An effect of neostigmine on the response of the rat anococcygeus muscle to field stimulation

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Neostigmine alters the shape of the response of the rat anococcygeus muscle to field stimulation, causing a 'shoulder' to appear during the relaxation phase (Figure 1).

Anococcygeus muscles from male Wistar rats (220–260 g) were suspended in Kreb's solution at 37°C gassed with 5% CO_2 in O_2. Field stimulation was applied via parallel platinum wire electrodes at 30 pulses/s, 1 ms and supramaximal voltage for 30 s every 6 min, and responses recorded isometrically.

The size of the 'shoulder' was dose dependent in the range 5×10^{-7} M to 5×10^{-6} M neostigmine, and was abolished by 5×10^{-8} M atropine, but was unaffected by 10^{-6} M (+)-tubocurarine. Physostigmine (10^{-5} M) produced a 'shoulder' which was abolished by atropine, whereas iso-OMPA (5×10^{-6}–10^{-4} M) and 1,5-bis (4-trimethylammoniumphenyl) pentan-3-one diiodide (3W 62 c 47; 10^{-7}–5×10^{-5} M) were without effect.

Total cholinesterase (ChE) activity of rat anococcygeus muscle was measured colorimetrically (Ellman, Courtney, Andres & Featherstone, 1961), and found to be 1.65 ± 0.13 μmol min^{-1} g^{-1} tissue. The slope of the plot of % inhibition of ChE against log concentration neostigmine was significantly different ($P < 0.001$) from the plot of the % maximum response against log concentration neostigmine for the neostigmine 'shoulder'. The ED_{50} for neostigmine was 1.4×10^{-5} M for ChE inhibition, but 9.6×10^{-7} M for the neostigmine 'shoulder'.

Preliminary experiments indicate that neostigmine enhances [^{3}H]-noradrenaline overflow from the rat anococcygeus muscle during field stimulation. Neostigmine might elicit repetitive firing of motor nerve terminals in skeletal muscle, by an effect unrelated to ChE inhibition (Riker, Roberts, Standaert & Fujimori, 1957; Blaber & Bowman, 1963; Blaber & Christ, 1967). The effect of neostigmine in the rat anococcygeus muscle could be elicited in an analogous way. Studies of the [^{3}H]-noradrenaline overflow from the rat anococcygeus muscle during field stimulation are being undertaken but have so far failed to yield conclusive results.

References

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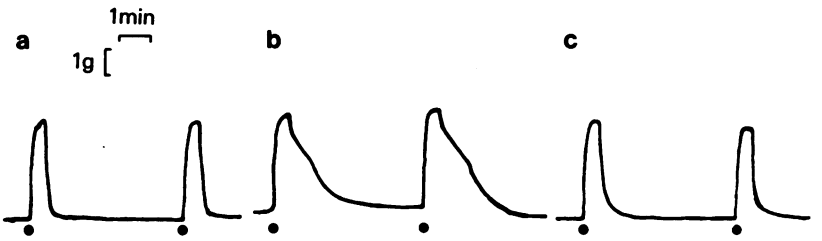

Figure 1 Responses of the rat anococcygeus muscle to field stimulation (●) (a) in drug-free Ringer, (b) in the presence of neostigmine (10^{-5} M), (c) in the presence of neostigmine (10^{-5} M) plus atropine (5×10^{-2} M).