The aftereffects of peripheral nerve stimulation: Change in psychophysical judgments and autonomic reactions during the scaling of cutaneous pain

NORMAN A. KRASNEGOR, J. RICHARD JENNINGS, WILLIAM C. ORR
and HOWARD L. FIELDS*
Walter Reed Army Institute of Research, Washington, D.C. 20012

Psychophysical estimates of pain intensity, experimentally induced in the index and third fingers with a dolorimeter, were compared for three "normal" human Ss before and after low-level electrical stimulation of the median nerve. Estimates of high, but not low, intensity thermal stimuli decreased after peripheral nerve stimulation. Psychophysiological indices mirrored the psychophysical data. Both the number and amplitude of the galvanic skin responses to the stimuli decreased after nerve stimulation.

One of the implications of the gate control theory of pain perception (Melzack & Wall, 1965) is that selective stimulation of large-diameter myelinated fibers should produce relief from chronic peripheral pain associated with spinothalamic discharge. Briefly, the theory holds that activity in the large-diameter myelinated fibers has an excitatory effect upon "gating" cells located in the substantia gelatinosa. Excitation of these "gating" cells is presumed to have an inhibitory effect upon input from small unmyelinated fibers which carry information concerning nociceptive stimuli to the "T-cells," the presumed transmission cells for pain located in the dorsal horn. Stimulation of the large myelinated fibers should presumably prevent or delay summation at the level of the T-cells and therefore alter pain perception by reducing the number of T-cells reaching threshold. Recent studies lend support to the gate control hypothesis. Wall & Sweet (1966) and Meyer & Fields (in press) both demonstrated in clinical settings that following selective stimulation of large myelinated fibers with low-level electrical stimulation, patients reported temporary relief from pain. In addition, Higgins, Tursky, & Schwartz (1971) demonstrated under laboratory conditions a reduction in affective responses of normal human Ss to electric shock during, but not necessarily following, application of a tactile stimulus to the shocked locus.

The present experiment is the first in a series of experiments planned to investigate the aftereffects of selectively stimulating large-diameter

fibers in peripheral nerves on the pain responses of "normal" Ss. Specifically, Ss were required to rate psychophysically the intensity of experimentally induced cutaneous pain both before and after low-level electrical stimulation of the peripheral nerves that supply the target area where pain was induced. In addition, galvanic skin responses (GSR) to the experimentally induced pain and skin temperature were monitored throughout each experimental session.

SUBJECTS AND APPARATUS

The authors served as Ss (N.A.K., J.R.J., and W.C.O.). Each was thoroughly familiar with the experimental procedure and an experienced psychophysical O.

A modified dolorimeter (Hardy, Wolfe, & Goodell, 1952), designed and built in the fabrication shop at the Walter Reed Army Institute of Research and calibrated for irradiance (m cal/sec/cm^2) by the thermometry section of the National Bureau of Standards, was used to produce the heat stimuli. The low-level electrical stimulation for peripheral nerves was provided by a Grass S4G stimulator. Skin resistance was monitored using silver-silver chloride electrodes containing an isotonic saline paste (Edelberg, 1967) and a Beckman two-channel polygraph. Skin temperature was measured with a Yellow Springs Instrument telethermometer and Yellow Springs thermistor.

PROCEDURE

Each S was run a total of 10 times, 5 training and 5 testing sessions. All sessions were composed of a preparatory and a scaling phase. During the preparatory phase, India ink was applied to the middle pad of the index and third fingers of the S's right hand (these fingers served as

alternating targets for thermal stimulation). This procedure helped to insure a uniform distribution of heat in the target areas. Next, GSR electrodes were attached using adhesive collars, an active electrode on the palmar-surface of the right hand, and a ground electrode on the right forearm. In addition, a temperature probe was taped in place on the forefinger of the left hand to monitor skin temperature.

The initial skin temperature was then noted, and a pain threshold was determined using the psychophysical method of limits. Three ascending and three descending series were used. If the S's skin temperature was less than 85°F or his threshold outside the range of 185 to $265 \text{ m cal/sec/cm}^2$, the session was discontinued. This occurred during less than 10% of the sessions.

During the scaling phase of a session, the intensities of 40 stimuli were scaled using a modified method of magnitude estimation. The 40 stimuli consisted of 20 pain stimuli and 20 catch trials. No heat was applied during catch trials. The 20 pain stimuli consisted of a series of five thermal stimuli ranging between 225 and $305 \text{ m cal/sec/cm}^2$ and separated by equal increments of $20 \text{ m cal/sec/cm}^2$. The five irradiance levels were presented four times each in a quasirandom order. Catch trials were interspersed randomly between stimulus trials. These trials provided an estimate of the Ss' response biases.

The Ss' task was to rate the intensity of the stimuli on a scale ranging from 1 to 5, with 1 representing the least painful stimulus and 5 the most painful. If no pain was experienced on a trial, the Ss were to respond "nothing." An anchoring point was provided at the start of each scaling session. Two $265 \text{ m cal/sec/cm}^2$ stimuli (one on the index finger and one on the third finger) were presented and assigned the value of 3 on the 5-point scale.

During both threshold and scaling determination, the duration of the thermal stimulus (a 1-cm^2 spot of focused light) on each trial was 3 sec and the intertrial interval (scheduled with a variable interval tape timer) was at least 30 sec. The index and third finger were used as target areas and were alternated from trial to trial. These procedures successfully prevented any injury to the irradiated areas.

Procedures for training and testing sessions were identical, except for the addition of low-level electrical stimulation of the median nerve during test sessions. Just prior to the psychophysical scaling, the median nerve which innervates the index and

*Present address: The Neurological Unit, Boston City Hospital, Boston, Mass. 02118.

Fig. 1. Psychophysical estimates of pain intensity before and after median nerve stimulation. Each point represents the mean of 20 observations averaged over the three Ss.

third fingers was stimulated, using square-wave stimuli similar to those reported by Wall & Sweet (1966), i.e., 0.1-msec pulses at 100 Hz with an amplitude of 80 V. Skin resistance on the volar surface of the right wrist was reduced by applying Sanborn Redux paste, and then the bipolar electrode from the Grass stimulator was applied. The electrode was rotated until the S reported feeling strong paresthesias in his index and third fingers. Stimulation lasted for a total of 3 min, with the provision that paresthesias had to be present in the target area for the entire duration of electrical stimulation. At the termination of stimulation, the Ss immediately began the scaling phase of the experiment.

RESULTS

Psychophysical Scaling

The pooled estimates of pain intensity made by the three Ss during the five training and five testing sessions are shown in Fig. 1. Each data point is based upon the mean of 20 observations averaged across the three Ss. The effect of median nerve stimulation upon the estimate of pain is reflected in the difference between the two curves. After selective stimulation of the median nerve, the Ss rated the intensity of the thermal pain lower than during the training phase of the experiment. In both training and testing sessions, the three Ss discriminated among the five stimulus levels. Their estimates of Stimuli 1 and 2 closely approximated absolute judgment. Stimuli 3, 4, and 5, however, were consistently underestimated by the Ss. Stimuli 4 and 5 were markedly underestimated after stimulation.

Using an analysis of variance (split

plot design¹), the decrease in the estimate of pain after stimulation was found to be statistically significant. Ss and pre- and poststimulation conditions were treated as experimental plots. The resulting design produced an analysis of variance with pre- vs poststimulation as whole plot factors, and sessions and levels of thermal stimulation as subplot factors. The effect of peripheral nerve stimulation on high (4 and 5), but not low (1, 2, and 3), levels of pain is demonstrated by the significant interaction of Thermal Stimulus Level by Pre- vs Poststimulation ($F = 2.33$, $df = 5, 100$, $p < .05$). The only other significant effects were the main effect of thermal stimulation level ($F = 299.8$, $df = 5, 100$, $p < .001$) and a Sessions by Pre- vs Poststimulation interaction ($F = 3.19$, $df = 4, 16$, $p < .05$). Across sessions, pain intensity judgment decreased within the poststimulation sessions but not within the prestimulation sessions. There was no measurable effect of median nerve stimulation on judging catch trials. Under both training and testing conditions, the Ss consistently detected all of the "noise" trials, i.e., the "false-alarm rate" was zero.

Psychophysiological Measures

Figure 2 shows the relationship between stimulus intensity and measures of change in skin resistance. In general, the data indicate that skin resistance activity mirrored the Ss' altered psychophysical ratings of pain intensity. The GSR to relatively intense thermal stimuli decreased after median nerve stimulation.

The left side of Fig. 2 shows the average GSR amplitude to the five stimulus levels during training and

testing phases of the experiment. The amplitude of the largest response to each thermal stimulus was measured from its onset to the peak level reached. A GSR was defined as a change in skin resistance of 1 kilohm or more which occurred between 0.4 and 5.0 sec after the onset of the thermal stimulus. This response period takes into account the relatively long latency of the GSR and is designed to include all responses initiated during thermal stimulation. The graph plotted on the right shows the number of discrete GSRs to the thermal stimuli during both the training and testing phases of the study. Responses were counted as relatively discrete if they showed an initial point of inflection followed by a peak and the initiation of a return toward the prereponse baseline.

Both measures, amplitude and total number of GSRs, show marked reductions after median nerve stimulation. The reductions are somewhat more marked for high, as opposed to low, levels of thermal stimulation for GSR amplitude. But in contrast to the psychophysical ratings of pain intensity, the effect of median nerve stimulation is not totally confined to Stimulus Levels 4 and 5. The statistical significance of the differences shown in the graphs plotted in Fig. 2 was tested using the same split plot analysis of variance described above. The interaction between intensity of the thermal stimulus and pre- vs poststimulation was marginally significant for the GSR amplitude ($F = 2.29$, $df = 5, 100$, $p = .06$). The data for GSR number approached significance ($F = 12.95$, $df = 1, 2$, $p < .10$) for the main effect of pre- vs poststimulation.

Fig. 2. Mean GSR amplitude (left) and mean number of GSRs (right) to thermal stimuli before and after median nerve stimulation.

Other Measures

Records of pain threshold and skin temperature were taken each session to determine whether either of these measures was related to differences between pre- and poststimulation conditions. No differences were found for average skin temperature or average pain threshold between the training and testing sessions of the experiment. The average pain threshold for the three Ss was identical for the five training and testing sessions (mean = 250 m cal/sec/cm², range = 225-265 m cal/sec/cm²) and is consistent with other reports in the literature (Hardy, Wolfe, & Goodell, 1952). The average skin temperature during training was 93.5°F, while the average during testing was 93.6°F for the three Ss.

DISCUSSION

The results in general support a gating mechanism interpretation of pain perception. In addition, the small but significant reduction in estimates of experimentally induced pain lends support to the clinical observations reported by both Wall & Sweet (1967) and Meyer & Fields (in press). One should, however, interpret the data of the present study with a note of caution. While the data suggest that selective stimulation of large fibers with low-level electrical stimulation produces a reduction in ratings of pain intensity, the Ss in the present study were quite familiar with the experimental procedure and the five stimulation sessions followed the training sessions. Thus, one could argue that the results obtained might be attributable to S bias or to an order effect. Two arguments question such an interpretation. First, the reduction in pain estimates occurred only at high pain levels. This result was unexpected. Second, since the present study was completed, a second experiment was initiated (Jennings, Lawson, & Krasnegor, unpublished data) incorporating a double-blind procedure and naive Ss. Preliminary

results from this study generally confirm the results obtained in the present study, i.e., naive Ss also show reduction in their estimates of judged pain intensity.

The GSR results parallel those of psychophysical scaling and provide important supporting evidence that the S's pain perception was altered by nerve stimulation. The GSRs reflected the intensity differences of the five stimulus levels during training and, after stimulation of large fibers, showed a decrease in both frequency and amplitude of response. These findings may reflect the sympathetic nervous system's sensitivity to changes in stimulus intensity (Sokolov, 1963). In the present situation, however, the finding may be related to the clinical syndrome of peripheral pain states. A low skin resistance is associated with states such as causalgia (Mountcastle, 1968). Fields (unpublished data) has observed a return to "normal" resistance level in a causalgia patient treated with peripheral nerve stimulation. The implication of this link between clinical and experimental findings is unclear at present.

The scaling data from the present experiment differ from other reports in the literature. Melzack, Wall, & Weisz (1963) found that after Ss received vibratory stimulation of the skin, they reported a decreased response to pain at threshold levels but an increased or enhanced response at intense levels of pain. Higgins et al (1971) reported that their Ss showed no change in pain response at threshold after receiving tactile stimulation of the target area but showed a uniform decrease in pain response to the three stimulus categories (uncomfortable, painful, and tolerance) above threshold. In the present study, the Ss showed no differential scaling of Stimuli 1, 2, and 3 poststimulation. They only showed reduced pain responses at Stimulus Levels 4 and 5. The differences observed between the three studies

may, in part, be attributable to the differences in stimuli used to induce pain, to the different intensity levels of the stimuli employed, the different methods used to rate pain levels, or the different methods used to alter the pain response.

In spite of the discrepancies found between the present study and previous experiments, the fact remains that each of the studies documents some attenuation of pain response after stimulation of peripheral nerves. The results of the present study clearly suggest the need for further research to determine the possible clinical implications of peripheral nerve stimulation as a nonsurgical alternative for the treatment of chronic peripheral pain.

REFERENCES

- EDLEBERG, R. Electrical properties of the skin. In C. C. Brown (Ed.), *Methods in psychophysiology*. Baltimore: Williams & Wilkins, 1967. Pp. 1-53.
- HARDY, J. D., WOLFF, H. G., & GOODELL, H. *Pain sensations and reactions*. New York: Hafner, 1952.
- HIGGINS, J. D., TURSKY, B., & SCHWARTZ, G. E. Shock elicited pain and its reduction by concurrent tactile stimulation. *Science*, 1971, 172, 886-887.
- MELZACK, R., & WALL, P. D. Pain mechanisms: A new theory. *Science*, 1965, 150, 971-979.
- MELZACK, R., WALL, P. D., & WEISZ, A. Z. Masking and metacontrast phenomena in the skin sensory system. *Experimental Neurology*, 1963, 8, 35-46.
- MEYER, G. A., & FIELDS, H. L. Causalgia treated by selected large fiber stimulation of peripheral nerves. *Brain*, in press.
- MOUNTCASTLE, V. B. Pain and temperature sensibilities. In V. B. Mountcastle (Ed.), *Medical physiology*. (12th ed.) St. Louis: Mosby, 1968. Pp. 1424-1464.
- SOKOLOV, Y. N. *Perception and the conditioned reflex*. New York: Pergamon Press, 1963.
- WALL, P. D., & SWEET, W. H. Temporary abolition of pain in man. *Science*, 1967, 155, 108-109.

NOTE

1. The authors acknowledge the assistance of Mr. Douglas Tang, Department of Biostatistics and Applied Mathematics, WRAIR, and thank him for his contributions on the analysis of the data presented in this study.