

# Pre-synaptic $\alpha$ -adrenoceptor regulation of the twitch response of the mouse vas deferens

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Noradrenaline inhibits the twitch response of the mouse vas deferens and this inhibition is blocked by phentolamine (Jenkins, Marshall & Nasmyth, 1976). The mechanism of this inhibition has now been investigated using drugs that selectively affect pre- and post-junctional  $\alpha$ -adrenoceptors.

The twitch response to electrical stimulation of the mouse vas deferens (256 mA at either 0.2 Hz, 2 ms, or 0.1 Hz, 1 ms) was inhibited by noradrenaline (0.06–48  $\mu$ M) with an  $ID_{50}$  of 1.5  $\mu$ M. Clonidine, a selective pre-synaptic  $\alpha$ -adrenoceptor agonist (Starke, Endo & Taube, 1975), also inhibited the twitch (0.56–56 nM,  $ID_{50}$  6.25 nM) as did tyramine (3–30  $\mu$ M), an indirect acting amine (Trendelenburg, 1961),  $ID_{50}$  18  $\mu$ M.

Inhibiting uptake with cocaine (10  $\mu$ M) and oestradiol (3.7  $\mu$ M) increased the noradrenaline inhibition, did not affect clonidine inhibition and abolished the tyramine response.

The  $\alpha$ -adrenoceptors mediating the inhibition were investigated using the selective pre-junctional antagonist yohimbine (Starke, Borowski & Endo, 1975). The twitch response of the mouse vas deferens (0.25–2.0 ms, 0.2 Hz) was potentiated by yohimbine, 3.2 to 128 nM in a dose-related manner. The inhibition produced by noradrenaline and clonidine was reduced by yohimbine in doses below 10 nM.

Phenylephrine, an agonist selective for post-junctional  $\alpha$ -adrenoceptors (Starke *et al.*, 1975) potentiates the twitch response and also produces a contraction of the vas deferens. Both effects were abolished by phentolamine (Jenkins *et al.*, 1976).

However, neither action of phenylephrine was antagonized by yohimbine (10 nM).

Thymoxamine (0.3  $\mu$ M) a selective post-junctional  $\alpha$ -adrenoceptor antagonist (Drew, 1976), inhibited the contraction and potentiation of the twitch produced by phenylephrine (0.15–3.0  $\mu$ M) but did not affect the inhibition produced by clonidine (3.0–18.0 nM).

These results demonstrate that agonists selective for presynaptic  $\alpha$ -adrenoceptors produce inhibition of the twitch response of the mouse vas deferens and this is blocked by the selective pre-synaptic antagonist yohimbine. Conversely, phenylephrine, an agonist selective for post-synaptic  $\alpha$  receptors, potentiated the twitch response and caused contractions of the vas deferens, effects which were selectively blocked by a post-synaptic  $\alpha$ -receptor antagonist. The inhibition produced by endogenous noradrenaline released by tyramine also appears to be mediated via pre-junctional  $\alpha$ -adrenoceptors. This, together with the potentiation of the twitch by yohimbine, suggests that the motor response of the mouse vas deferens to electrical stimulation may be controlled through pre-synaptic  $\alpha$ -adrenoceptors.

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## References

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