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Pain Perception: Modification of Threshold of Intolerance and Cortical Potentials by Cutaneous Stimulation

Abstract. *Cutaneous electrical stimulation temporarily raises the threshold of intolerance for pain elicited by electric shock. Similar stimulation suppresses the somatosensory cortical evoked potential.*

Threshold of intolerance for painful electrical stimuli was determined for three adult male subjects. The subjects in all cases faced away from the experimenter and the stimulation apparatus. In addition, their eyes were closed. Each subject was instructed to indicate when the limits of his pain tolerance had been exceeded by saying "stop." The pain stimuli were applied by silver electrodes 1 cm in diameter separated by a fixed distance of 3 cm. These electrodes were applied with pressure to the skin surface after cleansing and the application of standard electroencephalogram (EEG) electrode paste. Square-wave stimuli of constant duration were delivered at 1 sec^{-1} frequency to the skin of the dorsal surfaces of both great toes and thumbs, over the lateral malleolus of both ankles, and over the ulnar and radial borders of both wrists. Voltage was increased from 100 volts in 25-volt steps every 2 seconds to the point that the subject described it as intolerable. Subjects were given no cues other than the cutaneous shocks. Each subject was studied many times over several days so that the threshold for each area was determined a minimum of five times. The maximum tolerable voltage for a square-wave pulse of 0.2-msec duration was remarkably constant for all areas studied and among the three subjects (300 ± 25 volts).

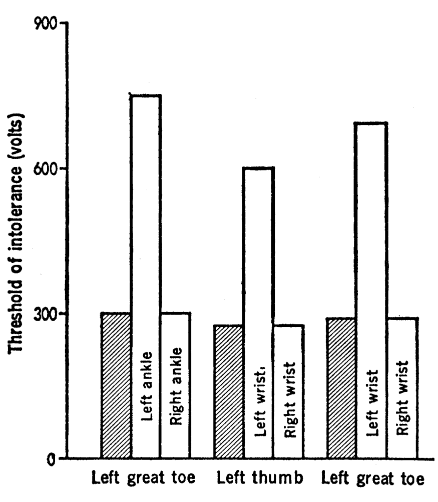

Fig. 1. Change in voltage tolerated after vibratory stimuli, subject J.B. Pain stimuli to areas labeled at bottom were given without previous vibratory stimuli (shaded bars) or immediately after vibratory stimuli to areas indicated in open bars. Four other series of determinations gave values within 25 volts of those diagrammed. Each cutaneous area was also studied five times in two other subjects, with similar results.

Vibratory electrical stimuli (50 sec^{-1}, 25 volts, 0.1-msec duration) were then delivered for 60 seconds to various portions of the extremities by electrodes constructed and applied in the same way as those used for the painful stimulation. After approximately 15 seconds, tingling sensations were reported by each subject in the extremity being stimulated. This tingling outlasted the stimulation by variable amounts of time. Pain thresholds were again determined immediately after the vibratory stimuli. In all observations, the vibratory points were at least 5 cm from the pain stimulation points, and usually the two points chosen were in cutaneous areas supplied by different peripheral nerves. A marked reproducible increase in maximum tolerance to the electrical impulse was noted after the vibration. This effect lasted for 20 minutes in our subjects, after which the original intolerance threshold values returned. Following the vibratory stimulus, the threshold for pain intolerance was often elevated in extremities other than the one receiving vibration. While this effect was primarily limited to ipsilateral limbs (Fig. 1), increased tolerance to the painful stimulus in contralateral limbs was observed several times. There was no evidence of tissue damage from the brief electrical stimulation used, despite high voltages.

Cortical evoked potentials (CEP) were obtained by averaging bipolar EEG recordings made with contralateral central region versus vertex electrodes while 100 nonpainful stimuli were delivered to the dorsal thumb (75 volts, 0.1-msec duration, 0.5 sec^{-1}) (Fig. 2). Following application of the vibratory stimulus described above, marked suppression of the CEP was observed. After the vibration, CEP's were recorded every 5 minutes until the original evoked potential configuration returned. Waves V and VI gradually reappeared, followed by a gradual increase in their voltage and then by return of the initial wave after 15 minutes. Configuration and latency of the CEP waves were identical to the initial recordings 20 minutes after the vibratory stimulus.

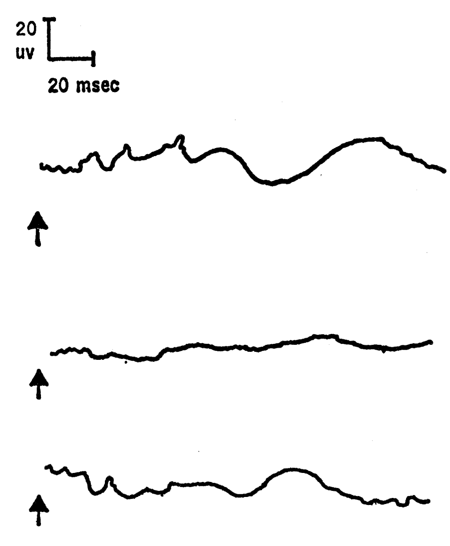

Fig. 2. Averaged cortical potentials evoked by cutaneous stimuli, subject J.B. Upper record was obtained prior to vibration (the irregular protuberance in the third major negative deflection represents artifactual reduplication of a point "dropped" by the averager). The middle record was obtained immediately after vibration; and the lower record, 15 minutes later. By 20 minutes after vibration, the CEP was indistinguishable from that in the upper trace. Arrows indicate stimulus marker. (Redrawn from photographic recordings.)

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.