ANTIDROMIC VASODILATATION IN THE PAW OF THE CAT

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One of the reasons why the chemical mediation of antidromic vasodilator effects has attracted the interest of numerous investigators is the proposal that the transmitter substance released might also act at central synapses.

Some years ago we made some observations on the cat's paw. Antidromic vasodilator effects were produced in the conventional way by stimulation of the exposed dorsal roots. Blood flow was recorded in one of the saphenal veins (1, 2).

Electrical, thermal (rapid heating to 45° C) and mechanical stimuli were observed to elicit marked vasodilatation in the paw. However, the preparation had a serious drawback. In spite of care being taken to minimize cooling and drying of the dorsal roots, the vasodilator responses progressively diminished, obviously due to declining of the excitability of the dorsal root fibers. Lately we therefore changed our technique somewhat. By aseptic procedures a sciatic nerve containing solely sensory fibers was prepared. In a first operation a unilateral abdominal sympathectomy was made; in a second the anterior roots L_6–S_4 were cut at the same side by an extradural approach just rostrally to the spinal ganglia. The cut efferent nerves were left to degenerate and the animals were allowed to recover for 2–3 weeks before they were used in the acute experiment. The animal was anesthetized with dial 60 mg./kg. given intravenously. The sciatic nerve was cut in the gluteal region and the peripheral stump placed on a Sherrington electrode. The electrical stimuli were sawtooth formed impulses from a thyratron stimulator.

The modified technique yielded a durable nerve preparation. Usually the fibers retained their excitability for more than 3 hours. As to the relation between stimulation frequency and vasodilator response the following observations were made. With a duration of each stimulation of 15 seconds, the responses reached a maximum at a frequency of about 5 impulses per second. With stimulation periods of longer duration, the peak of the curve might shift to even lower values. As few as 6 impulses delivered in 15 seconds sufficed to produce a recognizable vasodilatation.

If one compares vasodilator responses elicited by parasympathetic or sympathetic vasodilator impulses with those produced by antidromic impulses the differences are obvious. Fig. 1 shows vasodilator responses in the muscles of the hind limb to activation of the sympathetic vasodilator outflow (A), in the tongue to stimulation of the chorda tympani nerve (B) and in the paw to stimulation of the sciatic nerve (C), all in the cat. The first two responses have a rapid course. Observed with our technique they usually are over within less than a minute. The responses to antidromic impulses behave differently. The vasodilatation develops more slowly and reaches a plateau at which it stays for a longer or shorter time according to the intensity of the stimulus. The blood flow then slowly returns to its original level. As seen in Fig. 1 stimulation for 15

seconds was able to produce a vasodilatation in the paw that lasted for 10 minutes. Our technique does not allow any accurate determination of the latency of the responses but we have the impression that the responses to antidromic impulses occur with a considerably longer latency than those induced by parasympathetic and sympathetic impulses. The differences between the two types of vasodilator responses are illustrated in the schematic drawing in Fig. 1.

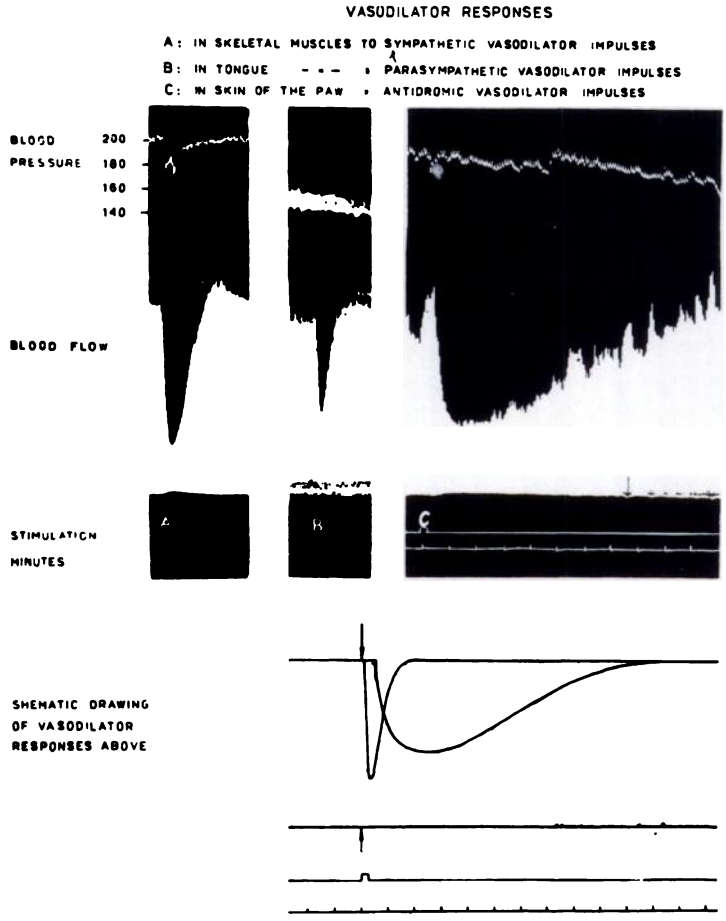

Fig. 1. Vasodilator responses in the cat. Above: A. Muscles of hind limb; response to activation of sympathetic vasodilator fibers by hypothalamic stimulation for 10 seconds. B. Tongue; response to stimulation of the chorda tympani nerve for 10 seconds. C. Left hind paw; response to stimulation of sensory fibers in a sciatic nerve for 15 seconds. From top to bottom: blood pressure, recorded with Hg-manometer (calibration on the left in mm Hg); bloodflow, recorded with optical drop recorder operating an ordinate writer (the ordinates are approximately inversely proportional to the rate of flow); signal line; time in minutes. Below: Schematic drawing illustrating the contrasts between the effects of impulses in parasympathetic and sympathetic vasodilator nerves and of antidromic vasodilator impulses in sensory fibers. In the diagram the vasodilator responses seen in A and C above are superimposed.

Mechanical stimulation (pinching with an arterial clamp 3 times), and thermal stimulation (heating to 45° C for 15 seconds) also produced vasodilatations that lasted for 5 to 10 minutes.

One can only speculate about the facts behind the different types of vasodilator response. In our experiments the vessels of the paw were sympathectomized and their responsiveness to the released vasodilator substance might have changed. However, let us assume that the vascular reactions to the released agent have not fundamentally changed. The long duration of the response indicates the release of a rather stable vasodilator substance that stubbornly clings to the receptors. The possibility exists that the character of the response might vary according to where in the periphery the vasodilatation occurs. The acetylcholine supposed to be released at parasympathetic and sympathetic vasodilator nerve terminals probably causes the arterioles to relax. We do not know where the antidromic vasodilator impulses attack. If I am not wrong, Pamela Holton thinks she has some evidence to indicate that they should reach the capillary bed. Sometimes I have an unorthodox thought and therefore a thought dangerous to reveal if one is not able to defend oneself. Are these fibers which carry the so called antidromic vasodilator impulses real vasodilator fibers in the sense that they terminate around the vessels? It is true that thermal, mechanical and chemical stimuli, able to produce pain, can elicit cutaneous vasodilatation. However, could one not imagine that the simultaneous activity of numerous pain fibers within an area leads to the release of some active substance at their terminals which by diffusion reaches and affects the minute vessels? Such a mechanism should explain the rather long latency and the slow increment of the antidromic vasodilator responses observed in our experiments.

In accordance with the observations of most investigators, no evidence was found to indicate that the antidromic vasodilator effects were produced by acetylcholine or histamine. Some observations have been presented to suggest that ATP should be the transmittor substance (3). Our observations do not permit any conclusions as to the validity of this proposal.

Whatever might be the chemical nature or the site of action of the vasodilator transmitter, the present observations do not indicate it to be a substance suitable as a synaptic transmitter. However, the possibility remains that the substance might have a central action fundamentally different from its peripheral action.

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