The initial CEP's conformed in all respects to the criteria published by others (1). As controls, similar repetitive CEP recordings were made without vibration. There was a gradual decrease in amplitude but never such marked suppression of the cortical response in these control studies.

Melzack and Wall (2) described a gating theory of pain perception. Some experience with stimulation of sensory nerves or nerve roots to treat pain has been reported (3). Dorsal spinal column stimulators have been implanted in patients with chronic pain, with good success (4). Our observations indicate that pain perception may also be altered for short periods of time by cutaneous stimulation. Although stimulating electrodes were applied carefully to ensure that the electrical current entered the limb rather than spread between the electrodes over the surface of the skin, the observations of increased pain tolerance in limbs other than those stimulated by the vibratory pulse are stronger evidence that the phenomena described here

cannot be explained simply by postulating local impedance phenomena. The changes in CEP subsequent to the vibratory stimuli, when taken with the above observation, suggest a central correlate. Cortical and subcortical structures need not be the only sites where this occurs. Further studies such as those reported here may provide more information on the mechanism of acupuncture (5).

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Kitten Visual Cortex: Short-Term, Stimulus-Induced Changes in Connectivity

Abstract. *Single neurons in the kitten visual cortex can be induced to increase their responsiveness to a repeated stimulus applied while the neurons are under observation. These short-term changes are in the same direction as the permanent modifications produced in whole populations of neurons following environmental manipulations during the "critical period" of cortical development, but are less pronounced and probably transient.*

If the visual experience of young cats is modified substantially, the population of neurons in the primary visual cortex is found, upon subsequent examination, to be abnormal. The abnormalities can be broadly described as a change of the selective responsiveness of the neurons to favor the patterns of experience they have received, and to produce these effects the modified experience must occur in the "critical period" (about 3 weeks to 3 months in cats) (1). The types of modification that have so far been tested, and the abnormalities produced, are as follows: Monocular lid suture (2) results in a decreased number of neurons connected to the lid-sutured eye. Artificial strabismus, or alternating occlusion of the two eyes so that they are not stimulated concurrently (3), leads to a decreased number of neurons connecting to both eyes. Exposure to either horizontal or vertical stripes and

deprivation of other visual experience (4) produces a preponderance of units selective for the orientation seen and an absence of units tuned to orthogonal orientations. Vertical deviation of one axis by interposing a prism (5) results in cortical receptive fields that are displaced up or down, so that the receptive fields of the two eyes superimpose with prism in place, not when it is removed.

These remarkable changes in the synaptic organization of the cortical cells appear to be permanent, but have so far only been studied some time after the experience that caused them. In this report we present results of testing single neurons in the kitten visual cortex for changes in their properties in response to conditioning stimulation applied while the neurons are under observation.

Single neurons were studied by extracellular recording with tungsten-in-

glass microelectrodes in the striate cortex of kittens between the ages of 18 and 35 days, a span chosen to coincide with the beginning and peak of the critical period. Anesthesia was initiated with Fluothane and maintained by forced ventilation with a mixture containing 80 percent nitrous oxide 18 percent oxygen, and 2 percent carbon dioxide. Eye movements were controlled with a continuous intravenous infusion of a mixture of Flaxedil and d-tubocurarine (6).

Stimuli of the desired configuration were cut from cards and moved in the object plane of an overhead projector by an arm attached to an X-Y recorder. Initial exploration of receptive field and stimulus positioning were performed by hand, by means of a control stick regulating two potentiometers. Once a given stimulus had been positioned accurately over the receptive field center, conditioning and testing runs were carried out by computer with a program designed to count spikes as it moved the stimulus over the receptive field center. Sweep velocity was set at a value judged to be optimal for the cell. Sweep amplitude was also adjusted to ensure that the whole field would be completely traversed in any direction. Counts were taken for a part of the sweep chosen to collect most of the response impulses, and also for control periods preceding each sweep. Ocular conditioning consisted in repeated presentation of a stimulus (generally a moving line) to one eye and not the other. Ocular testing consisted in presentation of sweeps or blocks of sweeps to the two eyes in alternation.

Cells in the cortex of normal adult cats (7) and of kittens about 3 weeks of age (8) range from those excited exclusively by the contralateral eye to those excited exclusively by the ipsilateral eye, the majority being excitable to a different extent by both. Some intermediate cells in the kitten cortex can be made relatively more susceptible to the influence of a chosen eye by several minutes of stimulation through that eye.

Figure 1 shows such an experiment. Initially the cell was dominated by the contralateral (right) eye, and gave a mean discharge of about 60 impulses each time the optimally oriented line stimulus passed across the receptive field for that eye. By contrast, stimulation of the ipsilateral eye gave less than a tenth of the response for the dominant eye, even when a long interval separated these tests and the preceding period of contralateral stimulation.

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When the ipsilateral eye was tested immediately after contralateral stimulation, no response was elicited for the first few trials. Repeated presentation of the stimulus to the nondominant eye led to a gradual increase in discharges until, after about 5 minutes, response had reached a level hitherto obtainable only from the contralateral eye. Testing of the contralateral eye at this stage gave only a weak response, revealing a reversal of eye preference. The changed dominance persisted for at least 30 minutes in spite of irregular stimulation of both eyes, but we do not have any evidence that it persists longer than about 1 hour.

Changes in which the cell came to favor the conditioned eye occurred in only 4 of the 60 units studied in five kittens. Our impression, however, is that most kitten binocular cells (47 of 60 studied) may be made to display weak and relatively impermanent shifts of ocular dominance such that the effectiveness of the eye opposite the stimulated eye will be reduced for a few seconds after conditioning.

We have no systematic observations of the age dependence of these effects. The youngest kitten of this study, 18 days of age, is noteworthy since none of ten cells which were intensively studied showed any change in its initial eye preference. Similarly, the cells of normal adult cats under the same experimental conditions have stable ocular dominance patterns (9).

We have attempted to change the orientational or disparity selectivity of cells by tests similar to those described above for ocular dominance. So far the results have suggested that the relative response to two orientations or disparities can be changed to favor that of the conditioning trial, but the results are not fully convincing, possibly for the following reason: A long sequence of trials is necessary to determine the optimal orientation or disparity, and this necessarily gives the cell visual experience that dilutes or perturbs that of the conditioning trial, and delays detection of the effects of conditioning.

The change in eye dominance with repetition of a stimulus is clearly different from the ordinary habituation, fatigue, or adaptation of excitable systems, since it involves an increase, not a decrease, in response to a frequently repeated stimulus. Furthermore, the changes we find are in the same direction as in experiments in which animals were studied some time after the conditioning stimulation (1, 4, 5, 10). But our changes are quite small; they are

not as dramatic as those described, and do not affect as many cells, nor do we have evidence that they extend beyond an hour.

There are many possible explanations for the weakness of effects we have obtained as compared to those
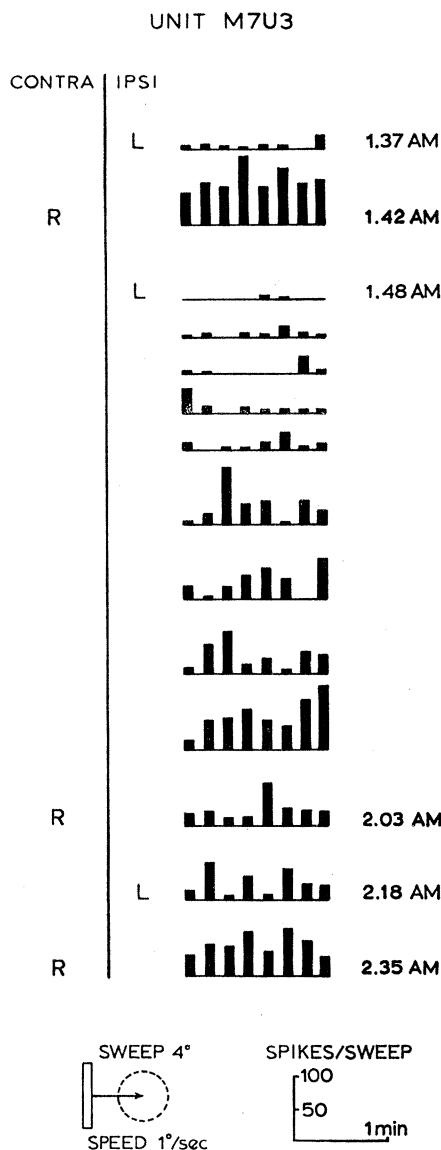
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Fig. 1. Shift in ocular dominance of kitten visual neuron caused by monocular conditioning. The neuron studied was from the left striate cortex of a kitten 4 weeks of age with no visual experience before the initiation of the experiment. The height of each bar represents the strength of the cell response to one sweep of the stimulus line. Observation times are at the right. At first the left (L) eye (line 1) was much less effective than the right (R) eye (line 2); but its effectiveness increased markedly during 15 minutes of continuous conditioning (lines 3 to 11); moreover, immediately following this period, the effectiveness of the right eye was reduced (line 12); the ocular dominance had, at this time, actually been reversed. The reversal was transient, and further testing (lines 13 and 14) revealed an incomplete drift back to the original pattern of dominance; contra, contralateral; ipsi, ipsilateral.

observed in experiments in which the cat is given selective experience during the critical period and studied at some later date. Perhaps in order for strong effects to occur the cat must be conscious or mobile (or both) at the time of exposure, as in the long-term experiments. Our cats were maintained on nitrous oxide and a relaxant. The length of time occupied by conditioning may also be important; our conditioning runs have, however, exceeded the single hour which Blakemore and Mitchell (10) suggest is long enough for producing a marked cortical bias in favor of vertical lines. The amount of stimulation provided to each individual unit is not the crucial factor; by finding and repeatedly presenting the favored stimulus of a cell we almost certainly excited it more during an hour of conditioning than it would have been excited during the few days of waking and active vision which Hubel and Wiesel (1) have shown to produce distinct effects. However, it is possible that movement of the whole visual field, which drives a huge number of cells suboptimally, is the stimulus of choice for conditioning of ocular dominance. A final speculation is that a period of "consolidation" may be required before experience produces large changes in the pattern of synaptic excitability. If so, the changes we describe here might be analogous to those underlying short-term, as opposed to long-term, memory (11).

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11. More recent experiments have been designed to increase the ratio of conditioning time to testing time. The results so far are striking and more in line with the findings of others (1, 4, 10). Large numbers of cells are affected in a relatively permanent way, but not until some hours after cessation of conditioning stimulation.
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