Short communications

Abolition of the nerve-induced responses of the isolated vas deferens of the young rat by agents blocking α-adrenoceptors

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The mechanical responses of isolated field-stimulated vasa deferentia from rats 3–10 days old were abolished by low doses of drugs blocking α-adrenoceptors. In preparations from older animals this effect was absent or there was a potentiation of the responses. The effect of atropine also changed during postnatal development. In the early period a moderate (10–40%) decline of the nerve-induced responses was generally observed, but later even high concentrations of atropine were without effect.

There have been some confusing findings with regard to the postganglionic adrenergic innervation of the vas deferens. One is the repeatedly reported observation that α-adrenoceptor blocking agents do not inhibit but rather enhance the responses of the isolated vas deferens to nerve stimulation in concentrations sufficient to abolish the responses to exogenous noradrenaline (for example, Boyd, Chang & Rand 1960). Concentrations 100–1000 times higher are generally needed to inhibit the nerve-induced contractions.

Another controversial topic has been the participation of cholinergic mechanisms in the motor innervation of the vas deferens. Cholinesterase inhibitors cause an atropine-sensitive potentiation of the mechanical response to nerve stimulation, but this response is usually not markedly influenced by atropine (Boyd *et al.*, 1960; Birmingham, 1966; Bell, 1967; Swedin, 1971a).

In a study on the postnatal development of the response of the rat isolated vas deferens to electrical stimulation it was noticed that the effects of α-adrenoceptor blocking agents and atropine were different in preparations from very young rats and changed into the adult pattern during the second to third week of life.

Methods.—Vas deferens preparations from young Sprague-Dawley rats were mounted in a superfusion bath (2ml) with two parallel platinum electrodes in the wall (Swedin 1971b, c). Tyrode solution (NaCl, 0·8%; KCl, 0·02%; $CaCl_2$, 0·02%; $MgCl_2$, 0·01%; $NaHCO_3$, 0·1%; NaH_2PO_4, 0·005%; and glucose, 0·1%) was equilibrated with 6·5% CO_2 and 93·5% O_2 at 36° C in an adjacent bath (25ml) and flowed at a constant rate of 3 ml/min through the organ bath via a short perspex tube at the bottom. The mechanical responses were recorded with an isotonic transducer on a Grass Polygraph. Transmural stimulation of the organs was performed by field stimulation (Birmingham & Wilson 1963) with biphasic pulses of supramaximal voltage, 10–25 Hz for 5 s at 1 min intervals. For nerve stimulation the duration of each pulse was 0·1–0·5 ms and for direct stimulation of the smooth muscle cells 10 ms.

Results.—Responses of the rat vas deferens to nerve stimulation were first obtained in preparations from animals aged 3 days (Swedin, 1971b). At all stages between 3 and 10 days phentolamine or phenoxybenzamine (0·2–2·0 μg/ml) caused complete inhibition of the nerve-induced contractions (Fig. 1A and B). Between the 11th and 15th day these drugs either became ineffective or potentiated the response to nerve stimulation (Fig. 1C).

The effect of atropine (0·5–2·0 μg/ml) also changed during the postnatal development. At earlier stages (3–15 days) there was generally a moderate decrease (10–40%) of the concentrations (Fig. 1B and C), which were not further influenced by increasing the concentration of atropine to 5 μg/ml. In preparations from older animals atropine was without effect in even higher concentrations.

Discussion.—The present study provides the first demonstration of a complete inhibition of the nerve-induced response of the vas deferens by phentolamine or phenoxybenzamine in concentrations which might be regarded as specific for the blockade of α-adrenoceptors.

The reason for the resistance of the adult vas deferens to α-adrenoceptor blocking agents appears to be the special arrangement of the terminal adrenergic network with a high proportion of very close neuromuscular junctions in this organ (Burn-

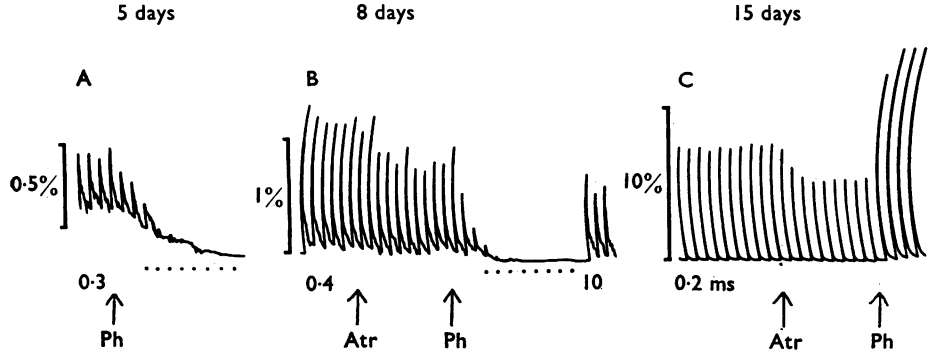

FIG. 1. Isolated vas deferens preparations from rats of different ages. The amplitude of the contractions in response to field stimulation is given as percentage of the total length of the preparations. A, 5 days old, length of preparation 17 mm; 20 V, 25 Hz, 0·3 ms pulse duration. Ph: phentolamine (2 μg/ml). B, 8 days old, length 23 mm; 20 V, 10 Hz, 0·4 or 10 ms duration. Atr: atropine (2 μg/ml). Ph: phentolamine (2 μg/ml). C, 15 days old, length 18 mm; 20 V, 10 Hz, 0·2 ms. Atr: atropine (1 μg/ml). Ph: phentolamine (1 μg/ml).

stock, 1970; Holman, 1970; Swedin, 1971c). The most probable explanation of the effect of α-adrenoceptor blocking drugs in the present study seems to be that these neuromuscular junctions might be immature and less intimate in the very young rats, even a considerable time after functional neurotransmission has been established (Swedin, 1971c); in this way the junctional receptors may be more susceptible to blockade by exogenous drugs. The altered reactivity to atropine during the first weeks of life also appears to speak in favour of such an unspecific mechanism.

The atropine sensitivity of a part of the mechanical response in preparations from rats younger than about 15 days seems to indicate that transmural stimulation liberates acetylcholine from some source within the rat vas deferens. The released amounts are, however, too low to evoke a registrable mechanical response after the α-adrenoceptors have been blocked.

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