It was possible to obtain a significant number of jumps after only six injections when morphine was administered three times daily in increasing doses. The number of jumps was a monotonic increasing function of both the number of injections and the total dose injected. When the same amount of morphine was given at each injection no such consistent relationship was found.

The behaviour of mice treated with methadone and pethidine was slightly different. It appeared necessary to inject pethidine more often (every three hours) to demonstrate physical dependence. Methadone, however, could be injected less frequently than morphine and still produce a significant number of jumps. This is consistent with what is found in man (Isbell & White, 1953). Way, Loh & Shen (1969) have published a quantal method for assessing precipitated abstinence in mice. In our method the response is graded and more detailed information about the abstinence syndrome can be obtained using fewer mice.

In conclusion it is suggested that the number of jumps elicited by an antagonist in chronically narcotized mice can be used as a quantitative measure of the withdrawal syndrome.

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Behavioural effects of a " smoking dose " of nicotine in rats

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Armitage, Hall & Morrison (1968) showed that nicotine can cause EEG activation and behavioural arousal, in terms of operant responding for water, with variations depending on the individual rat, the dose (in the range 50–400 μg/kg) and on the rate of injection. They estimated that a rat given 15–30 μg/kg intravenously receives a dose of nicotine equivalent to that inhaled by a man smoking a cigarette.

In the present experiments, the social behaviour of rats of two laboratory strains was observed, following the subcutaneous injection of nicotine base (25 μg/kg in 1 ml./kg of dilute saline). Paired male rats were separated daily and observed for 6 min after reintroduction. Acts and postures described by Grant & Mackintosh (1963) were recorded, and interpreted statistically by discriminant analysis.

There was a barely significant difference between the randomly selected experimental and control animals in the baseline observations. However, the difference was much greater after the administration of nicotine, and was greater still after the last of four daily injections intended to control for habituation. In a crossover test, where rats formerly given nicotine were injected with saline, and vice versa, the difference between the groups fell to insignificance. There seem to be individual differences between rats to which the effects of nicotine are additive. The latter were therefore shown more clearly by considering rats as their own controls.

The principal effect of nicotine was to reduce aggression. A linear regression equation showed that in both the albino and hooded strains the experimental rats showed less aggression than the control rats in the baseline observations, less still when they were given nicotine, but more when nicotine was given to the control rats instead.

The total activity of the rats was not consistently affected by nicotine, despite a slight reduction in other behaviour (investigation, sexual and submission) also involving approach to the other rat. There was a very slight, and probably independent, increase in escape. There was evidence that the behavioural changes were not secondary to side-effects.

Since the effect on aggression was fairly specific, and since the overall effect was both reversible and of the same order of magnitude as the difference between individuals, it seems that (in the words of Armitage *et al.*, 1968) nicotine is likely to " bring about a normal physiological response which can occur without intervention of a drug ".

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The effects of drugs on the hyper-reactivity of rats with bilateral anterior hypothalamic lesions

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The limbic system is known to be concerned with the mediation of emotional responses (Maclean, 1949; Pribram & Kruger, 1954; Grossman, 1967). Although the functional inter-relationships of the various limbic components and higher brain centres are not fully understood it is evident that emotional reactions are at least partially integrated and controlled at hypothalamic level. Kessler (1941) and Wheatley (1944) found that small bilateral lesions in or near the ventromedial nucleus of the hypothalamus in the cat produced a permanent increase in emotional reactivity. Similar results have been reported in the rat (Anand & Brobeck, 1951). In the work reported here small bilateral electrolytic lesions were placed stereotaxically in the anterior hypothalamus close to the anterior portions of the ventromedial nuclei. Rats with such lesions were found to be extremely vicious and to react in an exaggerated but fully co-ordinated and well directed manner to a variety of tactile stimuli. This hyper-reactivity persisted until animals were killed 6 months after lesion placement.

The effects of chlordiazepoxide, chlorpromazine, amylobarbitone, methaqualone and pethidine on the hyper-reactivity of these rats were assessed using a behavioural rating scale. All drugs were administered intraperitoneally. It was found that chlordiazepoxide and chlorpromazine reduced the hyper-reactivity in a dose-dependent manner; ED 50 values for these drugs were 9 and 4·7 mg/kg respectively.