Depolarizations recorded at locust excitatory nerve-muscle junctions in response to DL-ibotenic acid

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Two pharmacologically distinct populations of extrajunctional L-glutamate receptors, designated D (depolarizing) and H (hyperpolarizing), occur on locust skeletal muscle (Cull-Candy & Usherwood, 1973). It had seemingly been established that DL-ibotenic acid, a rigidly extended analogue of glutamate, activates H-receptors but not D-receptors and junctional glutamate receptors (Lea & Usherwood, 1973; Cull-Candy, 1976). However, we have recently obtained evidence which suggests the existence of ibotenic acid (Ib) receptors at locust glutamatergic neuromuscular junctions.

Iontophoresis of DL-ibotenic acid onto any part of the extra-junctional membrane of a locust muscle fibre evoked hyperpolarizations of up to 3 mV, but at certain locations usually either close to or within the cleft between adjacent fibres depolarizations of up to 15 mV were recorded. These Ib depolarizations were very localized. By using double-barrelled ibotenate/glutamate micropipettes, it was possible to show that regions of muscle membrane giving Ib depolarizations were excitatory junctional sites. By carefully mapping the distribution of ibotenate and glutamate sensitivities at these sites the Ib receptors were found to be restricted to a small area of junctional membrane. In many cases glutamate junctions were apparently devoid of Ib receptors.

Bath-applied glutamate (10^{-5} M) had no effect on the amplitude of currents evoked by iontophoretic application of ibotenic acid to voltage clamped muscle fibres. 10^{-4} M glutamate reversibly depressed the Ib currents by about 80%. Cross-desensitization studies using double-barrelled ibotenate/glutamate micropipettes, showed the desensitization effects of glutamate on the junctional responses and vice-versa to be dose dependent. Whereas it was possible to almost abolish the Ib response with prior application of L-glutamate the reverse was not true.

Reversal potentials of ibotenate and glutamate responses were determined by voltage-clamp. For Ib depolarizations the mean reversal potential ($\pm$s.d.) was -1.56 ± 3.27 mV ($n = 7$). Peak inward Ib current, at membrane potentials of -50 to -60 mV, was 30–40 nA for ibotenate doses of 1–5 nC. For similar membrane potentials peak inward glutamate currents were 80–100 nA. The mean reversal potential of these glutamate currents was -1.7 ± 5.3 mV ($n = 7$).

These results suggest that some of the glutamate receptors which occur at a minority of excitatory junctional sites on locust muscle are activated by DL-ibotenic acid.

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Interactions of methohexitone sodium and quaternary ammonium compounds at the avian neuromuscular junction

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Suxamethonium produces neuromuscular block of twitch fibres in the chick biventer cervicis muscle preparation and contracture of the multiply innervated slow fibres (Ginsburg & Warriner, 1960). The contracture is taken as a sign of a 'depolarizing' action. Elliott (1977) showed that a suitable concentration of methohexitone could block the contracture produced by suxamethonium without affecting its neuromuscular blocking action. During attempts to overcome this neuromuscular block produced by suxamethonium in the presence of methohexitone it was noted (unpublished observations) that tetraethylammonium bromide produced a small transient reduction in the block. A study of the interactions between tetraethylammonium and methohexitone is now reported together with observations on tetramethylammonium and tetra *n*-butylammonium.

The drugs used were: methohexitone sodium (METHO) (Eli Lilly), tetraethylammonium bromide