target stimulus after V4 and TEO lesions [9], we predicted that distracters would have a greater effect on the response of TE neurons to a target stimulus presented in the lesion-affected quadrant than in the normal quadrant, because in the former case, the distracters would not have been filtered out of the input to TE.

To test this prediction, we examined the effect of distracter stimuli on the responses of TE cells to attended targets. Average responses to targets surrounded by distracters were 14.0 s/s in the normal and 12.4 s/s in the lesion-affected quadrant, a small but overall significant decrease, compared to the response to the target alone, in both quadrants (paired *t*-tests, $p < 0.05$). However, we did notice that for some cells, the absolute magnitude of the response change caused by the distracter, whether an increase or a decrease, was larger in the lesion-affected than in the normal quadrant (Fig. 3a). To test this for the population of cells, we therefore computed, for each target stimulus, an index obtained by normalizing the absolute firing rate difference between target-alone (Ta) and target + distracters (TD) conditions: $|(Ta-TD)/(Ta+TD)|$ (Fig. 3b). On average, this index was indeed significantly larger in the lesion-affected quadrant (mean 0.31) than in the normal quadrant (mean 0.22; paired *t*-test, $p < 0.005$). Thus, these data suggest that distracters alter responses more in the lesion-affected than in the normal quadrant.

Responses to grating stimuli: We also analyzed the responses to the monochrome grating stimuli in the subset of neurons recorded while the monkey performed the orientation discrimination task. Although most units were far from optimally responsive to gratings, results were overall similar to those observed with complex stimuli, with no significant difference between responses to gratings presented alone in the normal (10.0 s/s) and lesion-affected (10.5 s/s) quadrants (paired *t*-test, $p > 0.05$), and with distracters affecting the responses to target gratings more in the lesion-affected quadrant (mean distracter impact index 0.32) than in the normal quadrant (mean 0.26), although the difference did not reach significance (paired *t*-test, $p > 0.05$).

Behavioral performance: We measured the monkey's behavioral performance to ensure that the animal consistently attended to the location of the target stimuli during the recordings, and to confirm the presence of behavioral deficits similar to those previously reported in the same monkey. Performance on the orientation discrimination task

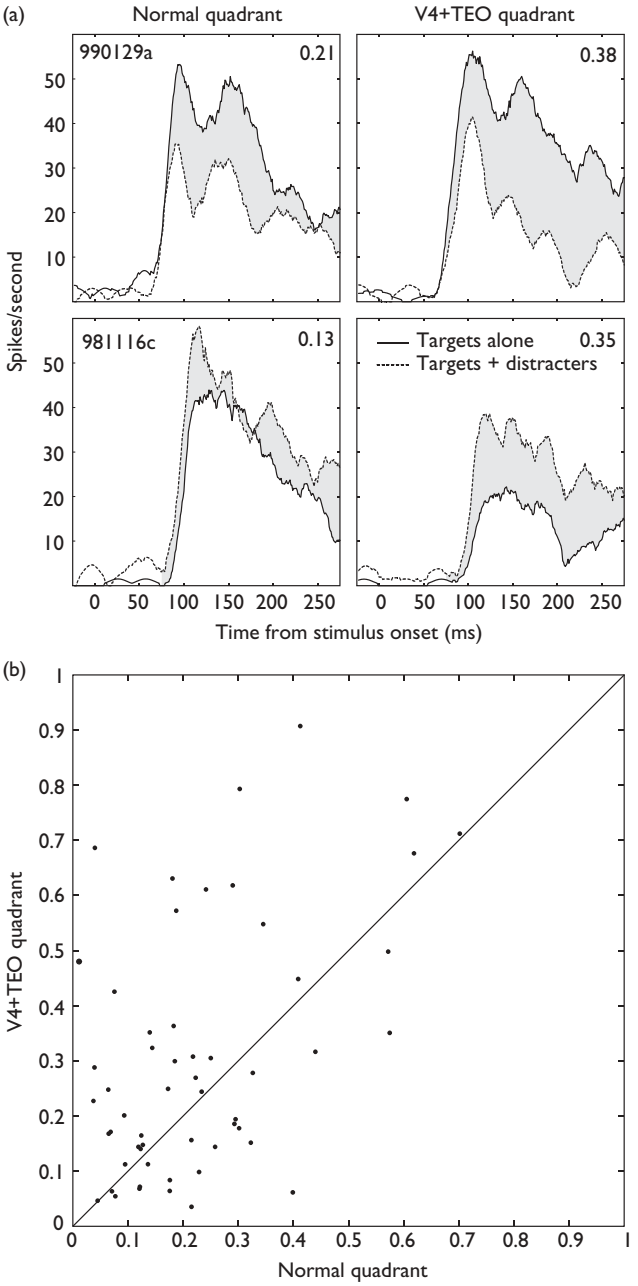

Fig. 3. Effect of distracters on responses to targets. (**a**) Responses of two sample neurons to stimuli presented either alone or surrounded by distracters. For one cell (top panels) distracters reduced the responses, compared to the target alone, while for another cell (bottom panels), responses were enhanced by the distracters. In both cases, distracters had a larger effect on the responses to target stimuli presented in the lesion-affected quadrant (right panels), compared to the normal quadrant (left panels). Numbers in the top-right corner of each plot are the normalized indices of distracter impact for these cells (see text). (**b**) Effect of distracters in the normal and lesion-affected quadrants in the population of cells. Each data point represents the average, for the two stimuli presented during the experiment, of the normalized indices of the impact that distracters had on a single neuron's response to targets (see text).

was similar to that reported previously for this monkey [9]. Briefly, orientation discrimination thresholds did not differ significantly for targets presented in the normal and the V4 + TEO-affected quadrants in the absence of distracters (*t*-test, $p > 0.05$). By contrast, the addition of distracters surrounding the target increased discrimination thresholds significantly more in the lesion-affected quadrant than in the normal quadrant (2-way ANOVA, significant interaction between quadrant and distracter effect, $p < 0.05$). These results provide evidence of an attentional deficit that was still present over 3 years after the lesions were made.

Although performance on the object discriminations varied greatly with the different stimulus pairs, on average performance was much better than on the more difficult orientation discriminations, which were at threshold. Thus, probably because performance was very often at ceiling on the object discrimination task, there was no overall significant difference in performance between the lesion-affected and normal quadrants, with or without distracters.

DISCUSSION

Neurons in area TE responded well to visual stimuli when presented in a visual field quadrant affected by a combined lesion in areas V4 and TEO. There was no significant difference in overall response level to targets presented alone in the normal and V4 + TEO-affected quadrants. Likewise, our behavioral findings demonstrated that the combined lesion of V4 and TEO did not impair the monkey's ability to successfully discriminate visual stimuli, confirming previous results [9]. Taken together, these data suggest that the spared neuronal responses in TE may contribute to the residual discrimination abilities in this monkey.

The robust responsiveness of TE neurons after deprivation of input from both V4 and TEO is interesting in itself. Feedforward anatomical projections in the ventral pathway are largely organized in a serial fashion, from area V1 to V2, to V4, to TEO, and finally to TE [13,14]. While evidence exists for feedforward connections bypassing a single processing stage [18], direct projections bypassing two stages along this pathway (e.g., from V2 to TE) have yet to be demonstrated. Thus, a lesion including both V4 and TEO certainly deprives area TE of important inputs. Alternative indirect anatomical routes from posterior visual areas to TE may thus be more important than hitherto imagined, or might become recruited after the lesion. One such route might involve the pulvinar, which receives inputs from many visual areas, including V1 and V2, and which projects to TE [19,20]. Alternatively, or in addition, there is evidence for cortico-cortical routes to TE through dorsal stream areas [21], areas in the superior temporal sulcus [22,23], and through the parahippocampal region [24]. In addition, remaining islands of tissue in V4 and TEO might provide a source of residual input to TE. While this last explanation cannot be discounted, it is worth pointing out that impairments in difficult shape discrimination tasks, even in the absence of distracters, following lesions of these areas argues against a significant sparing [11].

The addition of distracters around the target stimulus had a greater effect on the absolute magnitude of TE responses in the quadrant affected by the V4 and TEO lesions than in the normal quadrant. This suggests that the V4 and TEO lesion eliminated part of the mechanism by which distracting stimuli are filtered out of the input to TE. In a separate study, we have found that moving the distracting stimuli far enough from the target such that they would all

no longer be contained within a V4 receptive field dimension eliminates the loss of filtering caused by a V4 lesion, as would be expected [25].

CONCLUSION

Our data demonstrate that a lesion in V4 and TEO does not eliminate visual responses downstream in area TE, and suggest that these responses could contribute to the good residual discrimination abilities found after this lesion. In addition, the increased effect of distracters on the responses of TE neurons to target stimuli following the lesions may contribute to the reduced ability to ignore distracters during difficult visual discriminations.

REFERENCES

1. Moran J and Desimone R. Selective attention gates visual processing in the extrastriate cortex. *Science* 1985; **229**:782–784.
2. Connor CE, Preddie DC, Gallant JL and Van Essen DC. Spatial attention effects in macaque area V4. *J Neurosci* 1997; **17**:3201–3214.
3. Luck SJ, Chelazzi L, Hillyard SA and Desimone R. Neural mechanisms of spatial selective attention in areas V1, V2, and V4 of macaque visual cortex. *J Neurophysiol* 1997; **77**:24–42.
4. Reynolds JH, Chelazzi L and Desimone R. Competitive mechanisms subserve attention in macaque areas V2 and V4. *J Neurosci* 1999; **19**:1736–1753.
5. Schiller PH and Lee K. The role of the primate extrastriate area V4 in vision. *Science* 1991; **251**:1251–1253.
6. Schiller PH. The effects of V4 and middle temporal (MT) area lesions on visual performance in the rhesus monkey. *Vis Neurosci* 1993; **10**:717–746.
7. Schiller PH. Effect of lesions in visual cortical area V4 on the recognition of transformed objects. *Nature* 1995; **376**:342–344.
8. Merigan WH. Basic visual capacities and shape discrimination after lesions of extrastriate area V4 in macaques. *Vis Neurosci* 1996; **13**:51–60.
9. De Weerd P, Peralta MR, III, Desimone R and Ungerleider LG. Loss of attentional stimulus selection after extrastriate cortical lesions in macaques. *Nature Neurosci* 1999; **2**:753–758.
10. Walsh V, Le Mare C, Blaimire A and Cowey A. Normal discrimination performance accompanied by priming deficits in monkeys with V4 or TEO lesions. *Neuroreport* 2000; **11**:1459–1462.
11. De Weerd P, Desimone R and Ungerleider LG. Generalized deficits in visual selective attention after V4 and TEO lesions in macaques. *Eur J Neurosci* 2003; **18**:1–21.
12. Gallant JL, Shoup RE and Mazer JA. A human extrastriate area functionally homologous to macaque V4. *Neuron* 2000; **27**:227–235.
13. Ungerleider LG and Mishkin M. Two cortical visual systems. In: Ingle DJ, Goodal MA and Mansfield RJW (eds). *Analysis of Visual Behavior*. Cambridge, MA: MIT Press; 1982, pp. 549–586.
14. Felleman DJ and Van Essen DC. Distributed hierarchical processing in the primate cerebral cortex. *Cerebr Cortex* 1991; **1**:1–47.
15. Gross CG, Rocha-Miranda CE and Bender DB. Visual properties of neurons in inferotemporal cortex of the Macaque. *J Neurophysiol* 1972; **35**:96–111.
16. Desimone R, Albright TD, Gross CG and Bruce C. Stimulus-selective properties of inferior temporal neurons in the macaque. *J Neurosci* 1984; **4**:2051–2062.
17. Tanaka K, Saito H, Fukada Y and Moriya M. Coding visual images of objects in the inferotemporal cortex of the macaque monkey. *J Neurophysiol* 1991; **66**:170–189.
18. Nakamura H, Gattass R, Desimone R and Ungerleider LG. The modular organization of projections from areas V1 and V2 to areas V4 and TEO in macaques. *J Neurosci* 1993; **13**:3681–3691.
19. Baleydier C and Morel A. Segregated thalamocortical pathways to inferior parietal and inferotemporal cortex in macaque monkey. *Vis Neurosci* 1992; **8**:391–405.
20. Webster MJ, Bachevalier J and Ungerleider LG. Subcortical connections of inferior temporal areas TE and TEO in macaque monkeys. *J Comp Neurol* 1993; **335**:73–91.
21. Webster MJ, Bachevalier J and Ungerleider LG. Connections of inferior temporal areas TEO and TE with parietal and frontal cortex in macaque monkeys. *Cerebr Cortex* 1994; **4**:470–483.
22. Boussaoud D, Ungerleider LG and Desimone R. Pathways for motion analysis: cortical connections of the medial superior temporal and fundus of the superior temporal visual areas in the macaque. *J Comp Neurol* 1990; **296**:462–495.
23. Saleem KS, Suzuki W, Tanaka K and Hashikawa T. Connections between anterior inferotemporal cortex and superior temporal sulcus regions in the macaque monkey. *J Neurosci* 2000; **20**:5083–5101.
24. Martin-Elkins CL and Horel JA. Cortical afferents to behaviorally defined regions of the inferior temporal and parahippocampal gyri as demonstrated by WGA-HRP. *J Comp Neurol* 1992; **321**:177–192.
25. Buffalo EA, Bertini G, Ungerleider LG and Desimone R. Impaired filtering of distracter stimuli by TE neurons following V4 and TEO lesions in macaques. *Cerebr Cortex* 2004: in press.

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