terval (mean, 13 seconds) the signal and shock series was again introduced.

The results of this procedure are shown in Fig. 1*A*. All the subjects acquired the avoidance response—that is, they responded during the interval between signal onset and the first shock. This result could have been obtained if the procedure merely generated a high rate of response and had not established stimulus control over the lever-pressing habit. However, the fact that the ratio of the number of responses to the number of signal presentations tended to 1 supports a discrimination-learning interpretation.

Experiment 2 was designed so that the effects of the conventional training procedure, in which training occurs under an escape-avoidance contingency, could be examined. Three male hooded rats, approximately 120 days old, were used. The experiment was run in two phases. In phase 1, which lasted for seven 2-hour sessions, an escape-avoidance procedure was used; in phase 2, which lasted for six 2-hour sessions, the avoidance procedure outlined for experiment 1 was used.

The escape-avoidance procedure during phase 1 was as follows. Shortly after a rat was placed in the chamber, the warning signal was presented; 7.5 seconds later a shock was given which lasted for 10 seconds. If the rat pressed the lever during the interval between the onset of the signal and the onset of the shock, the signal was terminated and the shock was avoided. If the response occurred after the shock had started, the shock and signal were terminated and the response was scored as escape. The interval between successive signal-shock presentations was varied, the mean being 13 seconds. The procedure adopted for the second phase has already been described.

The results are shown in Fig. 1*B*. For each subject the percentage of escape and avoidance responses during phase 1 of the experiment and the percentage of the avoidance responses during phase 2 are given. The rats which were subjected to an escape-avoidance contingency primarily made escape responses. When the procedure was changed so as to eliminate the possibility of escape from ongoing shock, avoidance behavior was firmly and rapidly established. All three subjects avoided shock and reached an avoidance criterion of more than 85 percent.

The discriminative avoidance procedure described here has been used successfully to detect the effects of administering different, small doses of 5-hydroxytrytophan which had not been detectable by other behavioral methods (*2*).

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3. This work was supported by funds from the Medical Research Council, United Kingdom.

29 April 1964

Effects of Cutaneous and Muscle Sensory Nerve Volleys in Awake Cats: A Study in Perception

Abstract. *The hypothesis that discharges from afferent nerves from muscle stretch receptors do not participate in kinesthesis has been substantiated by test of discrimination thresholds. In awake, unrestrained cats, nerve stimulation activating group I and most group II sensory fibers (from muscle spindles and Golgi tendon organs) in pure muscular nerves failed to evoke sensory discrimination. Cutaneous nerve stimulation in the same animals produced sensory discrimination even below intensities required to elicit detectable nerve thresholds.*

Afferent groups Ia, Ib, and II from stretch receptors in striated musculature have often been implicated in kinesthesis (*1*). Recent evidence in the anesthetized cat suggests that thalamic and cortical areas receive little, if any, functional contributions from Ia and Ib afferent nerves (*2*). Analysis of unit firing patterns to graded somesthetic stimuli, moreover, reveal extensive areas of the reticular formation and red nucleus unresponsive to the influence of low-threshold group I sensory fibers (*3*). Stimulation of cutaneous nerves produced pronounced effects in these same areas with very weak volleys. The absence of evoked response activity with low-threshold muscle afferent volleys implies that subjective discriminations, such as perception of limb position or muscle tension, may not be subserved by afferent discharges from the Golgi tendon organ or muscle spindle. To test this hypothesis, experiments were performed in awake, freely moving cats with electrodes implanted on peripheral nerves.

Previous work on similar preparations has shown that group I afferent volleys in awake, unrestrained cats failed to elicit either responses in the electroencephalogram or behavioral reactions, whereas weak cutaneous volleys succeeded in eliciting orienting responses. This indicated indirectly that weak cutaneous volleys evoked conscious sensations whereas weak muscular volleys apparently did not (*4, 5*). Since these experiments depended upon a passive reaction on the part of the animal, it cannot be ruled out that group I sensory fibers elicited subjective sensations which were weaker in comparison with cutaneous fibers, and thereby failed to effect the electroencephalographic or behavioral activity to a degree sufficient to be noted. A more direct and accurate test of discrimination thresholds to weak somesthetic volleys was obtained by training animals to respond actively to direct stimulation of a peripheral nerve so as to indicate perception of sensory volleys.

Six cats were trained to press a bar for food rewards during a period when a signal light, or auditory click (four clicks per second), was presented. Rewards could be obtained only during these "on" periods. Bar-pressing was discouraged during "off" periods by withholding presentation of the "on" period until the animal had not pressed the pedal for at least 30 seconds. Those animals tending to press the bar in spite of continued withholding of the "on" periods learned to stop pressing during "off" periods after receiving a mild shock (0.1 ma) from the lever. Before the electrodes were implanted, training proceeded until bar-pressing performance was almost exclusively restricted to "on" periods.

Under barbiturate anesthesia electrodes for stimulating the peripheral nerves were implanted surgically on nerves in both forelimbs, a cutaneous nerve (superficial radial) on one side, and a muscular nerve (deep radial) on the other side, according to methods described elsewhere (*4*). In some cats the hamstring nerve of the hindlimb carried an electrode instead of the deep radial nerve. Both muscle nerves are believed to contain proportionate num-

bers of stretch-receptor afferent fibers; however, the deep radial nerve at the point of stimulation has joint receptor sensory fibers whereas the hamstring has few or none (*5*). To prevent indirect excitation of cutaneous and joint sensory fibers by muscular movements, muscle nerves were always ligated peripherally to the stimulating electrodes. After recovery, animals were returned to the training box where the same "on-off" schedules were resumed with the exception that stimulation of a given nerve, by way of a connecting cable to an implanted cranial socket, was paired with the presentation of light or clicks. Animals were free to move and press the bar as before. The auditory or visual cues were gradually diminished until the cats pressed the bar in response to sensations produced by peripheral nerve volleys alone. Painful stimuli were avoided at all times since animals withdrew and refused to press the bar for prolonged periods after such an experience.

The nerves were usually stimulated at a rate of four rectangular pulses per second; occasionally 100 pulses per second were employed with equal effect. The animals were prevented from responding to temporal intervals by making the durations of "on-off" stimulus periods highly irregular. Stimulus intensities, likewise, were varied in near random fashion.

With stimulus intensities supraliminal for discrimination of sensory nerve volleys, animals usually pressed the bar within 5 seconds of stimulus presentation. Stimulus trials were considered not to have evoked a discrimination if the latency exceeded 15 seconds. For reasons unknown, some animals tended to commit more errors after implantation of electrodes than before by pressing the bar occasionally during the "stimulus-off" periods; but these errors did not interfere with measurements of discrimination thresholds as shown in the bar-pressing records of cat 3 (see Fig. 1*B*). When the task of responding correctly and predictably to sensory volleys above discrimination threshold was acquired with stimulation of one nerve, stimulation of any other nerve above discrimination threshold usually caused the cat to press the bar with the first few presentations.

Stimulus trials were carried out daily

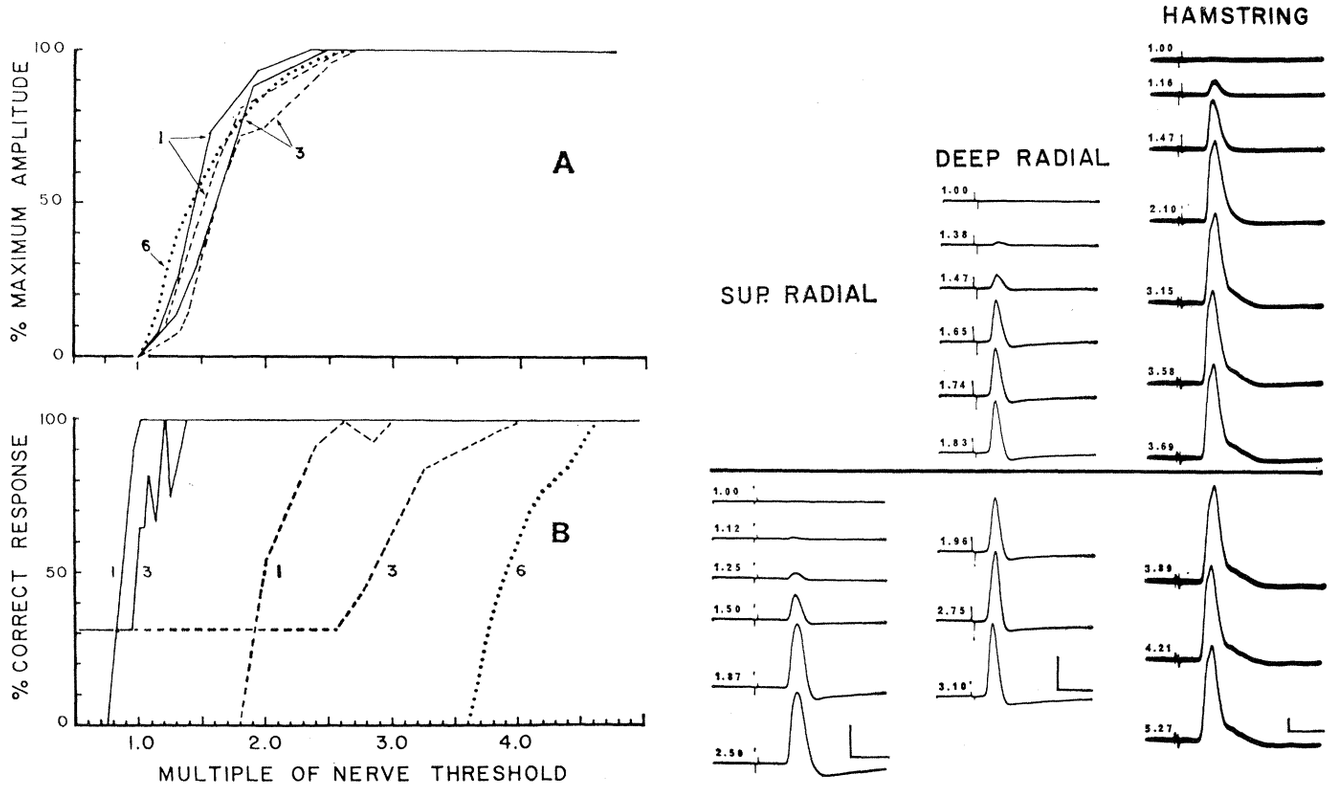

Fig. 1 (left). (*A*) After discrimination thresholds were obtained from the awake animal, the animal was anesthetized and compound action potentials were recorded from exposed nerve bundles. The results were plotted as the percentage of maximum development of the low threshold components of the superficial radial nerve (———), deep radial nerve (– – –), and hamstring nerve (. . .) according to intensities relative to nerve thresholds. Curves for the superficial and deep radial nerves of cats 1 and 3 and the hamstring nerve of cat 6 are shown (same abscissa as in *B*). (*B*) Results of behavioral trials with the same animals show clear distinction between thresholds for sensory discrimination with each type of nerve volley. The curves show the percentage of correct responses as a function of stimulus intensity relative to nerve threshold. In cats 1 and 3, minute cutaneous volleys (evoked by 4 or 100 rectangular pulses per second) produced 100 percent correct discrimination above 1.00 to 1.20*T*. Deep radial volleys were far less effective in the same animals. Hamstring volleys in cat 6 failed to elicit discrimination although all low-threshold muscular afferent nerves had been activated. Fig. 2 (right). Compound action potentials from two cats which had acquired discrimination thresholds. Stimulus intensities producing each response expressed in values relative to nerve thresholds. All traces below the horizontal line show the amplitudes and components of the sensory volleys necessary for evoking a bar-pressing response. The superficial and deep radial nerve traces from cat 3 (five superimposed sweeps per trace) show a phase of after-positivity due to recording from the very large, cut end of the posterior division of the brachial plexus. The records of the hamstring nerve from cat 6 (ten superimposed sweeps per trace) are taken from the cut end of the dorsal root of L_7. Compound action potentials from the superficial radial nerve of cat 6 (not shown) all fell below the horizontal line as in the case of cat 3. These may be compared with the behavioral response curves of the same animals in Fig. 1*B*. Calibration 1 mv; 1 msec.

for at least a week. If discrimination thresholds for each nerve remained constant throughout, the animals were again anesthetized and recordings were taken from the exposed peripheral nerve bundles conveying the sensory volleys. This control procedure allowed evaluation of the types of fibers activated with the various stimulus intensities used during the bar-pressing trials. Compound action potentials were recorded from the cut posterior division of the brachial plexus (for superficial and deep radial nerve volleys) with stimulus intensities identical to those utilized during testing procedures. Afferent volleys from the hamstring nerve were obtained from cut dorsal root bundles at the level of L_7. The threshold of nerve activation was taken as the stimulus intensity needed to produce a just noticeable deflection in the oscilloscope tracings. Stimulus intensities were then also plotted as multiples of the threshold intensity for the conducted action potentials. Figure 1*A* illustrates increase in amplitude, expressed as the percentage of maximum, of the low threshold afferent groups in superficial radial, deep radial, and hamstring nerve compound action potentials with graded stimulus intensities relative to the nerve threshold. Irrespective of nerve type, all attained maximum between 2.3*T* and 2.7*T* (where *T* is the multiple of the nerve threshold).

Figure 1*B* illustrates the number of correct responses expressed as a percentage of the total number of trials at different stimulus intensities. Except for cat 3, which made errors 31 percent of the time, all animals pressed the bar with essentially no errors. The animals commenced bar-pressing with cutaneous volleys at stimulus intensities slightly below 1.00*T*. A few nerve fibers were activated below observable nerve thresholds but because of the noise inherent in the recording system they could not be detected. Between 1.00*T* and 1.20*T*, cutaneous volleys induced correct responses in 100 percent of the trials. In contrast to this no significant responses occurred with deep radial volleys until stimulus intensities exceeded 1.8*T*. Above a critical intensity muscle afferent stimuli evoked correct responses in all trials, as with cutaneous stimuli, but the slope of the response curves for muscular volleys was less steep than that observed for cutaneous effects; this presumably is related to gradual inclusion of joint afferents in the deep radial sensory volleys which are known to reach thalamic levels (*6*).

An even greater divergence from the cutaneous response patterns was observed with hamstring volleys. The response curve for cutaneous volleys for cat 6 (not shown) was almost identical to that of cat 1, but, with hamstring volleys, essentially devoid of joint afferent discharges, and with a full complement of groups I and II stretch receptor afferents, the same cat failed to make any discrimination below 3.81*T*. Considering the exquisite sensitivity of cutaneous volleys in promoting active discrimination in all animals studied, it is all the more remarkable that comparatively strong muscular nerve stimulation always failed to produce a response in the same animals unless a sharply defined limit was passed.

Figure 2 illustrates monophasic recordings of a graded series of compound action potentials from cats 3 and 6. All conducted volleys placed above the horizontal line failed to evoke discrimination whereas all examples below the line initiated bar-pressing within 15 seconds.

It may be concluded from Figs. 1 and 2 that activation of only a very small number of cutaneous fibers is sufficient to elicit nonpainful sensations. Essentially the same findings have been recorded in humans (*7*). Group I volleys in the deep radial nerve, however, may attain 75 to 95 percent of maximum before any discrimination of the volley is evident. Results from the hamstring nerve in Fig. 2 show that 100 percent activation of group I components and extensive activation of group II occurred before discrimination thresholds were attained. This allows a more definitive interpretation concerning the central projections of the stretch receptor sensory fibers. Since secondary sensory fibers from muscle spindles become activated between 1.7*T* and 1.8*T* and are extensively activated at or above 3.5*T* (*3*, *5*), it seems likely that all myelinated sensory fibers originating from muscle stretch receptors in the mammal, whether in group I or II fiber spectrums, do not influence those rostral elements of the brain involved in conscious perception. It furthermore substantiates the hypothesis that afferent nerves from muscle stretch receptors play no direct role in kinesthesis.

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15 May 1964

Immunocompetent Cells: Committedness

The ability of peritoneal exudate cells from previously immunized mice to give a logarithmic antibody response in x-irradiated isogenic recipients without further antigenic stimulus (*1*) is remarkable for several reasons. This kind of nonspecific anamnestic response has been looked for by several investigators without success, and in general no important qualitative difference has been found between peritoneal exudate cells and lymph node or spleen cells. Several years ago I was attempting to induce a nonspecific anamnestic response in rabbits previously immunized with bovine serum albumin (BSA). When the animals were "nonspecifically" stimulated with aggregated rabbit γ-globulin (RGG), their level of serum antibody rose threefold within a few days. I was on the point of reporting a brilliant success when in a moment of caution it occurred to me that a truly nonspecific stimulus should give a proportionate rise in all types of γ-globulin. A test of serum γ-globulins showed no detectable rise during this period, and subsequently the RGG preparation was found to be contaminated with BSA (*2*).

In Weiler's experiments the number of cells transferred (10 to 40 $\times$ 10^6) is equivalent to at least 1 percent of