hydrates can be a source of some energy for the H^3NE uptake by isolated frog ventricle.

Resumen. El tratamiento con iodoacetato (IAA), no modifica la incorporación y retencion de H^3Norepinefrina (H^3NE) al ventriculo aislado de *Rana* oxigenado y suspendido en ringer con o sin glucosa. Bajo atmosfera de Nitrógeno y ausencia de glucosa, la incorporacion de H^3NE es bloqueada en un 58%; en estas condiciones el IAA produce un ulterior bloqueo del 33%.

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Pressor Response to Oxotremorine in Atropinized Rats

Oxotremorine, the active metabolite of tremorine, is known to produce parkinson like effects in experimental animals and has been widely recommended for evaluating potential antiparkinson drugs[1,2]. Oxotremorine has been typically classified as a muscarinic agent and reported to be devoid of nicotinic property[2,3]. Muscarinic potency of oxotremorine is comparable to acetylcholine[3]. Nicotine like effect of oxotremorine at neuromuscular junction manifested by muscular twitchings and subsequent paralysis has been reported recently[4]. We have now examined whether oxotremorine exhibits nicotinic effect on blood pressure in anesthetized and atropinized rats.

Methods. Albino rats of either sex (150 to 230 g) were anesthetized with urethane (1.4 g/kg, s.c.). Polythene tracheal, left carotid and left femoral cannulae were inserted: 100 U of heparin were then administered i.v. to each rat and these were artificially ventilated. In one set of experiment rats were pithed by inserting a suitable pithing needle through one orbit down the spinal cord. In another set of experiment bilateral adrenelactomy was performed through the abdominal route.

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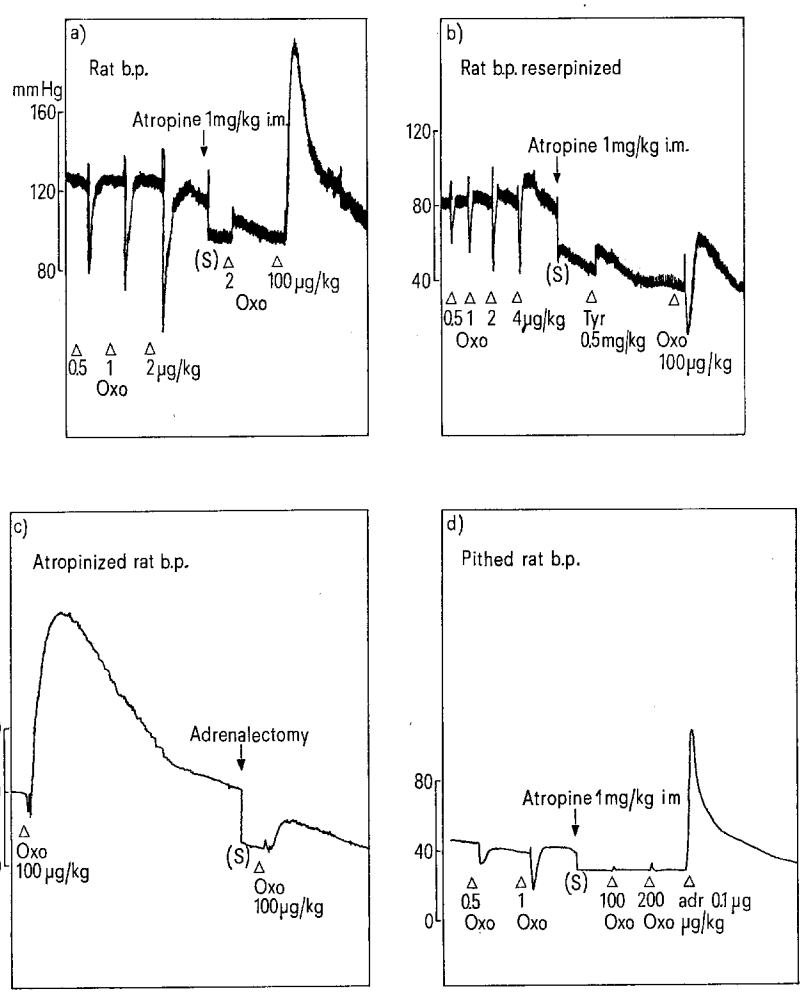

Effect of oxotremorine sesquifumarate (Oxo) on rat blood pressure. Tyr, tyramine sulfate; S, stopage of kymograph for 45 min.

Blood pressure was recorded on a smoked rotating drum through a mercury manometer from the left carotid artery. Drugs were injected in a constant volume of 0.2 ml, through a femoral vein. In all experiments atropine sulphate was injected at a dose of 1 mg/kg i.m. 45 min before administration of oxotremorine. At least 6 experiments were performed in each set.

Results. Administration of oxotremorine sesquifumarate (Aldrich) at doses between 0.5 to 2 µg/kg i.v. resulted in instantaneous and transient fall of blood pressure (Figure a). The vasodepressor effect of oxotremorine was abolished after atropine (Figure a). However, a 100-fold increase in dose of oxotremorine (50 to 200 µg/kg, i.v.) in atropinized rats resulted in a fast increase of blood pressure (Figure a). The vasopressor effect in atropinized rats lasted for 20 to 35 min followed by no subsequent vasodepression. The average percentage of pressor response of oxotremorine after a dose of 100 µg/kg i.v. was found to be 104 ± 12.4 (S.E.). Repeated administration of a vasopressor dose of oxotremorine resulted in complete trachyphylaxis.

The vasopressor effect of oxotremorine in atropinized rats was abolished when repeated 1 h after dibenzyline (1 mg/kg, i.m.) administration. The pressor response to oxotremorine after administration of atropine was absent in reserpinized (1 mg/kg/24 h, i.m. for 48 h) rats (Figure b). Reserpinization was ensured by abolition or marked reduction of i.v. administered tyramine (0.5 mg/kg).

Tetraethylammonium bromide (50 mg/kg, i.v.) similarly reduced the vasopressor response to oxotremorine. Bilateral adrenalectomy either markedly reduced or abolished the pressor response to oxotremorine in atropinized rats (Figure c).

In order to detect any central component in the pressor action of oxotremorine, its effect was investigated in pithed rats before and after atropine. The pressor effect to oxotremorine after atropine could not be demonstrated in pithed rats. However, the vasodepressor effect of low doses of oxotremorine before atropine remained unaltered in pithed rats (Figure d).

Discussion. The results obtained suggest that the pressor response to oxotremorine after cholinergic blockade by atropine is due to ganglionic stimulation and subsequent liberation of catecholamine from the suprarenal medulla. Abolition of pressor responses to oxotremorine by a) the adrenolytic agent dibenzyline; b) the ganglion blocking agent tetraethylammonium; c) bilateral adrenalectomy and d) reserpinization, provide validity for such conclusion. Pressor effect to oxotremorine could not be demonstrated in pithed atropinized rats which indicates that oxotremorine has no effect at peripheral nicotinic site like acetylcholine. However, the peripheral muscarinic action of oxotremorine remained unaltered in pithed rats. Absence of vasopressor response in atropinized pithed rat suggests that liberation of catecholamine from suprarenal medulla is entirely central y mediated. Nicotine has been shown to cause liberation of catecholamine from adrenal medulla through a central mechanism[5]. We, therefore, propose to qualify the pressor response to oxotremorine in atropinized rats as central nicotinic effect of the drug. A stimulant action on the superior cervical ganglion has been reported following close arterial injection of oxotremorine[6] but this may be blocked by atropine and appears to be analogous to the specific effects of other muscarinic agents on autonomic ganglia[7].

Zusammenfassung. Eine zentrale, nikotinartige Wirkung von Oxotremorin wird am Blutdruck der Ratte beschreiben.

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Effects of Tybamate and Pentylenetetrazol on Spinal Interneurons

It has recently been shown that the central muscle relaxant tybamate (Solacen) acts primarily by depressing spinal polysynaptic reflexes[1,2]. This effect can be adequately explained as a depressant action on spinal internuncial neuronal activity[2]. Similar studies with the analeptic pentylenetetrazol (Metrazol) indicate opposite results, that is, an enhancement of polysynaptic activity with a depression of the electrically evoked monosynaptic response[3,4]. Later reports, attempting to explain these effects by recording the activity of single Renshaw cells following pentylenetetrazol administration, were negative[5]. Also, it appears that pentylenetetrazol does not directly affect motoneuron excitability[6]. With this in mind, the present study was designed to determine whether pentylenetetrazol affected spinal internuncial neuronal activity and also if pentylenetetrazol antagonized the depressant effects of tybamate.

Materials and methods. The experimental procedures employed in this investigation have been previously described[1,2]. Briefly, midcollicular decerebrate cats were prepared under ether anesthesia. Arterial blood pressure was measured from the left common carotid artery and drug injection was via the radial vein. The contralateral polysynaptic extensor reflex was elicited by stimulating the central end of the cut left sciatic nerve and recording contractions of the contralateral quadriceps femoris. For the spinal interneuron studies, decerebration was followed by laminectomy at L_{1-2} and transection of the spinal cord. The animals were artificially ventilated with room air. The dorsal and ventral roots of L_7 were dissected free, sectioned and mounted on Palmer bipolar electrodes for orthodromic and antidromic stimulation, respectively. Extracellular unit activity was recorded from single spinal interneurons with the electrode positioned medial to or on the line of L_7 dorsal root entry and 1.5 to 3.5 mm below the cord surface. The exposed area of the cord was bathed in mineral oil and maintained at 36–37 °C.

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