

## FACILITATION BY PREVIOUS ACTIVITY IN A PACINIAN CORPUSCLE

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### ABSTRACT

A period of supernormal excitability is left by a propagated impulse in a Pacinian corpuscle. The increase in excitability is found 6 to 10 msec. after an impulse occurs in the corpuscle. Supernormality is produced by either mechanically elicited dromic impulses, or by electrically excited antidromic impulses. Generator potentials do not cause supernormality. Local potentials discharged spontaneously by the corpuscle, and which fall on the supernormal trail left by an antidromic impulse, become enhanced in amplitude, and eventually are turned into propagated dromic potentials. The supernormal period is interpreted as caused by a negative after-potential left at the first intracorporecular node of Ranvier which outlasts both the recovery time of the firing level and that of the generator potential during the corpuscle's relative refractory period.

### INTRODUCTION

In a preceding study a facilitatory state was described in Pacinian corpuscles (Loewenstein and Altamirano-Orrego, 1958). The facilitation was initially observed by sending an antidromic impulse into the corpuscle, and testing its threshold for mechanical stimulation at various intervals. It was then found that the threshold to mechanical stimuli becomes lowered for a short period following at approximately 7 msec. the arrival of an antidromic impulse to the corpuscle. This recalled the facilitation of the frog's cutaneous tactile receptor brought about by impulses travelling along sympathetic fibres to the skin (Loewenstein, 1956). In line with this earlier observation, it was at first thought that the facilitation in the Pacinian corpuscle was caused by dromic impulses conveyed to it by other fibres than its afferent axon. The assumption became further supported by the finding that sympathomimetic amines applied externally to the isolated Pacinian corpuscle rendered it more excitable to mechanical stimuli (Loewenstein and Altamirano-Orrego, 1956). The present experiments were done to examine the nature of the facilitation produced in the corpuscle by antidromic stimulation. They show that the aforementioned facilitatory state does not involve accessory fibres, but is the supernormal tail of the recovery cycle which each propagated impulse develops in the corpuscle travelling in either dromic or antidromic direction along the afferent axon.

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The experimental set-up and procedures have been described in the first of the present series of papers.

#### RESULTS

*Facilitation by a Dromic Impulse.*—In Fig. 3 of the first of the present series of papers a typical excitability curve is given for a Pacinian corpuscle. It can be seen that the threshold regains its normal resting value 9.5 msec. after the firing of a preceding propagated impulse. Just before recovering to normal, the excitability goes through a supernormal phase of 2 to 3 msec. duration. The change in excitability is small; it rarely amounted to more than a 15 per cent decrease of the normal threshold value at rest. During the supernormal period, an ordinarily subthreshold stimulus can be shown to reach the threshold for firing of a propagated impulse. An example is illustrated in Fig. 1 of the present paper. A mechanical test stimulus ( $S_2$ ), 14 per cent below threshold, is delivered to the corpuscle. When preceded by an 8 per cent subthreshold stimulus ( $S_1$ ),  $S_2$  is always unable to produce a propagated impulse (Fig. 1 *a*). If  $S_1$  is raised above firing threshold, a proportion of test stimuli sets up propagated impulses ( $P_2$ ) (*b*). The production of a supernormal phase in the corpuscle requires: (1) that the conditioning event ( $P_1$ ) be a propagated response. A facilitation could never be shown if a generator potential was used as conditioning event. (2) That the interval between conditioning and test response, as measured over 14 corpuscles, be from 6 to 10 msec. The intervals between  $P_1$  and  $P_2$  of Fig. 1 *b* and *c* demarcate the boundaries of the facilitatory period for this particular case.

*Facilitation by an Antidromic Impulse.*—The facilitatory state can also be evoked by an antidromic conditioning potential (Fig. 2). It is inconsequential to the resulting facilitation whether the antidromic impulse is produced by excitation of the axon with leads placed close to, or at several centimeters away from the corpuscle. Since in the latter instance the conditioning impulse must travel a considerable distance before entering the corpuscle, it appears that here again the facilitatory state is due to the trail of the propagated potential and not to a local conditioning potential.

In a few experiments the interval between arrival of the antidromic impulse to the corpuscle and occurrence of the facilitated response was calculated from data of axon distances and conduction velocity. To minimize errors, the axon was freed over a stretch of 5 to 8 cm. and the stimulating electrodes were placed at that distance from the corpuscle. The conduction speed was assumed to be uniform throughout the entire route of the impulse. If a change in velocity actually takes place over the *ca.* 0.5 mm. of intracorpuseular course of the axon (Quilliam and Sato, 1955), it may be expected to introduce an insignificant error in the calculation. An average interval of 7 msec. was found. This falls within the limits of facilitatory period resulting from dromically conducted impulses described in the preceding section.

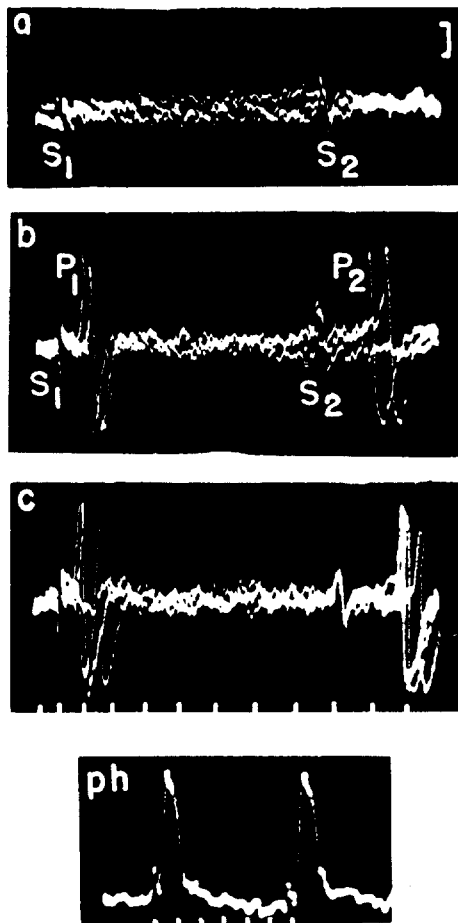


FIG. 1. Facilitation after a mechanically evoked propagated impulse. A subthreshold mechanical stimulus  $S_2$  is brought to firing threshold when preceded by a propagated potential  $P_1$ . *a*, Conditioning stimulus  $S_1$  is subthreshold. *b*, *c*,  $S_1$  is suprathreshold. Test stimulus  $S_2$  is of constant strength in all experiments. Three successive oscilloscope sweeps superimposed. Beyond the time limits demarcated in *b* and *c* by the interval between  $P_1$  and  $P_2$  a propagated response  $P_2$  is no longer observed. *ph*, photoelectric record of mechanical stimuli of magnitude as used in *b* and *c*. Time: 1 msec.

*Collision between Conditioning and Facilitated Response*—Our first observations were those of mechanically evoked responses facilitated by antidromic impulses. It seemed, at that stage, desirable to give a clear demonstration of the facilitation being actually caused by conditioning activity in the corpuscle's afferent axon, and not by that of any other fibre running along the same nerve into the corpuscle. For this purpose, an antidromic impulse (*A*) was set up by

electric stimulation of the axon before an ordinarily subthreshold mechanical stimulus. The interval between the two stimuli was so chosen that the mechani-

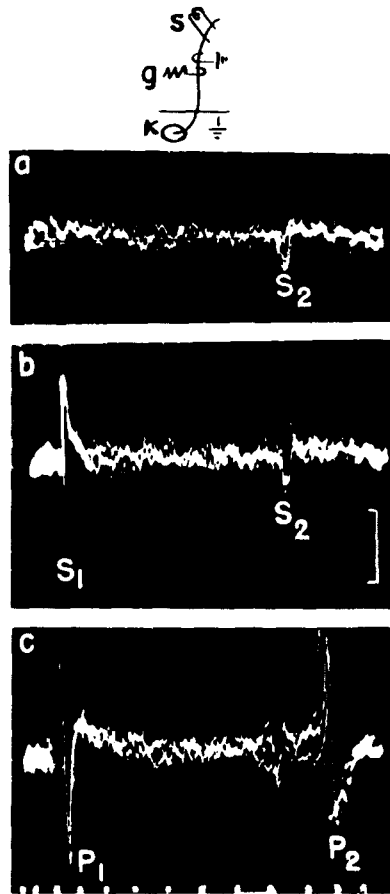


FIG. 2. Facilitation after an antidromic impulse. A constant mechanical stimulus  $S_2$  of subthreshold strength (*a*) satisfies threshold conditions when preceded by an antidromic impulse ( $P_1$ ) produced by electric stimulation of the axon (*c*). *a*, no antidromic stimulation; *b*, antidromic stimulus ( $S_1$ ) subthreshold; *c*, at threshold producing  $P_1$ . Three successive sweeps superimposed. Calibration: 1 msec.;  $50\mu\text{V}$ .

cal stimulus became facilitated to threshold. The antidromic stimulus was held at threshold strength throughout the experiment. The mechanical stimulus ( $S_2$ ) was then raised above threshold, producing upon repeated stimulation the constant appearance of a dromically propagated potential ( $M$ ) (Fig. 3 *a*). The conditioning stimulus ( $S_1$ ) was thereafter delayed so that its resulting response ( $A$ ) collided with, and abolished the dromically propagated mechani-

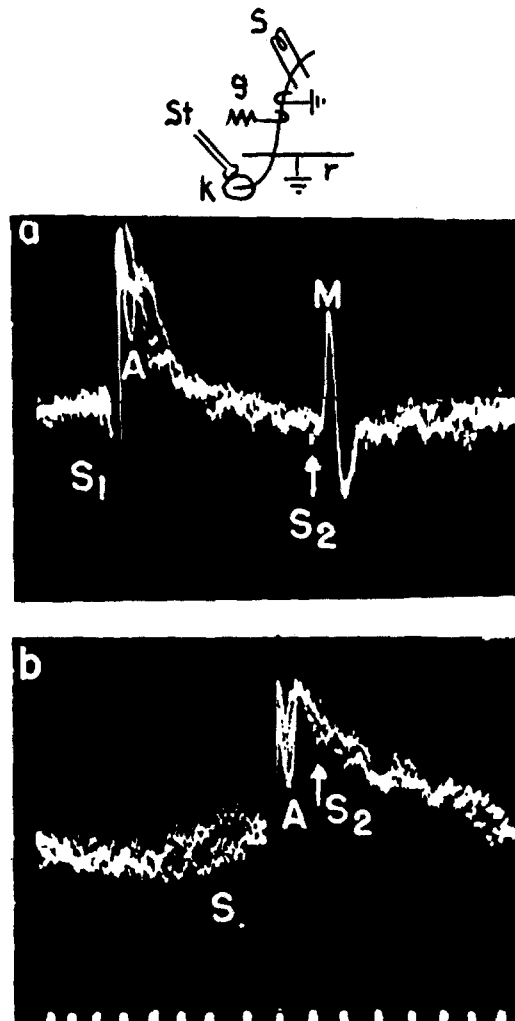


FIG. 3. Annulation of an orthodromic impulse by a preceding antidromic impulse. *a*, suprathreshold mechanical stimulus ( $S_2$ ) applied at arrow mark produces a potential ( $M$ ) which travels orthodromically to recording lead ( $r$ ) giving an initial upward deflection of oscilloscope beam. Antidromic impulse ( $A$ ) in response to electric stimulus  $S_1$  preceding  $S_2$  in 6.5 msec. does not interfere with  $M$  at this prolonged delay. *b*,  $S_1$  precedes  $S_2$  in 1.5 msec.;  $A$  collides with  $M$  before the latter reaches the recording lead. Superpositions of three successive sweeps. Distance between stimulating and recording leads was small. This caused the large initial upward deflection of the beam on top of which  $A$  is seen. Time: 1 msec. See text for further description.

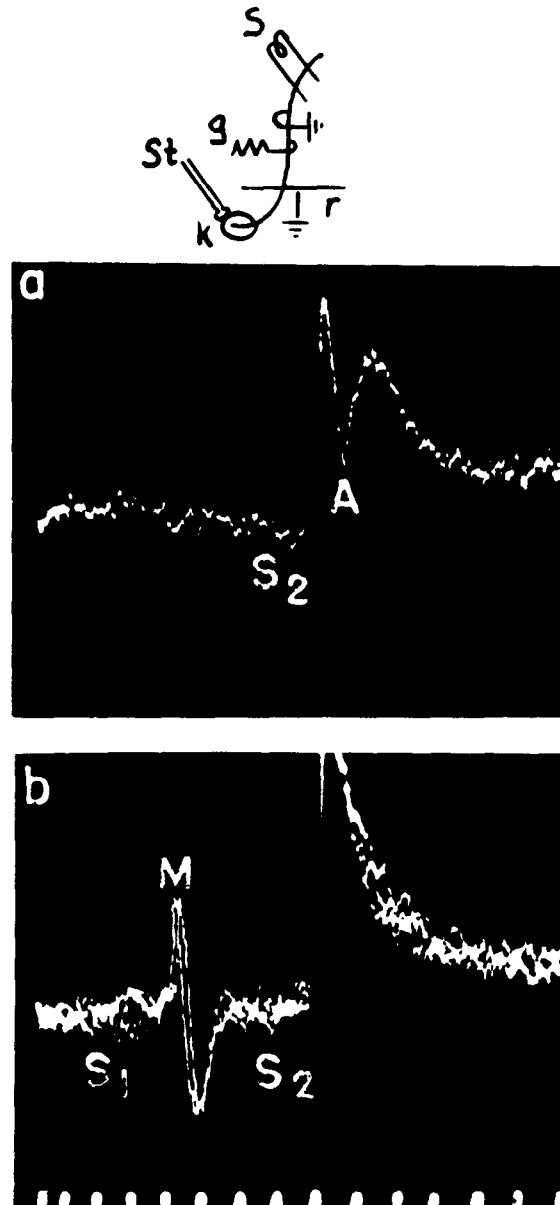


FIG. 4. Annulation of an antidromic impulse by collision with an orthodromic impulse. *a*, an antidromic impulse (*A*) is set up by an electric stimulus (*S*<sub>2</sub>) applied to the axon. *b*, an orthodromic impulse (*M*) caused by mechanical stimulation of the corpuscle 4 msec. before, cancels the antidromic impulse by refractoriness leaving no residual potential. Several sweeps have been superimposed. Time: 1 msec.

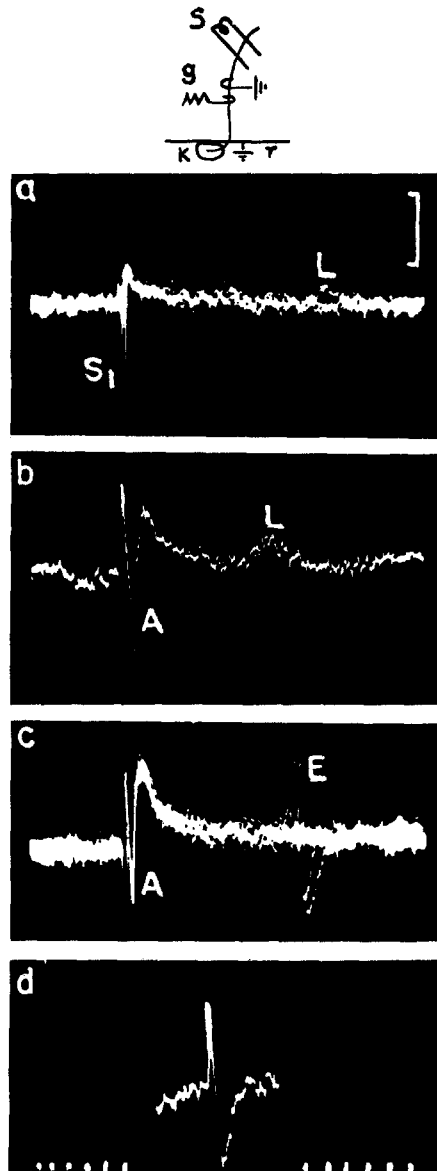


FIG. 5. Facilitation of subthreshold spontaneous activity. *a*, spontaneous local activity (*L*) discharged at random by the undisturbed corpuscle. *S*<sub>1</sub>, shock artefact of subthreshold antidromic stimulation. *b*, an antidromic impulse (*A*) travels towards the corpuscle causing in a proportion of applied stimuli an increment in the amplitude of local potentials or *c*, an orthodromic impulse (*E*) to appear as an echo at a relatively fixed delay from the antidromic impulse. Compare phases of "echo response" (*E*) with those of orthodromic impulse (*d*) produced by mechanical stimulation of the corpuscle. Several sweeps have been superimposed in *a* and *c*. Time: 1 msec.

before the latter reached the recording electrodes (*b*). Similar results were obtained by reversing the order of the events (Fig. 4). The antidromic response (*A*) then following after the dromic impulse (*M*) ran into the latter and was thus no longer detected. Since the collision leaves no detectable residual potential, it may be concluded that the facilitating as well as the facilitated impulse is conveyed by the same fibre, namely the corpuscle's afferent axon. Further support for this conclusion derived from the observation of facilitation of mechanically evoked responses by preceding mechanically evoked responses.

*Facilitation of Spontaneous Local Activity.*—Two mechanisms could account for the described facilitation: (1) the supernormal excitability is due to a diminution of the generator's firing level; (2) the generator potential becomes increased during the facilitatory period. The present facilitation, amounting at its best to 15 per cent increase in excitability, was too small, and the normal fluctuations of firing level, relatively too high, to allow meaningful information about small changes in firing level. Large decreases in firing level were not observed during the facilitatory period, and small reductions, if at all present, may have become masked by normal fluctuations.

To test the second possibility it was endeavoured to facilitate subthreshold spontaneous activity, in corpuscles which discharged non-propagated potentials "spontaneously." The randomly discharged local potentials (*L*) were recorded (Fig. 5 *a*). Besides, the axon was stimulated repetitively, each stimulus sending an antidromic impulse (*A*) into the corpuscle (Fig. 5 *b*). When a local potential (*L*) happened to fall within the above described limits of antidromic facilitation, it was usually seen to grow (*b*). Eventually, out of a number of antidromic impulses, some would cause the spontaneous local activity to be facilitated into dromically propagated potentials. These appeared then to arise from the corpuscle as an echo of the antidromic impulse, succeeding it at a fairly constant interval (*c*). By suitable placement of recording leads and by comparing the phases of the facilitated "echo"—potential with that of an impulse in response to mechanical stimulation (*d*), it was shown that the latter really originated within the corpuscle and travelled dromically along its afferent axon.

#### DISCUSSION

The present facilitation has several features in common with the supernormality known long ago in other excitable structures such as nerves (Adrian, 1920; Gasser and Grundfest, 1936) and cardiac muscle (Adrian, 1920 and 1921; *c.f.* Brooks, Hoffman, Suckling, and Orias, 1955). With the present recording conditions it is not possible to distinguish with certainty a "spontaneous" generator potential from an abortive "spontaneous" *T* potential, especially when the latter is small (*c.f.* Loewenstein and Altamirano-Orrego, 1958). Clear discernment requires, among other things, testing for the presence or absence of stepless gradations in potential with varying stimulus strength.



This, obviously, cannot be done with "spontaneous" potentials. The growing of local potentials during the corpuscles' facilitatory period does therefore not necessarily imply an increment in generator potential. On the contrary, the mutual independence which is found between recovery cycles of generator and propagated potentials (Loewenstein and Altamirano-Orrego, 1958; Loewenstein, 1958) makes it difficult to think of a propagated potential as cause of an increase in subsequent generator potential. It seems preferable to ascribe the growth of the local potential to the aborted *T* spike. A *T* potential, not existing in absence of facilitation may appear and summate with the generator potential under the present recording conditions; or an already existing "*T*" potential may receive an "all-or-none" addition during the period of facilitation (Loewenstein, 1958).

We are left therefore with the alternative that the facilitatory effects are due to a decrease in the minimal value of generator potential required for the firing of an impulse. This may in turn be brought about by a lowering of the critical transmembrane potential at which firing of propagated events occurs. No information was obtained at this respect, nor seems a lowering of the critical membrane level to have been shown for other structures which present similar supernormality. On the other hand it is likely that a negative after-potential will be associated with the lowering of minimal generator requirements. After-negativity is found in many types of nerve fibres and cells (Lorente de Nó, 1947; *c.f.* Grundfest, 1952; Brock, Coombs, and Eccles, 1952) and has been described for the frog muscle spindle (Katz, 1950) and for the slack stretch receptor cell of crustacean (Eyzaguirre and Kuffler, 1955). Let it be assumed that the propagated potential of the Pacinian corpuscle also leaves a prolonged depolarization behind at the first node of Ranvier. At the end of the relative refractory period the firing level at the node has reached its minimal value. By that time also the generator potential has fully recovered from refractoriness. If then the tail of after-negativity coincides with the end of the relative refractory period, the generator potential may add to the after-potential and thus reach the firing level with a subnormal stimulus strength. In the light of the present interpretation the presence or absence of a supernormal phase will depend on whether the after-negativity outlasts the 7 to 10 msec. of relative refractoriness.

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