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A potential screening test for minor tranquillizing drug action.

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Rats can be prevented from escaping from a maze by having the runways of the maze enclosed by walls or by using elevated runways with no side walls. Rats tend to explore enclosed runways more readily than elevated ones. In a Y-maze in which two arms have walls and the third is open-sided the rats avoid the open-sided arm (Montgomery, 1955).

Drugs were tested at three dose levels using thirty-two rats, eight at each dose level and eight controls. Twenty minutes after injection each rat was observed for 3 min in the maze. Entries to each arm and time spent in each arm were recorded. Exploration of the open-sided arm could be increased by minor tranquillizers (for example, chlordiazepoxide, 30 mg/kg subcutaneously) and sedatives (for example, amylobarbitone, 15 mg/kg subcutaneously). This test does not, however, detect other centrally active drugs such as chlorpromazine (2 mg/kg), imipramine (20 mg/kg), or atropine (2 mg/kg). Amphetamine (1·6 mg/kg) could increase, decrease or have no effect on time in the open arm, depending on control performance level. When measures other than time in the open arm were considered, however, amphetamine could always be distinguished from the tranquillizing drugs.

The compounds which are effective in this test are similar to those which increase bar-pressing behaviour which is simultaneously rewarded and punished (punished responding) (Geller & Seifter, 1960; Geller, Kulak & Seifter, 1962). The Y-maze has advantages over punished behaviour as a screening test for drugs similar in action to chlordiazepoxide, as it requires no complex equipment and results can be obtained quickly using untrained animals.

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Methods for detecting anti-anxiety drugs using baboons (*Papio cynocephalus*).

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Brody & Rosvold (1952), Maslow (1936) and Warden Fjeld & Koch (1940) showed that spontaneous social behaviour in monkey colonies was relatively simple and could be recorded and analysed; the patterns of behaviour that emerged in such studies could be modified by the administration of drugs. Delgado (1962) described a method for

studying social behaviour using timelapse photography (one frame every 2 s over a period of 8 hr) and analysed the behaviour of each member of the colony into twenty-two categories. One of the drawbacks of Delgado's method is the enormous amount of time required to analyse a single 8 hr experiment. We have used a video tape recorder to record behaviour patterns. Characteristic behaviour patterns occur during feeding or the introduction of a stranger, either man or baboon, to a colony of five baboons, one senior and two junior males, and two adult females. This provides a satisfactory model for examining the effects of new psycho-active substances on spontaneous behaviour, particularly where the suppression of aggression, either natural in origin or produced by anxiety, is indicative of effectiveness.

Some primate colonies show a social structure in which one male animal assumes dominance over all the other animals within the colony, both male and female. Introduction of another senior male or a human male to the colony—a challenge to the dominance of the leader—appears to induce anxiety in the dominant male. This is characterized by a marked increase in threatening behaviour towards other members of the colony, in particular, towards the junior males. The behavioural assessment of the interactions within the group and of the intruder or reaction to the human intruder is obtained by recording each time each of the animals is in one of the "attitudes" described by Delgado and then scoring according to a pre-determined system. The scoring system is biased towards aggression but can be adjusted to detect sedation, appetite suppression or other behaviour patterns.

Human intrusion into the colony appears to be the most effective and consistent means of producing anxiety-induced aggression in members of the colony, particularly in the leader of the colony. Medazepam (Ro 5-4556 2–5 mg/kg orally), chlordiazepoxide (2·5 mg/kg intramuscularly), pentobarbitone (5 mg/kg intramuscularly), chlorpromazine (3 mg/kg intramuscularly) all reduce the incidence of aggression. Medazepam, in particular, reduced anxiety to such a point that the animal under observation lost all fear of the intruder and resumed near normal behaviour patterns. No sedation was detected after Medazepam but some sedative effects were seen after pentobarbitone and chlorpromazine.

The suppression of aggression, particularly in the leader of a social colony of primates, seems to be a rapid and effective way of detecting potential psycho-active drugs, especially where aggression is indicative of an anxiety state.

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