structures, including their stereochemistry. It is of interest that the N^6 position of adenine is in the major groove of the DNA double helix, whereas the N^2 position of guanine is in the minor groove. The significance of attack by BPDE at these two different sites, with respect to stereochemical aspects, interference with base pairing, recognition by DNA repair enzymes, and the carcinogenic process, remains to be determined.

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14. The high-resolution spectrum was measured on a JEOL-01SG-2 instrument at 8 kV, 4.4 A; the probe temperature was 250°C. Further losses of 43 (CH_3CO) and 60 (CH_3COOH) mass units occurred from the *m/e* 444 fragment to give ions at 401 ($C_{24}H_{19}NO_5$, 50 percent) and 384 ($C_{24}H_{18}NO_4$, 100 percent). Consistent with the proposed structure were the ions corresponding to losses from the molecular ion of (i) CH_3COOH to give fragment 761 ($C_{40}H_{35}N_5O_{11}$, 20 percent), followed by losses of CH_3COO to 702 (20 percent) and CH_3COOH to 642 ($C_{36}H_{28}N_5O_7$, 85 percent); (ii) CH_3COO and the benzo(*a*)pyrene moiety to give an ion at *m/e* 334 ($C_{14}N_{16}N_5O_5$, 10 percent); and (iii) the ribose moiety and CH_3COO to give an ion at *m/e* 503 ($C_{29}H_{21}N_5O_4$, 10 percent), followed by a loss of CH_3CO to 460 ($C_{27}H_{18}N_5O_3$, 5 percent).
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Generation of Unidirectionally Propagated Action Potentials in a Peripheral Nerve by Brief Stimuli

Abstract. *Single, unidirectionally propagated action potentials can be elicited in peripheral nerves by electrical stimuli of short duration. Propagation in one direction is blocked anodically by means of a quasi-trapezoidal stimulus wave form and a modified tripolar electrode configuration. Propagation in the other direction proceeds unhindered. This technique may be applicable to collision blocking of motor nerves for neural prostheses.*

Electrical stimulation of a peripheral nerve ordinarily elicits two action potentials, which propagate in opposite directions from the stimulus site. We report a technique in which a single unidirectionally propagated action potential is generated by brief current pulses. This mode of stimulation could be used to effect motor-nerve blockage by introducing antidromic impulses in the peripheral nerve. The block would arise from the head-on collision (and subsequent mutual annihilation) of the natural efferent impulses and the artificially generated antidromic impulses. Directionally controlled stimulation is essential in producing antidromic impulses in order that the muscle receive no artificially generated neural activity.

We demonstrated the technique successfully in 15 cats by using the preparation shown in Fig. 1A. Regulated current pulses were delivered to the sciatic nerve through an asymmetrical tripolar cuff electrode (Fig. 1B). Of the current returning to the cathode, 10 to 30 percent originated from the proximal anode; the remainder flowed from the closer distal anode. Orthodromic propagation was blocked by the potential gradient arising between the cathode and distal anode, which interfered with the flow of excitatory action currents. Spurious orthodromic excitation that occurred distal to the block as a result of stimulus current spread was suppressed by the tripolar electrode configuration, which tended to contain current flow within the insulator. The stimulus wave form consisted of a square leading edge and a 350-μsec plateau phase followed by an exponential falling phase (*1*). Electromyogram (EMG) tracings were obtained by recording distally (R1) from the medial gastrocnemius with intramuscular electrodes of fine stainless steel wire. Compound sciatic neurogram tracings were obtained by recording proximally (R2) with 45-μm straight wires inserted into the nerve trunk with hypodermic needles (29 gauge).

Figure 2A shows a typical sequence of responses recorded at R1 and R2 with increasing stimulus amplitude. A maximal EMG response was elicited at an amplitude of 0.5 mA; as the amplitude was increased to 6 mA, the response disappeared. Simultaneously, the neurographic response grew to a maximum as smaller fibers were recruited. This demonstrates the feasibility of preventing orthodromic propagation from the stimulus site to the muscle. The persistence of the antidromic response is implied by the maximal sciatic discharge at R2. However, an additional experiment was required to demonstrate conclusively that the particular axons innervating the medial gastrocnemius were among those discharging antidromically. This was accomplished by establishing that, after the blocking stimulus, these axons were refractory on the proximal side of the blocking cuff.

Stimulating hook electrodes (S2) were placed proximal to the cuff and their stimulus amplitude was adjusted to produce a maximal EMG response with a 100-μsec pulse. Neurogram recording sensitivity was adjusted such that the compound action potential (recorded at R2) elicited by a maximal test stimulus at S1 to the medial gastrocnemius branch was clearly visible (trace a in Fig. 2B). Stimuli were then delivered at S2 immediately after the blocking pulse. The blocking pulse itself elicited a strong neural discharge at R2 (traces b to h). Stimulation at S2 failed to elicit any further neural activity when delayed from the onset of the blocking pulse by 1.75 msec or less (traces b and c). This indicates that all axons normally excited by stimulation at S2, including those innervating the medial gastrocnemius, were refractory in this time period, having already propagated an antidromic impulse in response to the blocking stimulus. As the delay was increased to 2.9 msec (traces c to g), the neural response gradually returned to normal and there was a simultaneous recovery of the maximal EMG response.

This stimulation technique may be applicable to development of a clinically useful motor-nerve block for spasticity control. For example, a short-term collision block may be very effective in controlling urinary sphincter spasticity (which interferes with efforts to urinate) after certain injuries to the spinal cord (*2*). Stimulus repetition rates adequate to block natural motor activity have been demonstrated, and successful biphasic coupling of the stimulus has been achieved (*3*). Although safe levels of electrical charge injection have not been determined for peripheral nerves, the stimulus strengths that we used appear to meet realistic electrode surface-area requirements (*4*).

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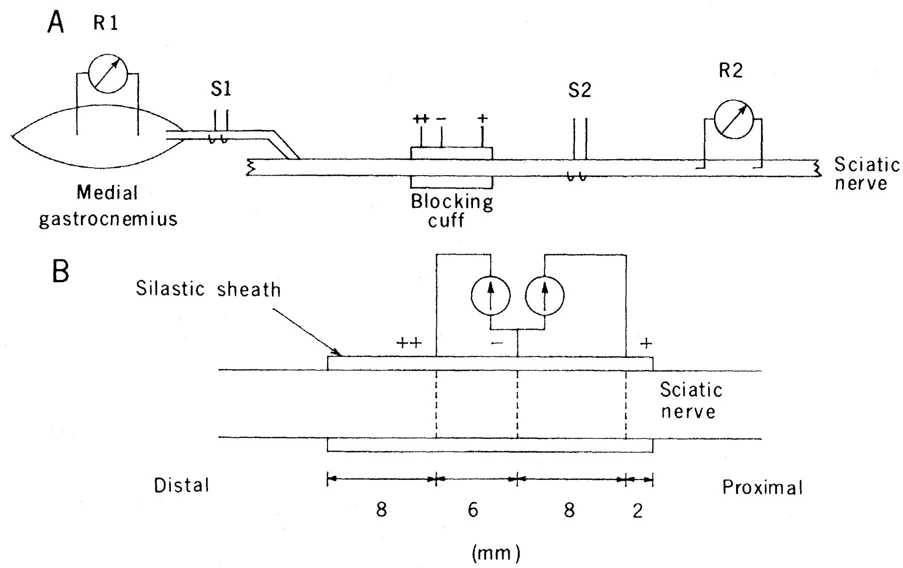

Fig. 1. (A) Experimental preparation: *R1* and *R2* represent EMG and neurogram recording sites, respectively; *S1* and *S2* represent silver hook electrodes. (B) Detail of insulated tripolar blocking electrode shown as blocking cuff in (A). Dashed lines represent rings within a silicone-rubber sheath (Silastic). Current is divided unevenly between the anodes.

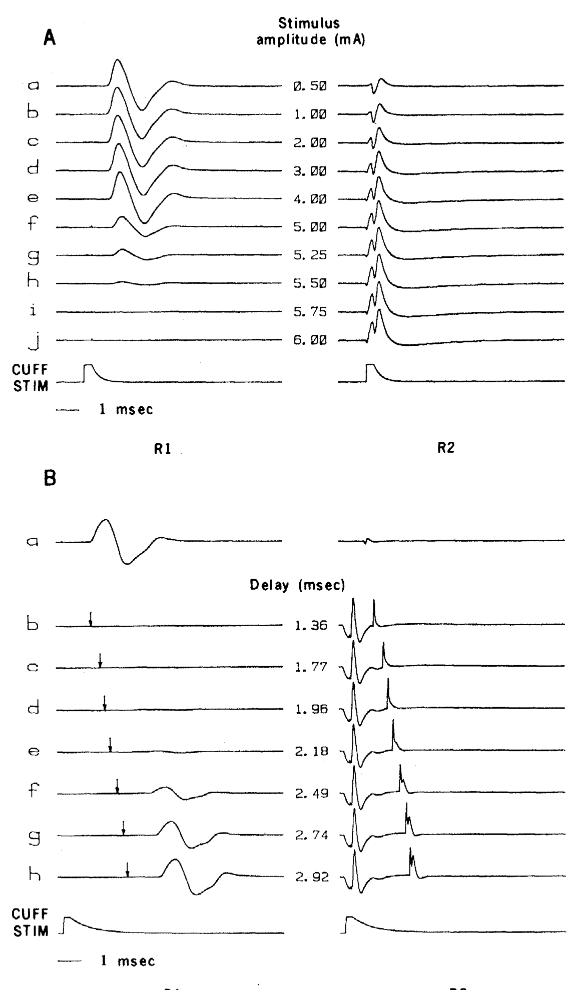

Fig. 2. (A) Electromyograms (*R1*) and sciatic neurograms (*R2*) of responses to blocking stimuli of increasing amplitude (350-μsec plateau, 350-μsec falling-phase time constant). (B) Confirmation of antidromically propagated excitation in response to the blocking stimulus. Trace a: test stimulus S1 elicits maximal EMG at R1 and compound action potential at R2 (axons to medial gastrocnemius only). Traces b to h: 100-μsec stimulus pulse at S2 delayed from the leading edge of blocking stimulus (2.8 mA, 1-msec falling-phase time constant). (Arrows indicate points of S2 stimulation on EMG traces.) Blocking stimulus elicits a maximal neural discharge at R2 (early deflection) but no EMG response. With a short delay (traces b and c), stimulus at S2 produces only a stimulus artifact at R2 (delayed deflection). With increased delay (traces d to h), neural response to stimulation at S2 develops as the delayed stimulus occurs outside the refractory period, and maximal EMG response develops.

References and Notes

1. These parameters represent the shortest stimulus pulse adequate to sustain an orthodromic block as determined by a study (C. van den Honert and J. T. Mortimer, in preparation) of responses to single pulses. Parameters investigated include pulse width (0 to 8 msec), linear (0 to 10 msec) and exponential (0- to 10-msec time constant) falling edges, fraction of current diverted to the proximal anode (0 to 100 percent), and electrode spacing. Of the current flowing through the proximal anode, the proportion necessary to suppress spurious excitation was never greater than 30 percent, and no adjustment during the course of an experiment was required.
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