It would seen that the rat mesentery offers a useful *in vitro* system on which the effect of permeability-reducing drugs can be investigated and these preliminary observations suggest that it behaves in some ways like the endothelium of blood vessels.

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Effect of Pyrogallol on Acute Learning in Rats

SIR,—Pyrogallol causes an increase in the contents of adrenaline and noradrenaline of the brain of mice (Izquierdo, J. A. and Biscardi, 1961) and rats (Izquierdo, J. A., Juorio and Dezza, unpublished) presumably by inhibition of their *O*-methylation. It seemed to us, therefore, a useful tool for a preliminary approach to the study of adrenergic mechanisms in learning.

At a dose of 200 mg.kg. i.p., in rats, it promoted habituation of investigatory-orienting and of arrest unconditioned reflexes to a buzzer to which there normally was none. The startle reflex was unaffected. The buzzer had a duration of 3 sec. and was presented 50 consecutive times (intervals between buzzes: 30–90 sec.) to 26 animals, 19 of which received pyrogallol and 7 water, 3 min before testing.

In other groups of rats, after 20 "control" presentations of this buzzer alone, it was paired with a shock (0·5 sec. of 150/sec. 100 V × 0·1 msec. rectangular pulses) delivered 1–2 sec. after it to a metallic grid on the floor of the training box. An instrumental response (lifting of one or both forepaws) appeared after 5–15 pairings, and reached a stable level of 50–90 per cent per block of 10 trials after 40–50 trials. The initial rate of appearance of the conditioned reflex was significantly lower in 9 rats to which pyrogallol was given 3 min. before the session began, as compared with 7 water-treated ones. In 8 other rats in which pyrogallol was given later during the reinforcement stage, when the instrumental response was already stabilised, its performance was unaffected.

In 7 rats, pyrogallol was injected 3 min. before beginning an extinction of the conditioned reflex; the rate of the extinction was significantly higher than in 7 other water-treated rats.

Pyrogallol is known to produce a slight increase in blood pressure which is counteracted by phentolamine (Izquierdo, 1962), and an increase in duodenal motility which is blocked by atropine (Izquierdo and Izquierdo, 1961; Izquierdo, 1962), both effects lasting 15–40 min. Neither phentolamine (10 mg./kg., 7 rats) nor atropine (1 mg./kg., 7 rats) given i.p. 1 min. before pyrogallol, modified the effect of the latter on extinction. Phentolamine alone (7 rats) had an effect not different from that of water, but atropine (7 rats) increased the extinction to a level not significantly different from that attained either with pyrogallol alone or with both drugs in combination.

Thus, any reflex influence of blood pressure or increase of duodenal motility by pyrogallol on extinction can be disregarded, and an effect on brain catecholamines is left as the most likely mechanism. But the action of atropine on extinction suggests, nevertheless, some interaction (other than duodenal) between both drugs.

Habituation and extinction, and possibly sleep, belong to the same category of phenomena, those of "internal inhibition." This is a process opposed by reinforcement, for it tends not to appear in its presence (Pavlov, 1960). This might explain the fact that in our rats a conditioned response was unaffected by pyrogallol during the reinforcement stage, whereas pyrogallol clearly enhanced internal inhibitory processes in situations where reinforcement was absent, like habituation, or extinction.

The decreased rate of establishment of a conditioned reflex, in view of the results on habituation, may be due to the fact that the "inhibitory property" of the conditioned stimulus (Konorski, 1948) was increased by pyrogallol.

In no experiment did our rats show any motor disturbance nor any apparent neurological symptom. The response to shock itself was obviously unmodified by pyrogallol.

Our data on enhanced internal inhibition by pyrogallol, if in fact due to the increase in cerebral catecholamines, may be in agreement with those that ascribe a "central inhibitory," sleep-inducing property to centrally active catecholamines (Bass, 1914; Domer and Feldberg, 1960). Attention is obviously drawn towards those diencephalic and mesencephalic structures which are normally rich in these transmitters (Vogt, 1954).

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December 6, 1962

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Lecithin-cholesterol Sols

SIR,—Further studies have been made of the clear lecithin-cholesterol sols formed by ultrasonic irradiation of coarse dispersions (Saunders, Perrin and Gammack, 1962). Electron micrographs of the residues obtained when the sols are dried down with sodium phosphotungstate as a negative stain, indicate that the lecithin sols alone give round particles many of which have a mean diameter in the range 100 to 200 Å, while the lecithin-cholesterol sols show many membrane-like structures of thickness 40 to 50 Å. A 1 : 1 molar ratio is the maximum cholesterol : lecithin ratio which gives stable dispersions.

The formation of interfacial membranes from concentrated lecithin-cholesterol sols has been examined. Since a cell membrane is probably formed by a precipitation reaction between the cell contents containing a high concentration of lipid and the environmental fluid, a film precipitated at an interface between a lecithin-cholesterol sol and another aqueous solution should give a realistic model of a natural membrane.