Isolation of male rats for 6–8 weeks after weaning, resulted in a marked increase in exploratory motor activity, rearing, sniffing and ambulation, when placed in an open field (novel) situation, compared to group-housed controls. Isolated rats were also more sensitive to the effects of isoprenaline, but not noradrenaline on the cardiovascular system.

(±)-Propranolol, 0·2–0·5 mg/kg (s.c. given 15 min before exposure to open field) reduced the hyperactivity of these rats to the control level found in group housed animals. Higher doses did not further reduce activity. Propranolol had no influence on motor activity of normal rats in doses below 20 mg/kg. The reduction of the hypermotility by (±)-propranolol could be attributed to any one of its pharmacological actions; blockade of β-adrenoceptors, membrane stabilization or a reduction in catecholamine release. We therefore compared its effects with those of (+)-propranolol which has only weak β-receptor blocking activity, and with practolol, which lacks the local anaesthetic effect, while both drugs retain the ability to reduce catecholamine release (Eliash & Weinstock, 1971 ; Weinstock, 1973).

Both (+)-propranolol and practolol, 0·5–1 mg/kg, reduced the hyperactivity of isolated rats without affecting motor activity of normal controls. This finding suggested that all three drugs may affect this form of abnormal behaviour by reducing an excessive release of central catecholamine.

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Atropine sensitivity of transmission and facilitation in the rabbit superior cervical ganglion

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Evidence has accumulated in recent years suggesting that muscarinic receptors play a part in transmission through sympathetic ganglia and particularly in the facilitation following trains of conditioning stimuli (Libet, 1964). The Late Negative (LN) wave seen after single or trains of ganglionic action potentials is thought to be involved in this facilitation, as both coincide in time of onset and the LN wave is very sensitive to atropine.

We investigated this problem using the excised ganglion maintained at 37° C in a bath which allowed continuous superfusion with Krebs solution. Stimuli supramaximal for the main (Sa) component of the postganglionic compound action potential were delivered to the preganglionic trunk 30 mm proximal to the ganglion; responses were recorded either from the ganglion or from the internal carotid nerve 3 mm distal to the ganglion. The action potentials recorded remained relatively stable for several hours, although a slow decline in amplitude was sometimes seen. Perfusion with 0·29 μM atropine sulphate, (0·1 μg/ml), caused a reduction in Sa amplitude. This reduction was maximal after approximately 25 min. 2·9 μM atropine (1 μg/ml) caused no further reduction. Allowing for any steady decline, spike amplitude was decreased by 9±1% (mean, S.E. of mean, n=14) by 2·9 μM atropine.

The pattern of facilitation following a single conditioning stimulus reveals phases of

early (peak 40–75 ms) and late facilitation (peak 700–2,000 ms), neither of which are significantly reduced by atropine (Brimble, Wallis & Woodward, 1972). The present results indeed suggest some variable increase in early facilitation in the presence of atropine, possibly due to an increase in the subliminal fringe. Increasing the number of conditioning stimuli increased the magnitude of late facilitation from 10±1% (n=6), following single stimuli to a value of 29±3% (n=5), following a 1 s, 30 Hz train. After a 1 s, 10 Hz train of stimuli a maximal facilitation of 20±2% (n=19), was obtained. Atropine, 2·9 μM, caused a marked though variable reduction (26±6%, n=6) in this facilitation. The facilitation following a 30 Hz train was also substantially reduced. However, we have been unable to demonstrate post-train facilitation with heterosynaptic testing.

In contrast to the lack of effect of atropine on the late facilitation following single conditioning stimuli, the LN wave was reduced after approximately 25 min by 70±4%, (n=5), in the presence of 2·9 μM atropine, but 29 μM atropine caused no further reduction. 0·29 μM atropine was also effective in reducing the LN wave. After trains of stimuli, measurement of the LN wave is difficult, as it is partially or totally submerged by the P wave (Libet, 1964). It appears superimposed on the declining phase of the P wave and, although 2·9 μM atropine reduced this LN wave, it was not possible to estimate the extent of the reduction.

We conclude that post-train facilitation is partly mediated via muscarinic receptors, but that these receptors apparently play no part in the late facilitation seen after a single conditioning stimulus. Experiments in progress using heterosynaptic testing suggest presynaptic mechanisms are primarily involved.

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Some studies on the convulsant action of folic acid

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It has been suggested that the anti-folate effect of anticonvulsants may be related to their therapeutic action (Reynolds, 1967) and it is known that folic acid (FA) is a convulsant when given intraventricularly to dogs (Hayashi, 1959) and rats (Hommes & Obbens, 1972; Noell, Magoss, Cohen, Holland & Walters, 1960). We have compared FA and some known convulsants by intracerebroventricular (I.C.V.) and intravenous injection in mice.

TABLE 1. *ED50 values to induce convulsions and hind-limb extension (HLE), and convulsion latencies, for folic acid and some known convulsants by intracerebroventricular and intravenous injection in mice. In the calculation of each ED50 a minimum of 50 mice was used disposed over at least 5 doses*

Response	Folic acid	Leptazol	Picro-toxin	Strych-nine	Bicucu-lline	Glutamic acid	Ouabain
A. Intracerebroventricular (i.c.v.) ED50							
μg/mouse							
Convulsions	17·8	330·0	1·3	2·2	1·1	145·0	1·3
HLE	20·5	617·0	6·8	6·3	6·5	780·0	>20
Conv. latency (secs)	104·0	18·8	134·8	83·1	26·8	6·3	140·4
B. Intravenous ED50							
mg/kg							
Convulsions	846·0	29·4	5·8	0·5	0·5	>1800	>20*
HLE	1,024·0	41·8	11·5	0·6	0·8	—	—
Conv. latency (secs)	5,843·0	3·1	157·0	53·1	4·3		
C. Ratio of doses i.v./i.c.v. × 0·05 (1 μg/mouse = approx. 0·05 mg/kg)							
Convulsions	950·0	1·7	89·2	4·5	9·1	—	—
HLE	996·0	1·3	33·8	1·8	2·4		
Conv. latency (secs)	56·2	0·2	1·1	0·6	0·2		

* Lethal dose.