arise because photocells pick up small movements, for example, head shaking (Rushton & Steinberg, 1963) which we did not score and which may constitute " stereotyped " activity (Randrup, Munkvad & Udsen, 1963). With some mixtures of amphetamine and amylobarbitone (Rushton & Steinberg, 1967), high proportions of amylobarbitone make animals walk more and rear less, probably because of ataxia (Rushton & Steinberg, 1963). This " dissociation " might again not be detected by photocells.

Despite the risks of observer bias, we suggest that the onus remains on the designers and users of more elaborate activity cages to show in what circumstances they surpass skilled observers.

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## Effects of muscarinic and nicotinic agents on avoidance learning of "complex" tasks in different strains of mice

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The effects of nicotine on learning and behaviour have been widely assessed (Bovet, 1965 ; Armitage & Hall, 1967). Nicotine enhances learning and memory and this effect is generally higher in strains or individuals characterized by low performance levels.

An analysis of the action of nicotine, physostigmine, arecoline and pilocarpine was conducted in different strains of inbred mice showing high or low performance levels in a " basic " test of shuttle-box avoidance learning. The strains performing at a high level in this preliminary task were trained with presumably more " difficult " schedules in which: (1) the length of the conditioned stimulus was very short (1 sec) and a long delay divided the conditioned from the unconditioned stimulus (delay conditioning) ; (2) the animals were given a sequence of trials in which when the light was first presented alone the mouse had to move to avoid a shock, while a light-sound complex stimulus required immobility because crossings were punished (" go–no go " schedule) ; (3) each session was divided into two sub-sessions, a visual stimulus (10 W lamp) being used during the first part and an auditory stimulus (pure tone) being used during the second part.

The results show that (*a*) nicotine (0.1–0.5 mg/kg) and physostigmine (0.03–0.06 mg/kg) enhanced avoidance learning in strains characterized by low avoidance

levels; (*b*) a clear facilitating effect was evident in high avoiding strains trained under the three types of complex tasks reported above; (*c*) arecoline and pilocarpine exerted an impairing effect independently of the dose (0.1–5.0 mg/kg).

These findings support the view that as at peripheral ganglionic sites, there is also a distinction between the muscarinic and nicotinic actions of acetylcholine in the CNS (Feldberg, 1945).

A comparison between the neurophysiological, biochemical and behavioural effects of the cholinergic agents is more complex and suggests that each of these drugs exerts different actions at different levels.

The effects of nicotine on the arousal levels appear to be completely different from those exerted by amphetamine. On the basis of a dual memory storage mechanism, the results are consistent with the hypothesis that memory consolidation processes are enhanced by nicotine and physostigmine.

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## The analgesic activity of levallorphan

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Levallorphan (N-allylnormorphinan), clinically employed as a morphine antagonist, is considered devoid of analgesic properties in animals and man (Flodes, Swerdlow & Siker, 1964). Other morphine antagonists, which are recognized as potent analgesics in man, only inhibit the painful reaction of inflamed tissues to noxious stimuli in animals. The analgesic activity of levallorphan tartrate (Roche) was therefore studied in comparison with morphine hydrochloride and nalorphine hydrochloride in CF1 mice (18–23 g) and Long Evans rats (140–180 g). Two types of experiments were carried out reproducing: (*a*) non-inflammatory pain according to Woolfe & MacDonald (1944), Bianchi & Franceschini (1954) and Randall & Selitto (1957); (*b*) inflammatory pain, according to Hendershot & Forsaith (1959) and Randall & Selitto (1957). In the latter test one paw was injected with carrageenin.

In "non-inflammatory" pain the ED50 of morphine was from 1 to 2.5 mg/kg subcutaneously with a clear dose/effect relationship. Levallorphan and nalorphine were inactive in doses up to 10–20 mg/kg subcutaneously. In "inflammatory" pain all the compounds were active. In the test of Hendershot & Forsaith (1959) the ED50 of morphine was 0.43 mg/kg subcutaneously; nalorphine and levallorphan induced a 50% inhibition of the responses at doses of 0.31–0.62 mg/kg subcutaneously, although a clear dose/effect curve was lacking. In the test of Randall & Selitto (1957) morphine was active at 2.5 mg/kg subcutaneously and nalorphine and levallorphan at 10 mg/kg subcutaneously.