electrical inhibition of pain: *experimental evaluation**

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RECENT neurophysiologic studies have raised the possibility of electrical inhibition of pain. Electronarcosis has been widely investigated[1-12] but no previous attempts are known of application of inhibiting currents to the spinal cord. Wall[13] demonstrated that activity in large peripheral sensory nerve fibers carrying nonpainful impulses inhibits in the spinal cord subsequent activity from the smallest fibers considered essential to pain conduction. Melzack and Wall[14] suggested using this knowledge to suppress pain. Mechanical surface activation of the nonpainful large fibers, such as rubbing or vibration, however, is not practical for prolonged use. Furthermore, it is probable that such stimuli must be applied to a wide area to block pain effectively from even a small focus.

Unfortunately, most "intractable" pain arises from diffusely involved structures. Thus it seems reasonable to concentrate on stimulation of the dorsal columns, where large fibers are compactly arranged, or of the anterolateral spinal cord where small fibers predominate.

Using the tegmental and medullary recording sites first described by Collins and Randt[15,16] (fig. 1) one finds a prolonged after-discharge (PSAD) upon electrical tetanic stimulation of a peripheral nerve above delta threshold. This response lasts from 500 msec. to many seconds. It has previously been demonstrated that most of this after-discharge is elicited by stimulation of C fibers, although a small early component comes from delta.[15-17]

When the whole nerve stimulus response is compared with isolated C stimulus response, however, the isolated C response is found to be of greater amplitude than the response to whole nerve stimulation.[17] Electrical stimulation of skin through two subcutaneous needles at current intensity sufficient to elicit pain in man (greater than 40 volts) also elicits prolonged small-fiber after-discharge in cats. Similarly, PSAD can be evoked by pinching a paw with a hemostat, by heat sufficient to produce tissue damage, and by subcutaneous injection of noxious substances. Nonpainful mechanical stimuli such as hair movement, deep rubbing

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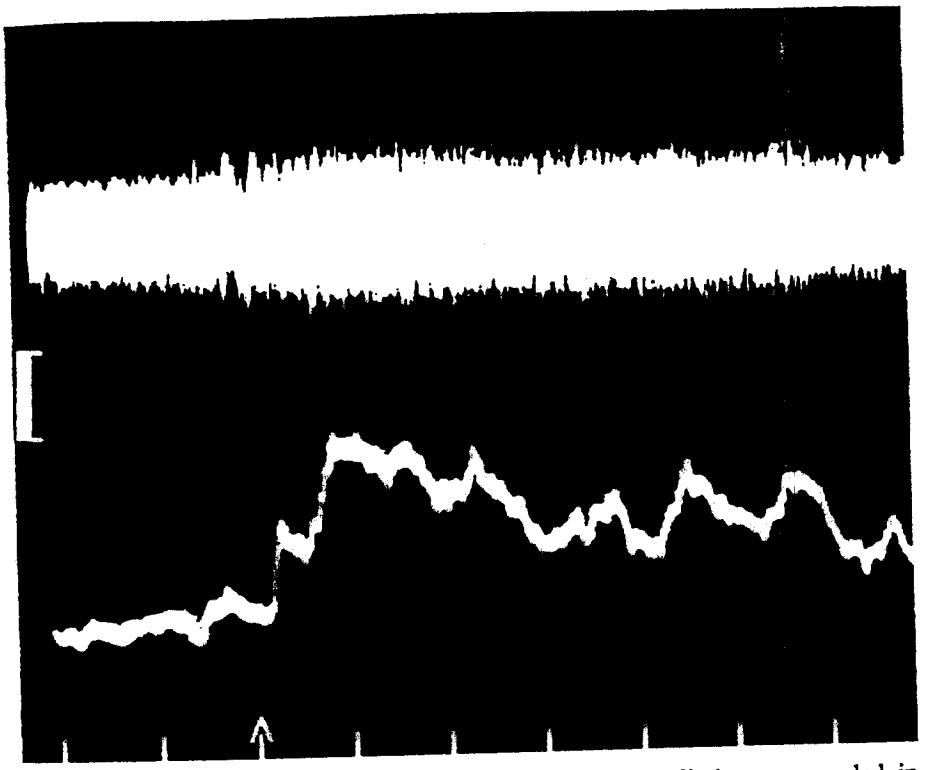

FIG. 1. Typical examples of prolonged small-fiber after-discharge, recorded in right ventral tegmentum. This particular potential was evoked by a 1-second pinch to left forepaw. Top line: Evoked response. Onset of pinch at arrow. Bottom line: Same response recorded through envelope detector. Time marks, 500 msec. Vertical marked=100 microvolts for top line. 2 volts for bottom trace. Note similarity of after-discharge to that in figure 2 evoked by electrical stimulation.

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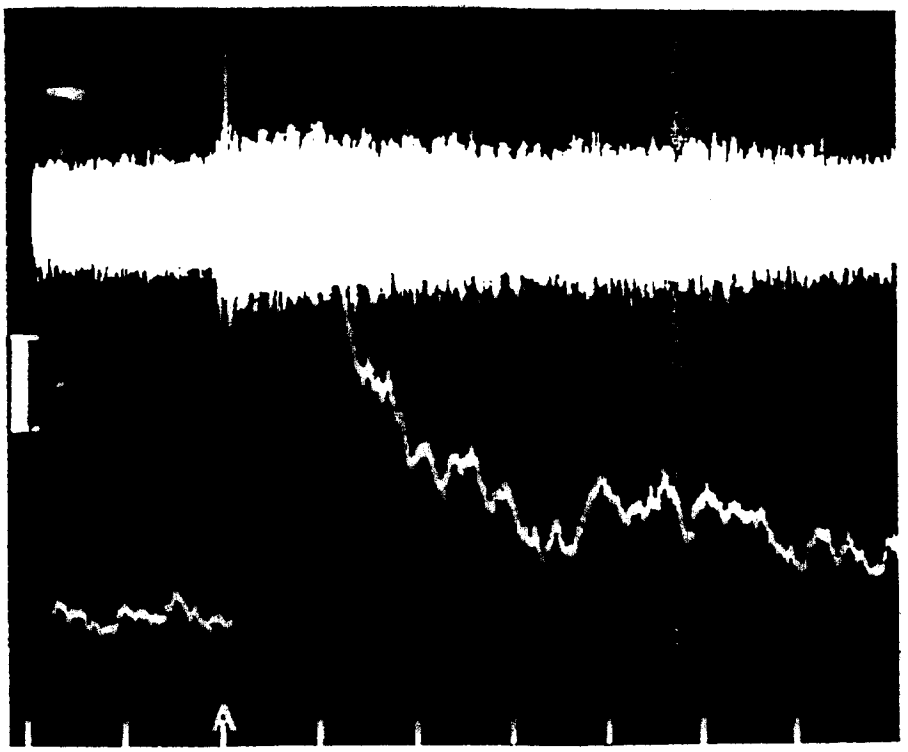

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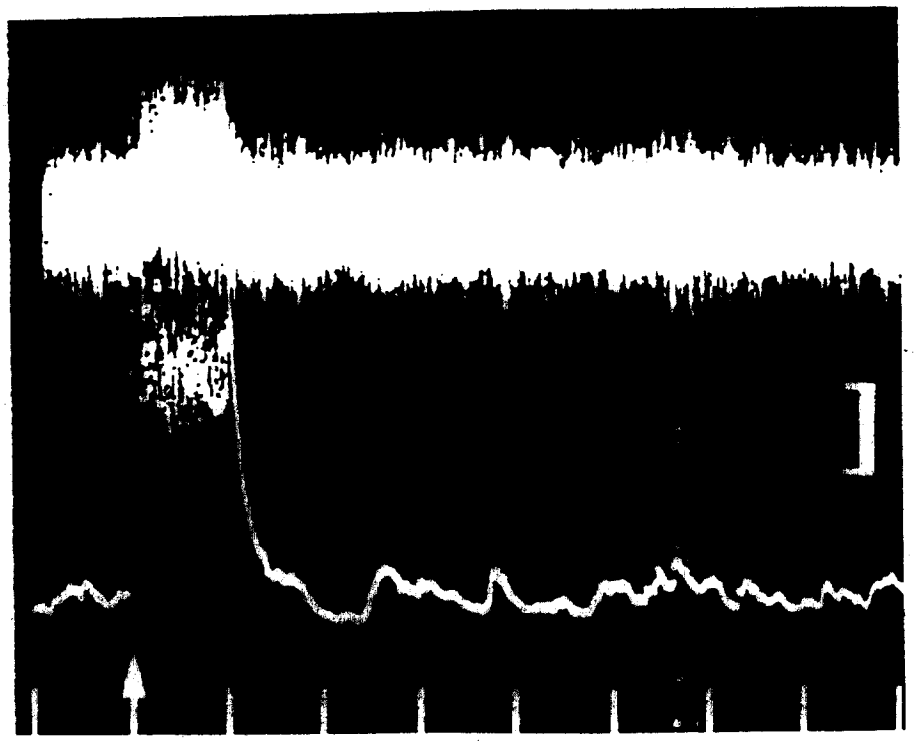

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FIG. 2. a. Control example of PSAD in right ventral tegmentum. Top line: Evoked response. Stimulus of 80 volts (at arrow), 500 second, 0.5 msec. pulses, 500 msec. train to left forepaw. Bottom line: Same response recorded through envelope detector. Time marks, 500 msec. Vertical marker=100 microvolts for top line, 2 volts for bottom trace. b. Same response during continuous application of 2 mamp. anodal current to cervical cord dorsum.

with a hand, vibration, and movement of joints have never elicited an after-discharge of greater duration than 200 msec.

Thus PSAD as elicited and reported in previous experiments[17] represents a central response uniquely relating to stimuli which would be painful in man and which has been absent when stimuli considered nonpainful are applied. A similar prolonged after-discharge has been recorded in the upper cervical spinal cord of one patient, the response being elicited only by pinching of his toe. This small-fiber system has been used in the current experiments to evaluate possible suppression of spinal cord transmission of pain.

METHODS

Thirty-five adult cats were used in this study. Initially they were anesthetized with Fluothane,[9] tracheotomized, and maintained in a Dann Infant Resuscitator with added 80 per cent nitrous oxide, 20 per cent oxygen until surgical procedures were completed, after which they were continued on Flaxedil.[9] Animals were placed in a stereotaxic headholder and extended to stretch the spine. A craniectomy was done for recording from tegmentum in the locations originally described by Collins and Randt.[15]

For medullary recording, also as reported by Collins and Randt,[16] an acute decerebration can be done by standard methods and 1 hour later the obex is exposed by an upper cervical laminectomy. Superficial radial or sural nerves are exposed for nerve stimulation and recording via platinum wire electrodes. Central recording electrodes are platinum-iridium wires with 30 micron tips, insulated within 30 microns of the tip. An AEL Stimulator is used for peripheral nerve stimulation. A Grass S4 Stimulator or the AEL Stimulator has been used for attempted blocking currents applied to various areas, but stimulus artifacts are troublesome.

Our most successful blocking current has been delivered from a 6-volt battery connected through a variable resistor and an ammeter in series to a platinum plate on the cord dorsum. "Blocking" currents as defined below and some mechanical stimulation have been applied to skin over various parts of the entire body, to peripheral nerves, and to the spinal cord. Physiologic controls consist of observations of evoked thalamic potentials which are related to nonpain-conducting large peripheral fibers.[15]

In six chronic-animal preparations small coils of platinum wire or solid platinum plates measuring about 2 x 2 mm. have been placed over the upper cervical or lower thoracic dorsal column with an indifferent subcutaneous plate. In two of these animals similar stimulating electrodes were also placed adjacent to the anterior spinal cord. These implanted electrodes were led subcutaneously for chronic stimulations under observation.

RESULTS

Using PSAD as a standard physiologic response to painful stimulus, we have applied additional mechanical stimuli to various portions of the body. Rubbing and low voltage electrical stimulation, through subcutaneous needles (up to 10 volts, 0.5 msec. duration, 10 to 1000 x/second) of many body areas has failed to yield consistent blocking of medullary or tegmentally recorded PSAD. Although suppression occurred in 5 animals, no PSAD depression was seen in another 15.

Unfortunately, *pulsed* currents applied to the dorsal columns introduce such large stimulus artifacts that these have not been useful in acute physiologic experiments. D.C. current of 1.0 to 2.7 mamps. delivered through a 3 x 3 mm. platinum plate to the exposed dorsal cord in the cervical region has suppressed PSAD in 12 animals (fig. 2). The circuit is completed through a stainless steel needle in adjacent muscle. Suppression is optimal just after onset of the blocking current and usually has been best with anodal current applied to the dorsal columns. On the other hand, occasionally with continuing anodal current to the dorsal columns and often if cathodal current is applied to the dorsal cord, there is marked enhancement of PSAD (fig. 3).

During the first 10 to 30 seconds of current application to the dorsal cord, there is continuous firing of a number of fibers. This same effect is seen in peripheral nerve when an anodal current is applied to the nerve for selective blocking of large fibers (unpublished personal observations). Similarly, when current to the cord dorsum is turned off, there is a burst of spontaneous firing lasting up to 30 seconds.

PSAD elicited from either fore or hind paw may be eliminated by application of D.C. current either to the lower thoracic or to the cervical dorsal spinal cord. Equally successful inhibition of PSAD has been obtained by application of 1.5 to 2.5 mamps.

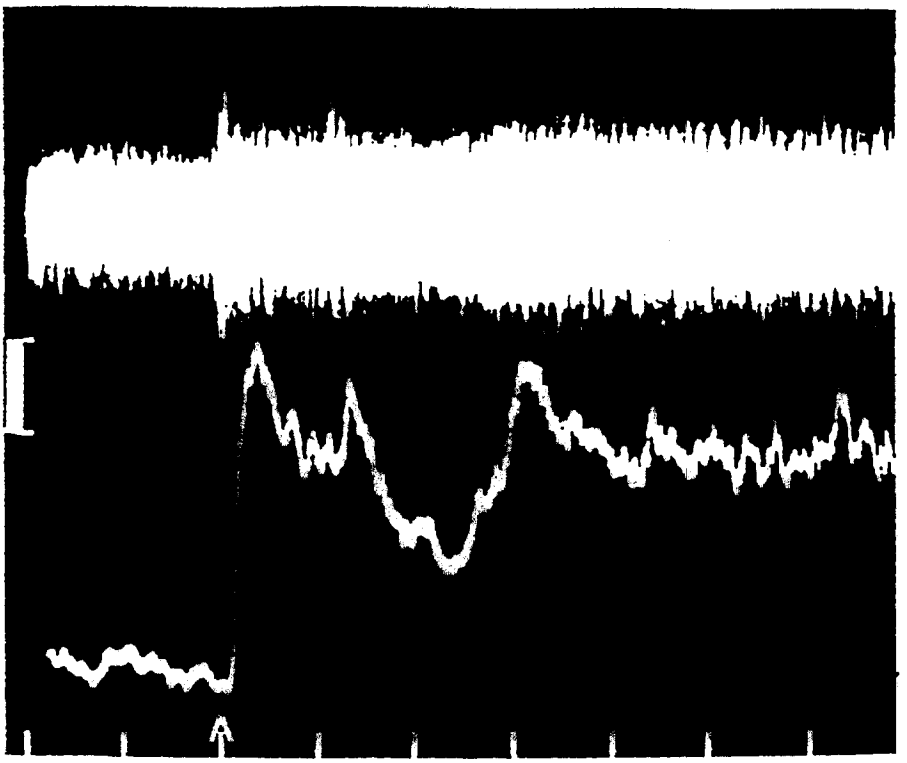

FIG. 3. Same response as figure 2b, but with continuing 2 mamp. *cathodal* current to cervical cord dorsum. Note increase in after-discharge.

of D.C. current to the anterolateral spinal cord, although this is best accomplished by anodal current. In this situation, however, *application of current to thoracic anterolateral cord inhibits PSAD from the hind paw but has no definitive effect upon PSAD elicited from the forepaw.* PSAD suppression may continue throughout application of

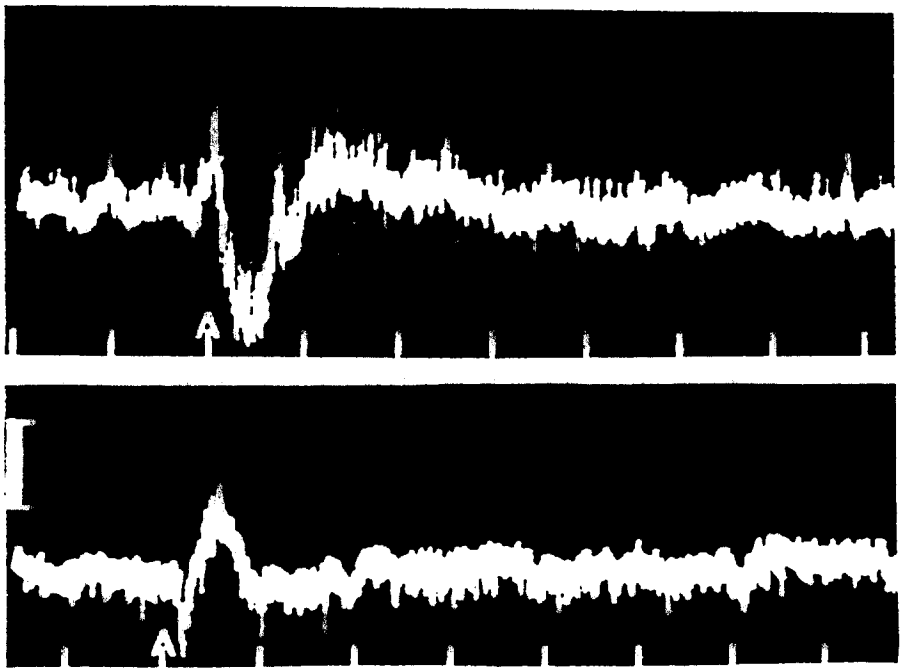

FIG. 4. Top: Control levels of evoked potentials to single stimulus (at arrow) of 0.5 msec. duration, 60 volts to left forepaw. Bottom: Similar response during anodal current of 2 mamp. to cord dorsum. Note reversal of polarity. Time markers = 50 msec.; vertical gain marker = 50 microvolts.

the current up to at least 1 minute. Enhancement of PSAD has not been seen with anterolateral cord polarization.

No significant change is found in the thalamic potentials during cord stimulation (fig. 4). In the chronic animals we have been able to observe the effects of various currents applied to the implanted cord electrodes. These animals are awake and alert. Normally pinching the tail or paw of the animals leads to meowing and vigorous withdrawal. Similarly, the cats flick an ear to avoid a hot soldering iron. However, when a pulsed D.C. current of 2 mamps. (0.3 volts) 50 x/second is applied to a dorsal column electrode over the cervical cord, *the animals allow prolonged pinching and intense heat to the point of tissue damage with no apparent discomfort.* They remain alert during the stimulus and sometimes will sit contentedly licking themselves during the dorsal column stimulation.

DISCUSSION

Melzack and associates[18] have attempted to mask pain by applying vigorous vibration or by a sudden slap. Although vibration raised the threshold for electric shock pain, it led to a decrease in the current needed to produce severe pain. A slap raised the threshold for electric shock pain, but had no influence on severe pain. Thus, surface stimulation in their experiments did not inhibit pain.

Andersen and coworkers[19] have demonstrated depolarization of primary afferent fibers by repetitive stimulation of sensory cortex. It is conceivable that thalamic and other descending influences might work similarly. Melzack and Wall[14] have postulated a spinal cord "gate" which is operated by balancing the input between large and small fibers. They have fully discussed synaptic depolarization at this entering "gate." Eccles and associates[20] reported that afferent dorsal root fibers can be depolarized or hyperpolarized by D.C. current applied between dorsal and anterolateral spinal cord. Hyperpolarization achieved by negative current in their experiments led to an increase in fiber spikes and in monosynaptic excitatory postsynaptic potentials; a positive dorsal root current producing depolarization suppressed afferent fiber spikes and monosynaptic excitatory postsynaptic potentials.

The physiologic experiments presented here with inhibition of PSAD suggest that spinal cord transmission of responses evoked by painful stimulation has been greatly influenced. The experiments with chronic animals indicate that similar stimulation in awake animals leads to apparent loss of appreciation of pain without other observable neurologic deficits. Considerable further experience is needed with long-term animal experiments and pathologic studies before spinal cord electric stimulation can be tried for inhibition of pain in man. Preliminary work, however, suggests that we may be able to inhibit pain electrically without destructive surgery and without narcosis.

SUMMARY

In cats, an electrophysiologic system activated by noxious stimuli is suppressed by stimulation of the dorsal columns or of the anterolateral spinal cord. In chronic-animal preparations, pulsed D.C. stimulation of the dorsal columns inhibits typical withdrawal from painful stimuli. The results are discussed in relation to possible future use of this technic for suppression of pain in man.

Generic and Trade Names of Drugs

Halothane—Fluothane
Gallamine triethiodide—Flaxedil

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CORRECTIONS

In the biographic sketch of Dr. Karl F. Urbach, on page 52 of the January-February 1967 issue, he should be listed as chief of the Anesthesiology Service at the U.S. Public Health Service Hospital, Staten Island, New York, and not as Chief of the Anesthesiology Service at Santa Clara Hospital and Medical Center, San Jose, California.

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A correction should be made in paragraph 2, page 205, of the Summary of the paper, "Intracardiac Epinephrine Versus Isoproterenol in Cardiac Arrest," by W. A. Warner, M.D., which appeared in the March-April 1967 issue.

The line, Blood pressure, heart rate, arterial pCO_2, pCO_2 and pH values . . . should read "Blood pressure, heart rate, arterial pO_2, pCO_2 and pH values. . . .