Local Analgesia From Percutaneous Electrical Stimulation

A Peripheral Mechanism

James N. Campbell, Arthur Taub, MD, PhD, New Haven, Conn

Pain and touch thresholds to a needle stimulus were measured on a finger of each of 11 subjects as a function of the presence or absence of continuous, 100-hertz, 1-msec electrical stimulation delivered proximally to the digital nerves of the finger tested at intensities of either 10 to 12 v, 22 v, or 50 v. At 10 to 12 v touch threshold alone was elevated; at 22 v both touch and pain thresholds were elevated; and at 50 v anesthesia and analgesia resulted. The averaged median nerve compound action potential resulting from either periodic bursts or continuous 50-v, 100-Hz, 0.5-msec duration electrical stimulation to the digital nerves of a finger was studied in each of five subjects. An A-delta wave was recorded with periodic bursts of stimuli, but was absent with continuous stimulation. These results indicate that analgesia from electrical stimulation results from peripheral blockade of A-delta fibers.
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In 1967, Wall and Sweet[1] delivered 100-hertz, 0.1-msec electrical stimulation to the infraorbital nerve of normal subjects via subcutaneous needle electrodes, and observed decreased appreciation of pinprick on the face in the region of its distribution. Patients with a variety of chronic pain syndromes then received similar electrical stimulation to the peripheral nerves innervating the region to which pain was referred, and temporary relief from pain was obtained. Since no pain was reported as resulting directly from the electrical stimulus, it was inferred, principally on the basis of studies in man indicating that some A-delta fiber stimulation is sufficient for the pain[2] experience, that only larger myelinated afferent fibers had been stimulated. Others have reported similar results in the treatment of clinical pain.[3,4]

Subsequently, relief of clinical pain has been reported[5,6] during electrical stimulation with electrodes placed upon the dorsal columns in man. Such stimulation was reported to be effective only when paresthesias were produced in the regions of pain referral.

Of the possible hypothetical mechanisms by which peripheral electrical stimulation may affect pain thresholds, those operating at central nervous system (CNS) levels have received the most attention.[7,8] It has been suggested that a "gate control" mechanism exists in the dorsal horn of the spinal cord, whereby large myelinated fiber input is said to inhibit central transmission of the overall effects of the sum of small fiber and large primary afferent fiber input.[7] Other CNS regions have also been postulated to be active in this respect.[8,9]

In the study reported here we demonstrate that percutaneous electrical stimulation of digital nerves in the median nerve distribution of man can produce analgesia and anesthesia in the distal portion of the finger stimulated. We present evidence to indicate that at least a portion of this effect is of peripheral origin, being a result of blockade of peripheral sensory fibers.

Experiment 1

This experiment was designed to investigate the effects of digital nerve electrical stimulation on touch and pain thresholds to a distal needle stimulus.

Subjects.—The subjects of this study were eight male and three female volunteers ranging in age from 20 to 27 years. They were informed of the general nature of the experiment, but not what specific results were to be expected.

Procedure and Apparatus.—Steel disk electrodes (1.5 cm in diameter) with electrode paste on the surface were taped firmly to the medial and lateral aspects of either the index or middle finger of either hand. Both digital nerves were stimulated by two separate synchronous sources. The cathode was placed proximally and the anode distally along the finger. A stimulating system consisting of a Devices Digitimer (type 3290), a Devices Counter-Timer (type 3251), and two Devices Isolated Stimulators (Mark IV) produced a square wave stimulus at 100 Hz, 1 msec.

The subjects were divided randomly into two groups. One group received a 10- to 12-v stimulus (three times threshold for sensation) to each digital nerve, and the other received a stimulus of 22 v. The 22-v stimulus could not be applied suddenly without protest of pain or discomfort. To reach this value, the stimulus voltage was increased gradually over a 5- to 20-minute period, depending on individual tolerance.

With the use of a servocontrolled tactile probe developed in this laboratory, the point of a 22-gauge needle was delivered to the skin at varying time intervals, with precise (within 10μ) control of the cutaneous deformation. The needle, moving vertically and continuously at a frequency of 1 Hz, was applied to the skin just proximal to the nailbed of the immobilized finger in 0.1-mm increments of deformation. The point of application was visualized by a stereomicroscope. Subjects were blindfolded. Touch thresholds were determined by the method of limits.[10] Pain thresholds were determined by lowering the needle to the point where pain was reported. The subjects were instructed not to report a "pricking" sensation as painful. The needle was then raised quickly to avoid the production of a lasting indentation of the skin, which was found to alter later threshold determinations. Each pain threshold determination was repeated three times.

Touch and pain thresholds were determined, for each subject, with and without electrical stimulation. In each group half of the subjects received electrical stimulation first, and in the other half the order was reversed.

A minimum of five minutes between trials was taken to minimize any effects electrical stimulation might have on subsequent determination of touch and pain thresholds. A problem encountered was

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From the Section of Neurosurgery, Department of Surgery, Yale University School of Medicine, New Haven, Conn.

Reprint requests to Section of Neurosurgery, Department of Surgery, Yale University School of Medicine, 789 Howard Ave, New Haven, Conn 06510 (Dr. Taub).

that when the 22-v repetitive electrical stimulus to the digital nerves was delivered, the testing needle would sometimes pierce the skin before pain was reported. This was thought to alter further threshold determinations, and data from these particular studies were discarded.

Results.—The sensation associated with low levels of electrical stimulation of the digital nerves was reported as being that of a paresthetic numbness. Paresthesias increased with electrical stimulus intensity to the point where pain was reported. The intensity of paresthesias decreased with time, despite constancy of the electrical stimulus. When voltage was increased to a level reported as painful, that pain also decreased within seconds to minutes. When the electrical stimulation was briefly discontinued and then immediately reapplied, pain was again reported.

The finger stimulated was no different in temperature from the other fingers on the hand, although at times the stimulated hand was somewhat cooler than the nonstimulated hand. Cyanosis of the stimulated finger was never noted.

Mean touch and pain thresholds with and without electrical stimulation are presented in Table 1. Threshold values are given in millimeters of cutaneous deformation. The threshold for touch without electrical stimulation was assigned the value 0. Paired statistical analysis of the effects of electrical stimulation on touch and pain thresholds was performed by means of Student *t* test.[11] In group 1 (10 to 12 v) electrical stimulation raised the touch threshold alone ($t = 3.19$, df = 3, $P < .50$). In group 2 (22 v) electrical stimulation raised touch ($t = 4.00$, df = 6, $P < .01$) and pain ($t = 5.75$, df = 6, $P < .001$) thresholds. The high-intensity stimulus produced a greater increase in touch threshold ($t = 2.65$, df = 9, $P < .05$) than did the low-intensity stimulus.

Table 2 shows the distance in millimeters between touch and pain thresholds in group 2 with and without electrical stimulation. The distance between the thresholds for touch and pain was greater ($t = 3.22$, df = 6, $P < .01$) with the electrical stimulus off than with it on.

Examination for other effects of electrical stimulation revealed none, except occasionally in adjacent fingers. These effects consisted of decreased appreciation of pinprick and an elevation of the pain threshold. With higher voltages (greater than 22 v) the effect on adjacent fingers was more noticeable. In one study the index and ring fingers were stimulated, and a marked increase of touch and pain thresholds was observed in the middle finger.

During threshold testing with the 22-v electrical stimulus on, the testing needle would sometimes puncture the skin, and bleeding would result. At these times subjects often reported a vaguely located pain, unlike that initially caused by the vertical movements of the needle. This pain was continuous, and was described as a feeling of "soreness" or "ache."

Table 1.—Thresholds for Pain and Touch*

Subject	Touch Threshold		Pain Threshold	
	Without Stimulation	With Stimulation	Without Stimulation	With Stimulation
		Group 1 (10 to 12v)		
1	0	0.03	0.20	0.38
2	0	0.18	1.08	1.10
3	0	0.30	2.10	2.10
4	0	0.20	1.55	1.55
		Group 2 (22v)		
1	0	2.62	2.57	3.12
2	0	3.45	2.33	3.45
3	0	1.30	1.57	2.00
4	0	0.63	0.70	1.05
5	0	0.53	0.90	1.40
6	0	2.86	2.39	2.86
7	0	1.05	0.63	1.05

*Measured by millimeters of skin deformation by a needle as a function of the presence or absence of proximal electrical stimulation.

Experiment 2

This experiment tested the hypothesis that analgesia produced by electrical stimulation results from blockade of peripheral sensory fibers.

Methods.—With a special-purpose digital computer (Biomac-1000), it was possible to record the averaged compound action potential of the median nerve transcutaneously at the wrist. A stimulus of 50 v, 100 Hz, 0.5 msec was delivered to both digital nerves of one finger, first in periodic bursts (every 30 seconds for 0.5 second) and then continuously.

Six subjects were tested. Steel disk electrodes were taped in place over the digital nerves of either the index or the middle finger. Identical electrodes were used for median nerve recording. The recording electrode was placed directly over the median nerve on the flexor side of the wrist. The "indifferent" electrode was placed on the extensor surface of the wrist. The ground electrode was a pliable metal strip wrapped around the palm. Electrode paste was used on the ground and electrode disks. It was found necessary to insulate the ground strip from the stimulating electrode with petroleum jelly since perspiration short-circuited the stimulating electrodes to ground. The compound action potential was amplified (×5,000) via a preamplifier (Grass P511). An average of 500 signals was taken. The periodic bursts of electrical stimuli were interrupted three times during the recording, for two minutes at a time, to minimize discomfort to the subject. Following the series of stimuli in periodic bursts, continuous electrical stimulation was delivered, but its intensity was gradually raised to a level of 50 v over a 5- to 20-minute period. Pain was reported with each increment of voltage, subsiding within seconds to minutes. When the stimulus level of 50 v had been reached, signal averaging commenced

Results.—With periodic bursts of stimuli at 50 v, the subjects were uncomfortable, perspired, and complained of pain. The bursts were perceived as painful during each, and as most painful at the beginning of a burst series and immediately upon resuming burst stimulation following each rest period. With continuous electrical stimulation at 50 v, five subjects did not feel pain once the final stimulus intensity had been reached. One subject noticed intermittent pain which was associated with involuntary movement of the finger. At the conclusion of the experiment, paresthesias were noted in the stimulated finger for approximately one half hour. Effects lasting longer than one half hour were not described by the subjects. During continuous stimulation at 50 v, a needle stimulus produced no sensation whatever at the fingertip except for a brief "jab" sensation if the needle was thrust through the skin.

An A-delta wave was always present in the averaged compound action potential record obtained during the series of periodic bursts, but was either diminished in amplitude or was entirely absent with continuous stimulation. The A-delta wave varied in configuration and latency to some extent from subject to subject. The Figure shows a representative example from a single subject.

The compound action potential in the

Table 2.—Distance in Millimeters Between Pain and Touch Thresholds in Group 2 (22)*

Subject	Without Stimulation	With Stimulation
1	1.67	0.50
2	2.33	0
3	1.67	0.70
4	2.50	0.43
5	1.90	0.87
6	2.33	0
7	1.83	0

*As a function of the presence or absence of electrical stimulation.

Median nerve averaged compound action potential (500 signals) recorded transcutaneously at wrist as function of 50-v, 100-Hz, 0.5-msec stimulation of both digital nerves of index finger; conduction distance 12 cm. Top, Electrical stimulus delivered in bursts for 0.5 second every 30 seconds; A-alpha latency, 3.6 msec (33.4 meters/sec); A-delta latency, 5.2 msec (16 meters/sec). Bottom, Continuous electrical stimulation; 50-v level reached over ten-minute period; A-alpha latency, 4.1 msec (29.3 meters/sec); no clearly defined A-delta wave.

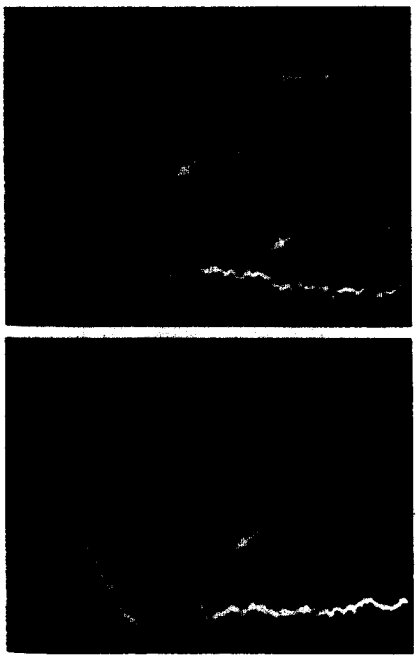

Figure (top) was recorded during the series of periodic bursts of electrical stimuli, and that in the Figure (bottom) during continuous electrical stimulation. An A-delta wave was present with periodic bursts of stimulation, and was absent with continuous stimulation. The A-alpha wave evoked by continuous stimulation was longer in latency and lower in amplitude (Figure, bottom) than the A-alpha wave evoked by the periodic stimulus in bursts (Figure, top).

The A-alpha wave in the Figure (top) begins at a latency corresponding to a velocity of 33.4 m/sec. In the Figure (bottom) the A-alpha wave begins at a latency corresponding to a velocity of 29.3 m/sec. The A-delta wave in the Figure (top) occurs at a latency corresponding to a velocity ranging from 16 to 23 m/sec.

Comment

These experiments indicate that a 10- to 12-v, 100-Hz, 1-msec continuous electrical stimulation to the digital nerves raised the threshold to touch but not that to pain in the tip of the finger stimulated. A 22-v stimulus, however, raised the thresholds both to touch and to pain, as tested by a distal needle stimulus. Further, the more intense electrical stimulus itself was painful if introduced suddenly; the pain caused by sudden introduction of the intense electrical stimulus diminished over a period of seconds.

When a 50-v electrical stimulus was delivered to the digital nerves in periodic bursts (100 Hz, 1 msec, for 0.5 second, every 30 seconds), an A-delta wave appeared in the averaged compound action potential of the median nerve, and subjects complained of pain. When the same stimulus was given continuously, the A-alpha elevation decreased in amplitude and increased in latency, and the A-delta wave disappeared, along with the sensation of pain.

A-delta fiber stimulation has been associated with a report of a sensation of pain in man.[2] The rise in threshold for pain, as tested by a needle stimulus, when electrical stimulation was applied proximally, associated with a marked decrease in the amplitude of the A-delta portion of the fiber spectrum, suggests that that portion of the A-delta fiber spectrum responsible for conduction of input from nociceptors[12] has been functionally blocked by high-frequency and high-intensity electrical stimulation. (It is not possible, however, to conclude, from the observation of the disappearance of the A-delta elevation, that *all* A-delta fibers in the volley have been blocked, as a portion of this decrement in size of the volley may be produced by decrease in size of individual action potentials, or by asynchrony in conduction of individual action potentials.) Functional blockade of the myelinated portion of the primary afferent fiber spectrum by application of cold and of high-frequency electrical stimulation was first demonstrated by Bishop,[13] and was used subsequently for the study of potentials evoked within the CNS by stimulation of an "isolated" volley derived from unmyelinated primary afferent fibers.[14,15]

The observation that the sensation of pain produced by the electrical stimulus itself decreased in intensity with time, was most intense at the onset of stimulation, and was always present when stimulation was delivered in short bursts is consistent with the assumption that a short period of time, measured in seconds, is required for the functional blockade of A-delta fibers to occur, and that recovery from such blockade is rapid. This assumption is confirmed by the continued presence of the A-delta elevation in the compound action potential when the electrical stimulus to the digital nerves is delivered in short bursts.

With respect to touch sensation, it was noted that both low and high intensities of continuous electrical stimulation to the digital nerves produced a rise in the touch threshold as tested by a needle, but that the rise in threshold was significantly greater during high-intensity electrical stimulation. It was also noted that the intensity of tactile sensation produced at any given level of electrical stimulation decreased with time. These observations suggest that a similar blockade of A-alpha fibers, stimulation of which has been associated with a report of the sensation of touch in man,[2] had occurred. The A-alpha elevation of the median nerve compound action potential decreased in amplitude during continuous stimulation, more so than during periodic bursts of stimuli, an observation compatible with this hypothesis.

During continuous electrical stimulation with the 50-v stimulus, the latency of the A-alpha fiber group and the amplitude of the A-alpha fiber elevation were seen to decrease. This suggests that the larger fibers within the A-alpha volley were preferential-

ly blocked. In Table 2, derived from measurements of touch and pain thresholds to a needle stimulus during continuous electrical stimulation at 22 v, it is seen that while both touch and pain are appreciated and their thresholds elevated, such elevation does not occur uniformly; the touch threshold approaches that of pain. This again suggests a nonuniform blockade of larger and smaller myelinated fibers, the larger fibers being preferentially blocked.

The observation that during continuous electrical stimulation with the 50-v stimulus, tactile sensation was absent despite the presence of a definite A-alpha elevation in the median nerve compound action potential suggests the necessity for the activation of a minimal number of A-alpha fibers as a requisite for the touch experience.

It was noted that high-intensity electrical stimulation often caused a decreased appreciation of pinprick in adjacent fingers. An elevation of pain threshold was especially seen when the finger between two electrically stimulated fingers was tested. This particular effect may result from antidromic stimulation and blockade of digital nerves in the palm, although CNS effects cannot be excluded.

Other cutaneous stimuli have been reported to alter local pain threshold in man. Wall and Cronly-Dillon[16] reported that vibration (60 Hz, peak-to-peak amplitude 3/16 inch) raised the threshold to warmth and pain (tested with heat and electric shock) in the areas stimulated. Melzack et al[17] studied the effects of vibration on local touch, prick, and pain thresholds to electric shock. Some subjects showed an increased threshold to touch and prick when vibrated, but no effect on mild pain, and a decreased threshold to severe pain. It would appear that vibration has a variable effect on pain threshold.

The observation of previous investigators[1-3] that it was possible to stimulate peripheral nerves electrically without producing pain, and yet producing temporary, local relief of pain in patients with chronic pain syndromes was thought to be compatible with the "gate control" hypothesis[6]: that is, with the notion that a central inhibitory effect was at the basis of the hypalgesia produced. It was proposed that electrical stimulation of a peripheral nerve in man produced hypalgesia while stimulating large myelinated fibers only.[1-3] The portion of the primary afferent spectrum stimulated was inferred from the lack of a report of pain, and no action potential data were presented. The data presented here make an alternate view likely: that in those clinical situations in which relief of pain was reported, a peripheral effect, that is, peripheral blockade of smaller myelinated fibers, had occurred, preventing transmission of information derived from A-delta nociceptors.[12] In our study, pain was experienced initially during continuous stimulation, but only transiently. Once intensities of stimulation sufficient to produce A-delta blockade were reached, pain was not reported. It is possible that where pain preexists chronically, a brief period of pain produced by electrical stimulation, and preceding blockade of A-delta fibers and hypalgesia, is apt to be overlooked. It remains to be seen whether analgesia can be produced by stimulation of large myelinated fibers alone, but it appears unlikely to be the case.

The brief "jab" of pain experienced when the skin was pierced during electrically induced local analgesia in our study may, perhaps, be attributable to stimulation of peripheral receptors provided with C fiber primary afferents, as these were not blocked at the intensities of stimulation used.[2,13]

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