condition, subjects would have trouble focusing their attention in the right place. Subjects read a brief sample of prose in half-space type shortly before the experiment to become accustomed to words printed in this style. A pilot experiment with normally spaced type and no reading sample produced virtually identical results.

6. Details of a very similar procedure and a replica of the type of mask used are given in (*3*).
7. W. M. Kincaid, *Biometrics* **19**, 224 (1962).
8. The degree of facilitation produced by position cueing with unrelated letter stimuli (6.5 percent) may provide a rough estimate of the strength of the factors working against the word-letter difference in this experiment. The factors mentioned may explain why the word-letter difference obtained is smaller than that reported under similar visual conditions comparing a word to a single letter alone (*3*).
9. I. Biederman [*Science* **177**, 77 (1972)] found that although items in "real world scenes" (for instance, objects arrayed along a street) are perceived better in their normal arrangement than when scrambled, a particular item is perceived still more accurately when subjects are told where to look for it. Biederman's evidence may mean that the phenomenon reported here does not hold when stimuli are related to one another, but not so strongly as to form a single coherent whole. Alternatively, our results may not be obtainable with stimuli as large as Biederman's (3.5° by 5° of visual angle).
10. Supported by NSF predoctoral fellowships to J.C.J. and J.L.M. and by a grant from the Spencer Foundation. We thank L. Paris and E. Moynihan for their assistance and H. Feldman, L. Johnston, J. Jonides, J. Nachmias, and P. Rozin for their helpful comments.

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Operant Conditioning of Single-Unit Response Patterns in Visual Cortex

Abstract. *Unit responses to photic stimuli were studied in cat visual cortex. After the baseline response pattern of a cell was determined, conditioning trials were given during which reinforcement was contingent upon increased firing during a selected segment of the poststimulus interval. Density of reinforcement increased substantially in about half the cells studied; significant increases in firing occurred within, but not outside, the criterion segment.*

One promising approach to studying neural mechanisms of conditioning and learning treats neural occurrences as conditionable responses, rather than simply as neural correlates of behavioral conditioning. Thus, classical conditioning of both electroencephalographic rhythms and evoked patterns of unit activity has been demonstrated, and a variety of neural events—including theta waves, spontaneous discharge rates of single units, and gross visual evoked potentials—have been brought under operant or reinforcement control (*1*).

To our knowledge, the present report is the first to show that the operant paradigm can be applied also to modify the temporal pattern of activity evoked in a single unit by a sensory stimulus. We recorded the response patterns of cortical neurons to a visual stimulus in temporarily immobilized cats, and then attempted to produce specified changes in these patterns by using electrical stimulation of lateral hypothalamus as a reinforcer.

Adult cats were implanted under surgical anesthesia with bilateral tripolar stimulating electrodes aimed at the lateral hypothalamus. A U-shaped aluminum frame with slotted sides was also cemented to the skull so that the cat could be returned later to the stereotaxic instrument and held firmly in place without pressure and with a clear visual field. After recovery, each cat was tested in a standard operant chamber for self-stimulation on each of the hypothalamic probes, and preferred points and the optimal current for reinforcing intracranial stimulation (ICS) were determined. To maximize the effectiveness of ICS as a reinforcer in the subsequent recording sessions, a relatively stringent behavioral requirement was imposed: Of a large number of implanted subjects, 13 that made more than 200 bar presses in an 8-minute test were used in the remainder of the experiment. Cats that were used repeatedly in two or more recording sessions received additional tests for behavioral self-stimulation interspersed with the recording sessions.

For recording, subjects were placed in the stereotaxic instrument on a circulating warm water coil and prepared under ether anesthesia. Pupils were dilated with Isopto atropine (1 percent), and nictitating membranes were retracted by using ophthalmic Neo-Synephrine hydrochloride (10 percent). All wound margins were infiltrated with a long-lasting local anesthetic (Zyljectin), and proparacaine hydrochloride (Ophthetic) (0.5 percent) was applied topically on the corneal surfaces. Ether was then discontinued, and the subject was immobilized with intravenous gallamine triethiodide (Flaxedil) (20 mg/ml) and artificially respired. Each eye was focused on a tangent screen by appropriate corneal contact lenses. The optic disk and area centralis were projected onto the tangent screen and mapped separately for each eye. During the remainder of the session, Flaxedil was administered (about 1 ml/hr), and heart rate and rectal temperature were monitored and kept at about 200 beats per minute and 38°C. After ether was discontinued, at least 3 hours elapsed before recording began.

Extracellular unit action potentials were recorded from the visual cortex with tungsten microelectrodes and sent to an amplitude discriminator that pulsed a computer of average transients (Mnemotron CAT 400B); the computer generated a 1- or 2-second peristimulus time histogram (PSTH) of the cell's response to a stimulus. Visual stimuli were back-projected onto the translucent gray tangent screen 50 cm from the subject. The eye ipsilateral to the cell being studied was covered, and stimuli were presented to the contralateral eye. For many cells, a 15° spot centered on the area centralis was effective in producing a clear, patterned response; other cells were activated by using smaller spots or slits of various widths centered on the cell's receptive field.

During recording from a cell, trials were generated every 5 seconds by pulses that synchronized the occurrence of the computer sweep and a 25-msec presentation of the visual stimulus 200 msec after sweep onset. For each cell, trials without reinforcement (baseline trials) were first given; PSTH's showing the baseline response pattern were made and the number of spikes during a selected time segment (the criterion period) was recorded and printed for each trial. A criterion spike count that was exceeded on about one-fourth of the trials was selected. Then conditioning trials were given during which the reinforcement contingency was in effect: On each trial, a comparator circuit counted the number of spikes during the criterion period; if the criterion had been exceeded, a 500-msec train of ICS was delivered starting 300 msec after the end of the criterion period. The criterion period began 300 msec after presentation of the visual stimulus and lasted 500 msec (other values were occasionally chosen).

Baseline or conditioning PSTH's were made for 75 cortical cells. Some cells were studied for an insufficient time to complete conditioning trials,

and others served as control cells to test the stability of repeated baseline PSTH's or to test the effects of reinforcement delivered at random. The present sample consists of 40 cells that either showed conditioned changes in firing pattern as described below, or were studied for 50 to 200 baseline trials followed by 100 to 500 conditioning trials during which such changes were not observed. A cell's response was arbitrarily designated as conditioned if the frequency with which the reinforcement criterion was met (the hit rate) was greater by at least 30 percent during the final 50 conditioning trials than during the final 50 baseline trials. Of the 21 cells classified as conditioned, 20 met this criterion and one showed a distinct pattern change but was lost during the first block of 100 conditioning trials.

The conditioning procedure produced significant changes in firing within, but not outside, the criterion period. For the entire sample of cells, the average change in firing rate from the final baseline PSTH to the final conditioning PSTH was +2.06 spikes per second in the criterion period ($t = 2.35$, $P < .05$) and +0.54 spike per second over the remainder of the PSTH ($t = 0.83$, $P > .40$). The increased hit rates exhibited by conditioned cells were due, on the average, to a significant increase in firing during the criterion segment of the PSTH rather than to overall changes in spontaneous rate or even in responsiveness to the stimulus. The average rate change produced in the criterion period by the reinforcement contingency, minus the corresponding change outside the cri-

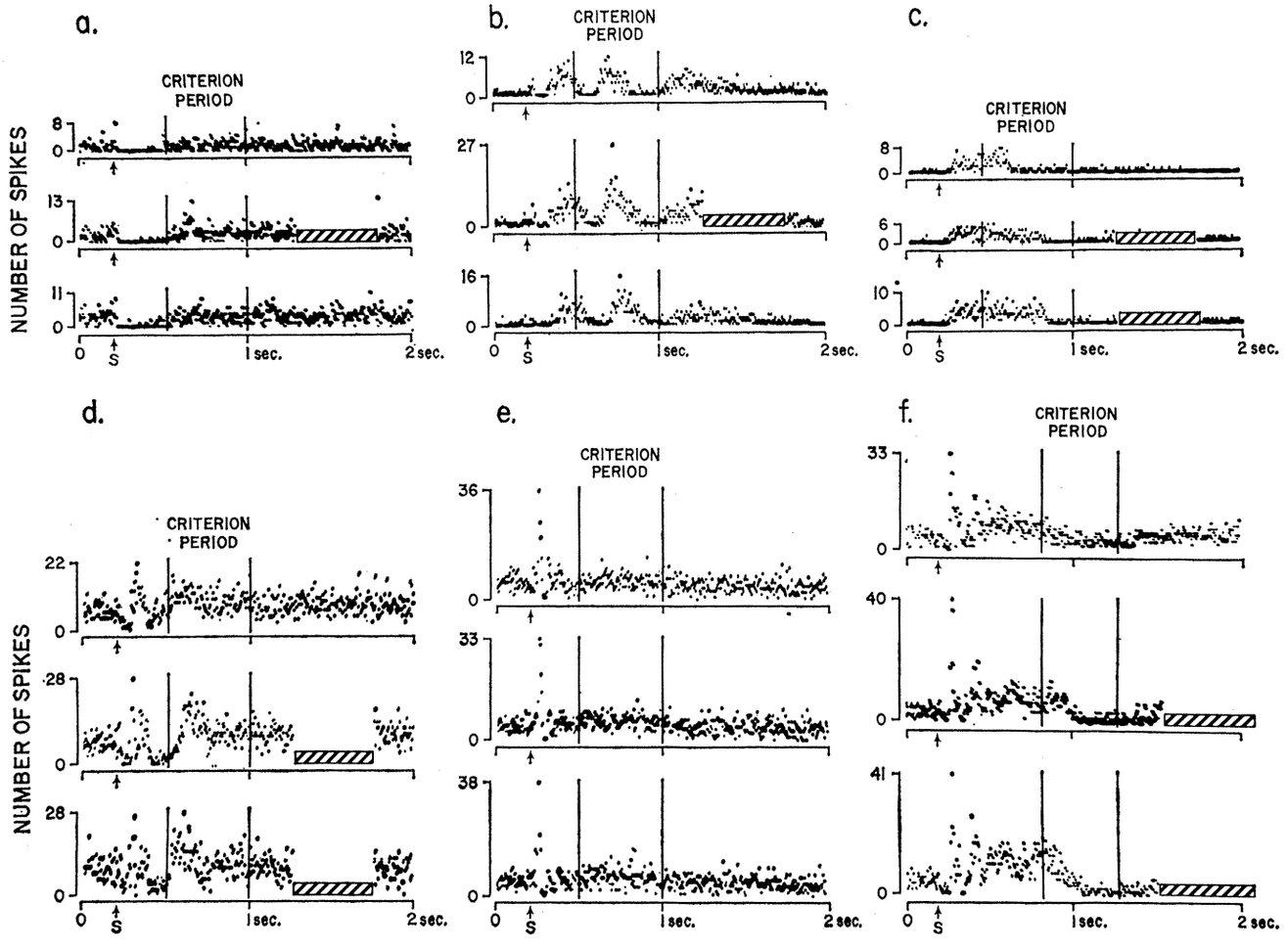

Fig. 1. Effects of a reinforcement contingency on temporal patterns of response of visual cortical cells. Each lettered column shows PSTH's from one cell, taken sequentially from top to bottom. Histograms compiled during conditioning trials have a 500-msec artifact (the diagonally hatched bar at right) corresponding to the delivery of ICS; this artifact is absent from baseline and extinction PSTH's. Sweep duration, vertical calibration, and onset of the 25-msec visual stimulus are the same for all PSTH's. The criterion period, during which increased firing led to reinforcement, extended from 500 to 1000 msec after sweep onset [except in (f)]. (a) The upper PSTH shows final 25 baseline trials; the middle PSTH, final 25 of 125 conditioning trials; and the lower PSTH, final 25 of 250 extinction trials. (b) The upper PSTH shows 100 baseline trials; the middle PSTH, 100 conditioning trials; and the lower PSTH, 100 extinction trials. (c) A baseline excitatory response (upper PSTH, 50 sweeps) showed increased duration early in conditioning (middle PSTH, conditioning trials 101 to 150); a pronounced effect was seen by the end of the conditioning (lower PSTH, conditioning trials 401 to 450). (d) Upper PSTH shows baseline response pattern (100 sweeps); the secondary excitatory peak became sharper during the first block of 100 conditioning trials (middle PSTH) and became larger than the early excitatory peak during the next 100 conditioning trials (lower PSTH). (e) Successive blocks of 50 baseline trials each, taken from a cell encountered in the same columnar penetration as the cell in (b), show the stability of response patterns in the absence of any reinforcement. (f) Upper PSTH shows baseline response pattern (50 sweeps); when a clear conditioned response appeared (middle PSTH, conditioning trials 151 to 200), the cat was given an intravenous injection to block any possible residual eye movements, after which the conditioned response persisted (lower PSTH, conditioning trials 201 to 250). For this cell only, the criterion period extended from 900 to 1300 msec after sweep onset.

terion period, was +3.47 spikes per second for cells in the conditioned category ($t = 2.90$, $P < .01$), and −0.90 spike per second for cells in the nonconditioned category ($t = 1.48$, $P > .10$). The firing changes that brought about increased hit rates were not altogether specific to the criterion period, however; most of the conditioned cells showed some increase in firing throughout the poststimulus period. Figure 1 shows examples of changes in cellular firing patterns brought about by the reinforcement contingency, along with a representative control cell for which reinforcement was omitted. To control for the possibility that the reinforcing brain stimulation caused a tonic increase in responsiveness to the visual stimulus which happened to be greatest during the arbitrarily selected criterion period, 12 cells were studied during baseline trials followed by 100 to 400 pseudoconditioning trials in which reinforcement was delivered randomly (33 percent of trials for seven cells and 50 percent for five cells.) Firing rates for these cells were not changed from baseline to pseudoconditioning trials, either in the criterion period (average change, −0.83 spike per second; $t = 0.39$, $P > .70$) or outside it (average change, +0.55 spike per second; $t = 1.00$, $P > .30$).

Several factors appeared to be unimportant in producing conditioned changes in firing. For instance, the levels of ICS current used during recording sessions were determined individually for each subject in behavioral tests, as described above, and ranged from 75 to 330 μa; individual rates of bar pressing in the behavioral tests varied from 25 to 94 responses per minute. Conditioned cells were encountered in subjects receiving both high and low levels of current and in subjects that had exhibited both high and low response rates during the behavioral tests. Also, ICS was delivered to the hemisphere contralateral to the recording site in some subjects and to the ipsilateral hemisphere in others; this variable was unrelated to the appearance of conditioned changes. The nature of the visual stimulus seemed not to matter: Conditioned cells included some stimulated with the large standard spot of light and others for which the stimulus corresponded to the cell's receptive field. Conditioned cells were located equally often in the posterolateral and suprasylvian gyri.

Subjects were immobilized with Flaxedil rather than curare because of the latter drug's undesirable cardiovascular side effects. It was therefore necessary to control for the possibility that the observed conditioning effects were trivially mediated by residual eye movements. Figure 1f shows PSTH's from a cell in which conditioned changes obtained after Flaxedil treatment persisted after intravenous injection of a mixture of Flaxedil (5 mg/kg) and *d*-tubocurarine chloride (0.5 mg/kg), which blocks all but the smallest (6 deg/hr) eye movements (*2*). This procedure, repeated with the same result, permitted us to rule out eye movements as a mechanism for generating the required response pattern.

Two factors might be significant in the observed conditioning. First, many temporal patterns of response occur in visual cortical neurons (*3*). In this experiment, conditioned changes were generally not observed in cells with brief, short-latency, single-peak response patterns; the activity of such cells returned to a spontaneous level by the beginning of the criterion period. The cells that showed conditioned changes had lengthy or multiple peaks or troughs of evoked activity, usually extending several hundred milliseconds into the poststimulus period. Second, the likelihood that conditioned changes would appear in a cell was related to the number of reinforced trials the animal had received (prior reinforcements), up to but not including trials for that cell. Thus the conditioned category included 15 of 34 cells for which there had been up to 300 prior reinforcements and all of six cells with 300 to 600 prior reinforcements ($P = .028$, Fisher's exact test, two-tailed).

For 12 of the 21 conditioned cells, reinforcement trials were followed by 50 to 500 extinction trials in which reinforcement was omitted. Of these, six showed a decrease in hit rate during extinction but only two returned to the baseline hit rate. The failure to find clear extinction effects in all cases may be analogous to a partial reinforcement effect in behavioral conditioning, since the average hit rate of conditioned cells during the final 50 trials was 56 percent, and only three cells achieved hit rates greater than 75 percent. Furthermore, as an aid in detecting the presence of a cell, the visual stimulus was usually flashed repeatedly as the microelectrode was lowered through the cortical layers. The subject had no basis for discriminating these probe flashes from baseline or conditioning trials except for the occurrence of ICS; reinforcement was quite intermittent from the subject's point of view.

The conditioning effects we observed, and their relation to the subject's previous experience as reflected in prior reinforcements, appear to support the interpretation that the subject learned to increase the probability of the required response pattern in the unit under study (and probably in other units as well). However, the cells studied here are not necessarily involved in normal learning in which behavior is changed.

The general significance of these results is twofold. First, the data provide a cellular basis for operant conditioning of gross visual evoked potentials (*4*) and, because of the use of an immobilized subject, help to rule out alternative explanations based on receptor orientation, motor feedback, and so forth. Second, the technique of simultaneously isolating the critical neural events in location and time offers promise for an analysis of the neural circuitry involved. For instance, spontaneous bursts of activity in neurons in monkey motor cortex have been operantly conditioned (*5*); the present paradigm, with altered temporal parameters, would readily lend itself to the study of units in various areas of cat cortex, both motor and association. Such an analysis may enhance our understanding of the neural events underlying instrumental conditioning.

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