TABLE 1. *Effects of drugs on the exploratory behaviour of septal rats placed in a Y-box*

Drug	Dose mg/kg s.c.	Mean entries in the arms ± S.E. Controls	Septal rats
Saline	—	3·06±0·44 (16)	5·12±0·75 (8)‡
Hyoscine	0·5	8·31±1·25 (16)*	1·9±0·73 (8)†§
Amphetamine	5·0	10·56±1·89 (16)*	15·0±4·18 (8)†

Number of rats in brackets.
* Different from saline with $P=0{\cdot}01$. † Different from saline with $P=0{\cdot}01$.
‡ Different from controls with $P=0{\cdot}02$. § Different from controls with $P=0{\cdot}01$.

These results support the view that the septum plays a role in the central cholinergic pathways as also suggested by the work of Lewis, Shute & Silver (1967) and of Szerb (1967).

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The brain acetylcholine system in barbitone-dependent and withdrawn rats

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Hypotheses to explain development of physical dependence and central nervous tolerance suggest that the mechanisms involved represent a compensatory reaction to the altered pattern of nervous activity produced by the drug in question. One type of theory supposes that the synthesis, release and/or destruction of transmitter(s) is affected, while a second type supposes that neuronal sensitivity to normal amounts of transmitter is altered (Collier, 1965, 1968). Although many workers have studied the effect of chronic morphine administration and withdrawal on brain neurochemical systems, few have studied drug dependence of the barbiturate type.

Female Wistar rats were made dependent on barbiturate by the administration of up to 400 mg/kg per day of barbitone sodium in the drinking water for 4 weeks. Withdrawal was effected by replacing barbitone solution with drinking water.

Chronic barbitone administration and withdrawal did not produce any change in the following, all determinations being made on the brains removed from control, barbitone-dependent and 48 h withdrawn animals: (1) acetylcholine content, cholinesterase and choline acetyltransferase activity of frozen brain removed from animals killed by total submersion in liquid air; (2) the ability of cerebral slices to synthesize acetylcholine; (3) the ratio of "free" to "bound" acetylcholine extracted from freshly excised brain.

To determine whether chronic barbitone administration or withdrawal affects sensitivity to acetylcholine-like drugs, the effects were studied of physostigmine (3 μg) or pilocarpine (50 μg) administered intraventricularly, on rectal temperature. All animals were pretreated (30 min) with atropine methylnitrate (2 mg/kg intraperitoneally). Body temperature was chosen because: (1) it is decreased by injection of acetylcholine, carbachol or oxotremorine into the hypothalamus or cerebral ventricles, an effect prevented by atropine (Lomax & Jenden, 1966; Lomax & Kirkpatrick, 1969); (2) barbiturates depress the hypothalamic temperature regulating centre and the barbitone dependent rat is partially tolerant to this effect. Thus the mean body temperature of barbitone dependent animals (37·3$\pm$1·1 (20) °C) was only slightly below that of a control group (37·6$\pm$0·7 (24) °C); (3) the tolerance mechanisms involved at this site may be the same as those in other parts of the brain.

The fall in body temperature produced by either drug was similar in control and withdrawn animals, but a slower return to normal was observed in the withdrawn group. In contrast, a prolonged hyperthermia followed pilocarpine in barbitone-dependent rats; with physostigmine a biphasic response was observed, an initial rise in temperature followed by a fall, with a return to normal after 2 h.

Thus, in the rat, chronic barbitone administration and withdrawal can affect, both qualitatively and quantitatively, the change in body temperature caused by pilocarpine and physostigmine.

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The relationship between the anti-inflammatory and irritant properties of inflammatory exudate

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A possible mechanism for the systemic anti-inflammatory effects of counter-irritants is that at a site of inflammation a factor or factors are produced which then enter the blood stream and exert the action at a distant site (Laden, Blackwell & Fosdick, 1958). This hypothesis gained support from Robinson & Robson (1966), who showed that inflammatory exudate, obtained from polyester sponges implanted subcutaneously in rats, exerted anti-inflammatory effects, possibly due to the presence of the humoral mediators postulated by Laden, Blackwell & Fosdick (1958). However, results obtained by Atkinson, Boura & Hicks (1969) indicated that the anti-inflammatory activity of sponge exudate was itself mediated through a counter-irritant mechanism.

Contrary to the findings of Robinson & Robson (1966), sponge exudate was found to be markedly irritant. Furthermore, such material was shown to exert systemic but no local anti-inflammatory activity. The object of the present work was a confirmation of the possible relationship between the two activities of sponge exudate.