Visual feature selectivity in frontal eye fields induced by experience in mature macaques

Narcisse P. Bichot, Jeffrey D. Schall & Kirk G. Thompson

Vanderbilt Vision Research Center, Department of Psychology, Vanderbilt University, Nashville, Tennessee 37240, USA

When examining a complex image, the eye movements of expert observers differ from those of novices; experts have learned to ignore features that are visually salient but are not relevant to the interpretation of the image[1–3]. We have studied the neural basis of this form of perceptual-motor learning using monkeys that have learned to search for a visual target among distractors. Monkeys trained to search only for, say, a red stimulus among green distractors will ignore green stimuli even if they subsequently appear as targets in a complementary search array, that is, among red distractors. We recorded from neurons in the frontal eye field (FEF), a cortical area that responds to visual stimuli and controls purposive eye movements[4–6]. Normally, FEF neurons do not exhibit feature selectivity, but their activity evolves to signal the target for an incipient eye movement[7]. In monkeys trained exclusively on targets of one colour, however, FEF neurons show selectivity for stimuli of that colour. Because this selective response occurs so soon after presentation of the stimulus array, and is independent of location within the visual field, we propose that it reflects a form of experience-dependent plasticity that mediates the learning of arbitrary stimulus–response associations.

To investigate the effects of training experience on gaze behaviour and the underlying neural activity, a between-subjects experimental design was used. Control monkeys were trained to make saccades to the single item of one colour among an array of elements of a different colour, in two complementary search arrays (red target among green distractors, and green target among red distractors). Experimental monkeys were given exclusive experience with only one of the two complementary search arrays. Control monkeys shift their gaze according to visual salience (Fig. 1, left column), but experimental monkeys persistently direct gaze to stimuli possessing a specific colour (right column). Despite this difference, the saccade latencies of experimental monkeys were not different from those of control monkeys (experimental, mean 199 ms, s.e.m. 0.5 ms; control, mean 198 ms, s.e.m. 0.8 ms; $t_{9386} = 1.40$). Similar experiments using humans have demonstrated a significant increase in response times when the colours of the target and distractors reverse unpredictably across trials compared to when they remain constant[8]. No such difference was observed in our data, probably because we changed the target and distractor colours across, but not within, blocks of trials with the control monkeys.

The FEF, located in the rostral bank of the arcuate sulcus in the frontal cortex, receives topographic, convergent input from visual areas responsible for form and object processing, as well as from areas involved in motion and spatial vision[9]. The FEF also projects strongly onto the subcortical structures that control the generation of eye movements, and stimulation of FEF with low currents evokes saccades[6]. Therefore, FEF is uniquely positioned to play a central role in the generation of a command to shift gaze, based on the product of visual processing[4–6]. Different classes of neurons in the FEF responded to visual stimuli or discharge in association with eye movements[10,11]. We recorded from 80 neurons that responded to visual stimuli in 90 penetrations from the FEF in

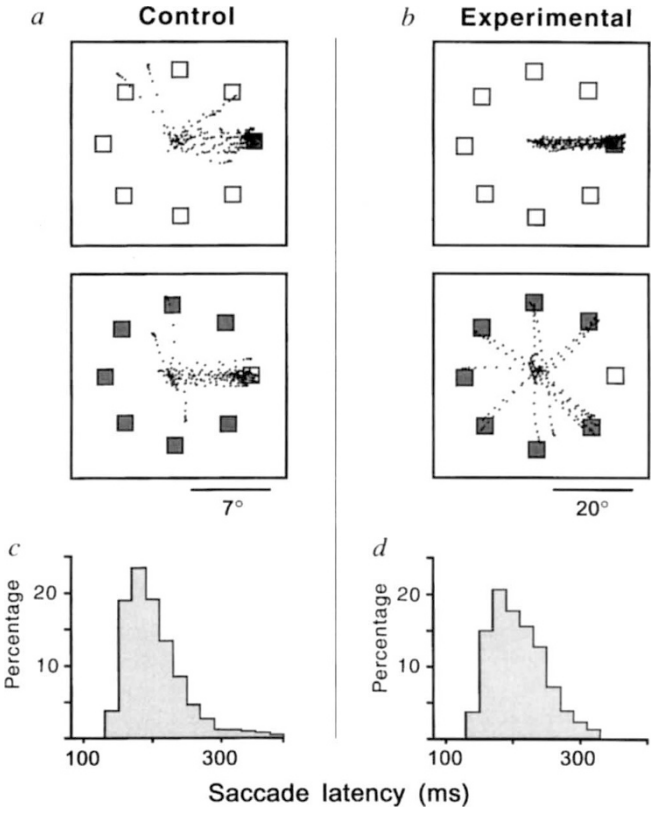

FIG. 1 Effects of experience on eye-movement responses to visual search arrays. Data were collected from 4 macaques, *Macaca mulatta*, of mass 4–10 kg. The behavioural and physiological methods have been described[7]. Each trial began when the monkey fixated a central white spot on a video monitor (60 Hz refresh rate). After an interval of fixation (400–500 ms) the target was presented either alone or with distractors. Within each block the target was presented at one of eight positions varying randomly in direction at each cell's optimal eccentricity. A trigger signal was given by a colour change of the fixation spot (simultaneous with stimulus presentation) to make a saccade to the target. If the monkey failed to direct its gaze properly at any time, the trial was aborted and no reinforcement was given. Targets and distractors were distinguished by colour (red versus green). Stimuli were presented on a grey background and were adjusted to be isoluminant. Saccades were detected using a previously described algorithm[7]. The key manipulation was that experimental monkeys were trained exclusively with one visual search array. One experimental monkey only experienced a green target among red distractors, and the other experimental monkey only experienced a red target among green distractors. The two monkeys were trained on each of the complementary search arrays to rule out possible stimulus confounds. *a*, Gaze behaviour of a control monkey trained with both complements of a search stimulus array. The target is shown at the right horizontal position. The first saccade was made to fixate the red target among green distractors (top) or the green target among red distractors (bottom) except for infrequent errors. *b*, Gaze behaviour of an experimental monkey. In response to the overtrained search array the monkey made saccades directly to the salient red target (top). When presented with the complementary search array of a green target among red distractors (bottom), the monkey shifted gaze to the distractors and not to the target. These trials were errors, and no reward was given. *c*, *d*, Distribution of visual search saccade latencies for all trials collected during recordings from all cells. The gaze behaviour of experimental monkeys in response to the unlearned stimulus array was probed with a few trials every week to insure the stability of the behavioural response bias. We did not expose the monkeys to the unlearned array for too many trials to prevent them from learning to shift gaze to the salient stimulus, thereby losing the behavioural response bias. Future studies will investigate how visual responsiveness in FEF changes as monkeys learn to generalize across search arrays.

the two experimental monkeys; 47 neurons had visually evoked activity and provided sufficient data for this report. These data were compared to corresponding unit activity in the control monkeys[7]. The activity of representative cells from each of the experimental monkeys is shown in Fig. 2. In striking contrast to our findings in the control monkeys, the initial visual response to the distractors of the search array was significantly less than the initial visual response to the target.

The ratios of 'initial visual response to target' to 'initial visual response to distractors' for all cells from the experimental monkeys were significantly greater than the comparable ratios for control monkeys (experimental response ratio, mean 1.70, s.e.m. 0.17, range 0.61–6.50; control response ratio, mean 1.17, s.e.m. 0.04, range 0.62–1.92; Mann–Whitney U test, $U = 631.0$, $P < 0.01$). Figure 3 plots the probability that the initial visual responses to the target were the same as the responses to distractors, as a function of visual response latency for the cells from control (open circles) and experimental (filled circles) monkeys. In control monkeys there was no systematic tendency for cells to respond preferentially to the target or the distractor. However, in each case of initial visual discrimination in experimental monkeys (in 21 of 47 neurons), the initial visual response to the target was greater than the response to distractors. The magnitude of response of the colour-selective cells evoked by the target was no different from the magnitude of response of the non-selective cells. Instead, the visual selectivity occurred because of an attenuated and/or delayed response to the distractor. The sample of colour-selective cells in the FEF had receptive fields representing all parts of the visual field from 4° to 20° eccentricity.

The visual latencies of the subset of cells from the experimental monkeys that discriminated the target from distractors in their initial response ranged from 50 to 129 ms, with a mean of 79 ms. The incidence of cells exhibiting an initial target-selective visual response was significantly higher in experimental monkeys in both early (<70 ms; Fisher exact test, $P = 0.01$) and late (>70 ms; Fisher exact test, $P = 0.02$) ranges of visual response latencies. The distribution of visual response latencies for all cells recorded in control monkeys was significantly earlier than the distribution for all cells recorded in experimental monkeys (control, mean 60 ms, s.e.m. 3.5; experimental, mean 71 ms, s.e.m. 3.0; Mann–Whitney U test, $U = 675.0$, $P < 0.01$).

The characteristic differences in gaze behaviour observed in the experimental and control monkeys indicate that different behavioural search strategies arose through experience with either constant or changing visual search arrays. By overtraining mon-

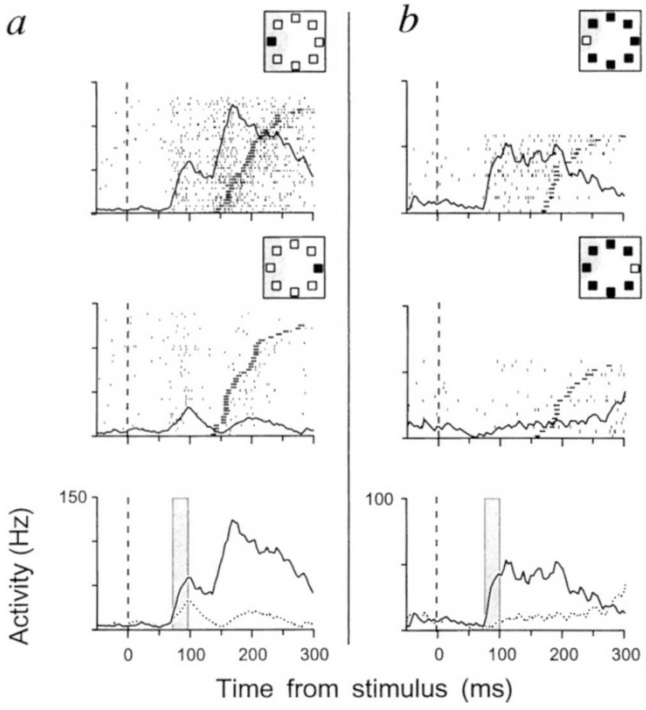

FIG. 2 Apparent colour-selective visual response of FEF neurons in experimental monkeys. Neural activity is represented by a raster plot; each vertical tick mark indicates the time of an action potential, the horizontal line in each raster indicates the time of saccade initiation, and rasters are ordered by saccade latency. Superimposed on the raster is the average spike density function; the ordinate scale represents the discharge rate. The rasters and spike density function are aligned on the time of stimulus presentation at time zero (vertical broken lines). Visual responses were identified by their consistent latency relative to the time of stimulus appearance. Stimulus configuration in relation to the cell's response field (shaded) is indicated. Responses of cells when the target was in their receptive field (top) were compared with responses to only distractors in their receptive field (middle). The average spike density functions from these two conditions are superimposed (bottom; solid line, target in receptive field; dotted line, only distractors in receptive field). We analysed all neurons that responded to the visual search stimulus array at eccentricities ranging from 4° to 20°. To determine whether the initial response of cells discriminated whether the target or a distractor was in the response field, we counted the spikes in the first 25 ms of visually evoked activation (bottom, shaded area). The resulting spike count values for all trials were submitted to an analysis of the relative variances using an F-test. Then, depending on the outcome, we applied a two-tailed t-test for equal or unequal variances to test for differences in the response to the target of the search array versus the distractors in the receptive field. This analysis depended on accurately determining the visual response latency of the cell. Application of a spike-train analysis that detects periods of significantly elevated activity in single trials to the visual responses of cells allowed an accurate estimation of the visual response latency[24]. Visual latency estimates were corrected for the raster scan time based on the location of the receptive field on the video monitor; average correction, 7.4 ms. For both of these neurons, the initial visual response was significantly greater when the target was in the response field than when only distractors were in the response field in the 25 ms after the beginning of the visual response (a, $t_{80} = 3.38$, $P < 0.01$; b, $t_{23} = 4.83$, $P < 0.01$).

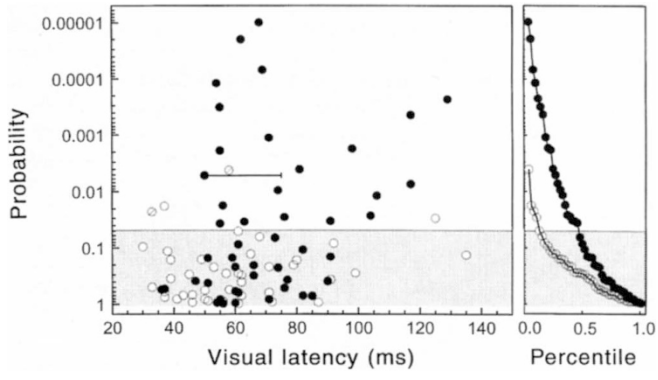

FIG. 3 Statistical analysis of the initial visual activation of neurons recorded in control (open circles) and experimental (filled circles) monkeys. The probability of the initial response to the target in the response field being the same as the initial response to the distractors in the response field is plotted as a function of the visual response latency (left). The shaded region indicates nonsignificant probability values greater than 0.05. Of the 43 neurons from control monkeys, 39 fell in the nonsignificant area, two responded preferentially to the target, and two responded preferentially to the distractors of the search array field (marked by diagonal lines). In contrast, 21 of 47 neurons recorded from the experimental monkeys exhibited significantly greater initial responses when the search array target fell in the response field, and none showed the opposite effect. The greater magnitude and incidence of the early visual discrimination observed in experimental as compared with control monkeys is highlighted by the plot of the cumulative distributions of the probabilities (right). The earliest response latency at which a cell from an experimental monkey exhibited a significant difference was 50 ms, representing an interval of analysis extending to 75 ms (indicated by the horizontal bar to the right of the point).

keys on one search array, we created a condition in which FEF cells express a visual stimulus selectivity they would not otherwise have[7,12,13]. Overtraining also led to an apparent increase in the distribution of visual response latencies of FEF neurons. Further work is needed to establish whether the latencies of individual neurons change, or whether different populations of neurons have been recorded in the control and experimental monkeys.

Our finding is probably related to the enhancement of the visual responses of neurons in visuomotor structures including FEF observed specifically when the stimulus in a neuron's receptive field is used as the target for a gaze shift[13,14]. However, unlike earlier studies that presented one or two stimuli in blocks of trials, in our experiment distractors were always present, and target location was much less predictable. Therefore, the early visual selectivity we observed in the experimental monkeys is unlikely to be due only to directed attention or motor planning specific for a particular visual field location.

Discrimination of a target from distractors based on visual salience or the subject's instructed preference has been observed in visual cortex[15–19]. This discrimination occurs typically 140–150 ms after stimulus presentation, a time which coincides with the time of visual target discrimination by FEF neurons measured in control monkeys[20]. The latency of the colour based discrimination observed in FEF of the experimental monkeys was markedly shorter than the attention-related modulations observed in extrastriate visual cortex. Indeed, the timecourse of the early visual discrimination in FEF coincides with or shortly follows the latency of activation of colour-selective cells in macaque primary visual cortex, having estimated mean values ranging from 45 ms (ref. 21) to 80 ms (ref. 22). If there is insufficient time for attentional modulation based on stimulus evaluation, it is possible that the attenuated response of FEF neurons to the distractors is mediated by a reduction in the synaptic efficacy of neurons representing the constant distractor feature. The present data do not show whether the hypothetical synaptic plasticity occurs in FEF or in visual areas that register the colour of the search stimuli.

If plasticity underlies the FEF visual selectivity observed here, then this finding contrasts with previous work, because it demonstrates a change in neural selectivity due to selective experience that was not localized in a topographic map. Previous reports of neural plasticity based on experience in adult primates have described expansions of representations within topographic maps that are associated with perceptual or motor skill acquisition[23]. The experience-dependent, early visual selectivity we observed in FEF was not due to a topographically limited pattern of sensory stimulation or motor output, but rather was contingent on a particular stimulus–response mapping. This finding may indicate another form of adaptation of the mature brain that is associated with the establishment of a habit, if not a skill. □

Received 30 January; accepted 8 May 1996.

1. Fisher, D. F., Monty, R. A. & Senders, J. W. *Eye Movements: Cognition and Visual Perception* (Erlbaum, Hillsdale, NJ, 1981).
2. Groner, R., McConkie, G. W. & Menz, C. *Eye Movements and Human Information Processing* (Elsevier, New York, 1985).
3. O'Regan, J. K. & Levy-Schoen, A. *Eye Movements: From Physiology to Cognition* (Elsevier, New York, 1987).
4. Goldberg, M. E. & Segraves, M. A. in *The Neurobiology of Saccadic Eye Movements* (eds Wurtz, R. H. & Goldberg, M. E.) 283–313 (Elsevier, New York, 1989).
5. Bruce, C. J. in *Signals and Sense, Local and Global Order in Perceptual Maps* (eds Edelman, G. M., Gall, W. E. & Cowan, W. M.) 261–314 (Wiley, New York, 1990).
6. Schall, J. D. in *The Neural Basis of Visual Function* (ed. Leventhal, A. G.) 388–442 (Macmillan, London, 1991).
7. Schall, J. D., Hanes, D. P., Thompson, K. G. & King, D. J. *J. Neurosci.* **15,** 6905–6918 (1995).
8. Bravo, M. J. & Nakayama, K. *Percept. Psychophys.* **51,** 465–472 (1992).
9. Schall, J. D., Morel, A., King, D. J. & Bullier, J. *J. Neurosci.* **15,** 4464–4487 (1995).
10. Bruce, C. J. & Goldberg, M. E. *J. Neurophysiol.* **53,** 603–635 (1985).
11. Schall, J. D. *J. Neurophysiol.* **66,** 559–579 (1991).
12. Mohler, C. W., Goldberg, M. E. & Wurtz, R. H. *Brain Res.* **61,** 385–389 (1973).
13. Goldberg, M. E. & Bushnell, M. C. *J. Neurophysiol.* **46,** 773–787 (1981).
14. Wurtz, R. H. & Mohler, C. W. *J. Neurophysiol.* **39,** 766–772 (1976).
15. Moran, J. & Desimone, R. *Science* **229,** 782–784 (1985).
16. Chelazzi, L., Miller, E. K., Duncan, J. & Desimone, R. *Nature* **363,** 345–347 (1993).
17. Motter, B. C. *J. Neurosci.* **14,** 2178–2189 (1994).
18. Lamme, V. A. F. *J. Neurosci.* **15,** 1605–1615 (1995).
19. Maunsell, J. H. R. *Science* **270,** 764–769 (1995).
20. Thompson, K. G., Hanes, D. P. & Schall, J. D. *Soc. Neurosci. Abstr.* **21,** 1270 (1995).
21. Maunsell, J. H. R. & Gibson, J. R. *J. Neurophysiol.* **68,** 1332–1344 (1992).
22. Nowak, L. G., Munk, M. H. J., Girard, P. & Bullier, J. *Vis. Neurosci.* **12,** 371–384 (1995).
23. Weinberger, N. M. *A. Rev. Neurosci.* **18,** 129–158 (1995).
24. Hanes, D. P., Thompson, K. G. & Schall, J. D. *Expl Brain Res.* **103,** 85–96 (1995).

ACKNOWLEDGEMENTS. Authorship is alphabetical. We thank D. Hanes for data, and R. Blake, F. Ebner, J. Kaas and D. Hanes for comments on the manuscript. This work was supported by the National Eye Institute and the McDonnell–Pew Program in Cognitive Neuroscience. J. Schall is a Kennedy Center investigator.

CORRESPONDENCE and requests for materials should be addressed to J.D.S. (e-mail: schalljd@ctrvax.vanderbilt.edu).

The neurobiology of sign language and its implications for the neural basis of language

Gregory Hickok*, Ursula Bellugi* & Edward S. Klima*†

* The Salk Institute for Biological Studies, 10010 North Torrey Pines Road, La Jolla, California 92037, USA
† The University of California, San Diego, California 92186, USA

THE left cerebral hemisphere is dominant for language, and many aspects of language use are more impaired by damage to the left than the right hemisphere. The basis for this asymmetry, however, is a matter of debate; the left hemisphere may be specialized for processing linguistic information[1–3] or for some more general function on which language depends, such as the processing of rapidly changing temporal information[4] or execution of complex motor patterns[5]. To investigate these possibilities, we examined the linguistic abilities of 23 sign-language users with unilateral brain lesions. Despite the fact that sign language relies on visuospatial rather than rapid temporal information, the same left-hemispheric dominance emerged. Correlation analyses of the production of sign language versus non-linguistic hand gestures suggest that these processes are largely independent. Our findings support the view that the left-hemisphere dominance for language is not reducible solely to more general sensory or motor processes.

Like spoken languages, sign languages used by the deaf are highly structured linguistic systems, with a rigid developmental course, including a critical period for acquisition[6]. There is no universal sign language, nor are they manual forms of surrounding spoken languages: American sign language (ASL) and British sign language, for example, are mutually incomprehensible. Signed languages have linguistic structure at phonological, morphological and syntactic levels. At the phonological level, signs are fractionated into sublexical elements, including recurring hand shapes, articulation locations, and limb/hand movements[7,8]. There are even systematic 'phonetic' differences between sign languages leading to an 'accent' when native users of one sign language learn another[3,9]. At the morphological level, ASL has developed grammatical markers that serve as inflectional and derivational morphemes[9]. At the syntactic level, ASL specifies relations between signs through, among other things, the manipulation of signs in space, where different spatial relations convey systematic differences in meaning[10–12] (Fig. 1).

Thus, although sign language has linguistic structuring at the same levels as spoken language, the surface form is radically different, with spatial contrasts prominent at every level. The time course between the shortest linguistically relevant transitions during a sign, such as a change in hand shape, is approximately 200 ms (ref. 13), significantly longer than the time course of the shortest transitions within a spoken word (~40 ms) that have been