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Effects of Experimenter and Test Location Novelty on Nonspecific Activity in Rats and its Modification by Methamphetamine

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Levels of nonspecific motor activity in female rats were determined by an interation between familiarity of the experimenter and the room in which the testing occurred. In a second experiment, 2.0 mg/kg methamphetamine increased activity when the rats were tested by a familiar experimenter in either a familiar or novel room, and by an unfamiliar experimenter in a familiar room. However, the effect did not appear when both the experimenter and the test location were unfamiliar. The results indicated the need to consider such influences in studies of drug effects on unconditioned behaviour.

Although it is generally accepted that experimenter characteristics can affect the performance of human subjects in psychological research (Rosenthal, 1966; Silverman, Shulman & Wiesenthal, 1972), this influence is less widely recognised in experimentation with laboratory animals. In most studies of animal learning the degree of experimental control is sufficient to minimise such effects. However, in studies of unconditional behaviour where fewer restraints are imposed upon the subjects it is conceivable that experimenter characteristics could to some extent determine behavioural outcomes. Although apparatus novelty is known to affect various activities in rats (e.g. Bindra & Spinner, 1958; Rushton & Steinberg, 1964), novelty of the experimenter or room in which the apparatus is situated has not been generally recognised as an influential factor. It is particularly important to be aware of any confounding by these influences when assessing the behavioural effects of experimental manipulations such as psychotropic drug administration.

It is now apparent that the effects of many psychotropic drugs on various forms of unconditioned behaviour can to a large extent be determined by a number of nonpharmacological influences. For example, gender (Hughes & Syme, 1972), strain (Broadhurst, 1964), early experiences (Rushton & Steinberg, 1966) and social isolation (Hughes & Syme, 1972) have all been shown to influence either the nature or intensity of drug effects on rats. Likewise details of the testing procedure such as familiarity (Rushton & Steinberg, 1964) and complexity of the apparatus (Hughes, 1973) and pre-testing stress (Gray et al, 1976) have also been shown to modify the behavioural action of certain compounds. It is therefore possible that experimenter and room novelty could be important particularly in relatively unstructured behavioural tests such as those assessments of nonspecific motor activity which are widely used for determining effects of drugs on overall activity levels. As the procedure usually involves automatic recording and a minimum of handling, measurements might not be expected to depend greatly on extraneous influences such as novelty characteristics of the experimenter and the test room. However, the present paper demonstrates that nonspecific activity of rats and its modification by methamphetamine can indeed be influenced by such factors.

Experiment 1

In this experiment novelty of both the experimenter and the test location were simultaneously varied to determine their effects on nonspecific motor activity.

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Materials and Methods

Subjects and apparatus. The subjects were 40 female hooded rats of a randomly derived strain approximately 130 days old. The apparatus comprised a clear Perspex cage measuring 30 x 30 x 30 cm with a wire mesh floor. This sat on a Lafayette A501 Activity Platform which consisted of a square metal frame mounted on four springs. Any displacement of the platform interrupted a light beam beneath the frame thereby activating a photocell. Numbers of light beam interruptions were recorded on a standard digital counter. The complete apparatus stood on a rubber-wheeled trolley which could be rapidly moved from one room to another.

Procedure. Half the subjects were tested by the first author (RNH) and half by the second author (IJB) in either the rat colony room or a nearby research room. As IJB is responsible for the breeding, maintenance and general welfare of all animals in this laboratory, it was assumed that subjects would find him more familiar than RNH whose animal contact is confined to specific research and teaching exercises. It was likewise assumed that the colony room in which the rats were normally housed would be a more familiar environment than a research room never previously encountered by the present subjects.

Testing involved an experimenter removing a rat from its home cage, stroking it for a few seconds, placing it in the appparatus and then sitting on a nearby stool for 5 min while its activity was automatically recorded. After returning the animal to its home cage, the apparatus was washed out with a disinfectant solution. The same procedure was adopted in both rooms by the two experimenters except that, in the colony room, a distance of 24 paces was walked before the held rat was placed in the apparatus. This modification controlled for the distance each experimenter had to walk between a subject's home cage and the research room. A series of 2 to 4 subjects were individually tested in both locations by one experimenter followed by another series who were tested by the other experimenter, and so on. The experiment was conducted during two afternoons with each rat being tested once only.

Results and Discussion

Mean activity scores for the four groups are displayed in Figure 1.

According to a 2 x 2 analysis of variance, the experimenter and location main effects were not significant but there was a significant interaction between them, $F(1,36 = 28.61$, p *0.001.* Subsequent *a posteriori* t-tests ($df = 36$) showed the differences between experimenters to be significant in both the colony, $t = 3.21$, $p < 0.01$, and research rooms, $t = 4.35$, $p < 0.001$

Clearly, nonspecific activity was differentially affected by characteristics of the experimenters and the test location. The

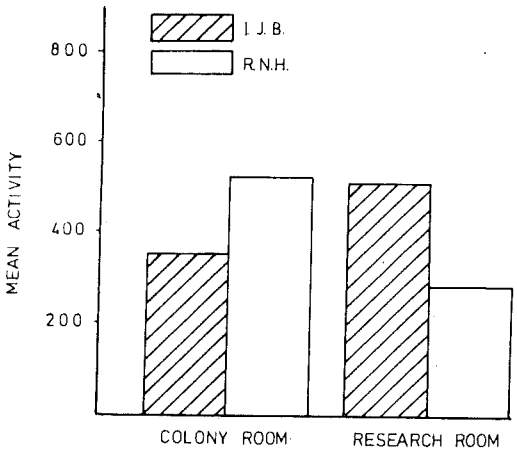

Figure 1. Light beam interruptions (mean activity) with each experimenter and test location.

direction of differences between the groups cannot be adequately accounted for by such factors as differences in handling skills between experimenters or presence and absence of other rats in the two locations. Instead the data are consistent with novelty-related changes in activity observed in other settings i.e., increases with mild degrees of novelty followed by decreases with higher degrees (Russell, 1973). It is conceivable that, in the present study, combined novelty effects from experimenter and test location increased in the order IJB colony (least or insufficiently novel); RNH colony; IJB research; RNH research (most or excessively novel). The levels of activity which occurred at each of these novelty values could then be interpreted as reflecting an inverted U relationship between novelty and activity (Lester, 1967). If the recorded behaviour comprised a large exploratory component (as is believed by many researchers e.g., Grant, 1974) then the results are in line with the view that moderate degrees of novelty produce curiosity whereas higher degrees produce fear and lower degrees fail to initiate interest (Montgomery, 1955).

Experiment 2

This experiment was intended to merely illustrate how the effects of a drug on nonspecific activity can in part depend upon the extraneous influences investigated in Experiment 1.

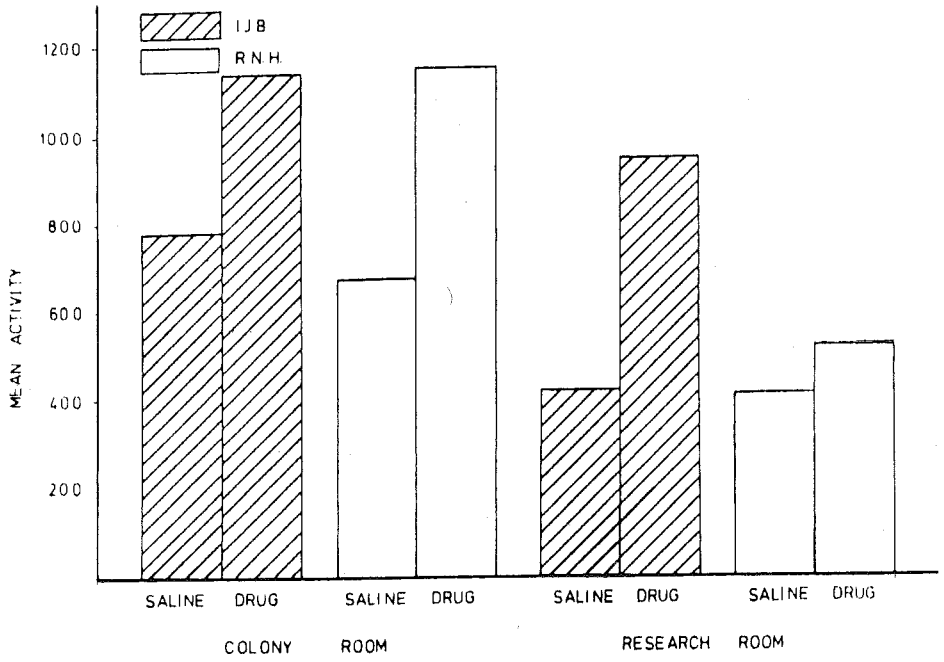

Figure 2. Saline and drug light beam interrruptions (mean activity) with each experimenter and test location.

Materials and Methods

Procedure. The procedure was the same as in Experiment 1 except that each rat was intraperitoneally injected with either isotonic saline or 2.0 mg/kg methamphetamine hydrochloride 10 min before testing. This dose has been shown to markedly increase activity in another setting (Hughes & Greig, 1976). To avoid possible effects of experimenter differences in injection procedures, all rats were injected by IJB. Equal numbers of animals were tested by RNH and IJB in the colony and research rooms during four afternoons.

Results and Discussion

Mean activity scores for the eight groups can be seen in Figure 2.

According to a 2 x 2 x 2 analysis of variance, all three main effects were significant (df = 1,40) i.e., experimenter, $F = 4.41$, $p < 0.05$; location, $F = 33.36$, $p < 0.001$; and drug, $F = 35.87$, $p < 0.001$. However, as the interaction between the three factors was also significant, $F = 5.28$, $p < 0.05$, t-tests ($df = 40$) were applied to differences between the saline and drug groups represented in Figure 2. All differences were significant except for rats tested by RNH in the novel research room i.e., colony room: IJB $t = 2.84$, $p < 0.02$, RNH $t = 3.92$, $p < 0.001$; research room: IJB $t = 4.37$, $p < 0.001$, RNH $t = 0.85$, *ns.*

The most striking aspect of this experiment was the finding that whether or not methamphetamine increased non specific activity depended on the nature of the experimenter and in which room testing occurred. When the experimenter was familiar to the rats (IJB) the drug heightened activity regardless of test location. But when they were tested by an unfamiliar experimenter (RNH) the drug was effective only in the familiar colony room. The novel handler in the novel research room may have attentuated the drug's action by an overall suppression of activity levels. If this suppression were a result of possible aversiveness of excessive experimenter and location novelty, then the result would be consistent with the lack of effects of amphetamines on low rates of operant responding maintained by punishment procedures (Sanger & Blackman, 1976).

Considering saline and drug groups separately (Figure 2) the distributions of activity responses (in relation to the degrees of novelty outlined in Experiment 1) appear to fall within a similar U-shaped novelty-activity relationship to that proposed earlier provided the injection procedure was seen

as a further novel experience which added to test location effects and thus forced all groups into the *latter* half of such a curve. This interpretation would account for the fact that most activity occurred in saline-treated rats with the lowest degree of novelty (IJB in the colony room) i.e. at the height of the curve, and least activity occurred with the highest degree of novelty (RNH in the research room). Even though there was a pharmacological elevation of activity at each novelty level the same relationship appeared to typify methamphetamine-treated animals.

The most important conclusion to be drawn from the present experiment is that, in the preclinical evaluation of drugs, experimenter and test location characteristics deserve consideration in studies of nonspecific motor activity. Clearly it must be determined to what extent these factors may account for the effects of other drugs, particularly compounds less extensively investigated than the amphetamines, as well as various other nonpharmacological manipulations e.g., brain lesions. Although this suggestion is immediately applicable to tests of nonspecific motor activity, it is likely that other forms of unconditional behaviour are equally susceptible to such influences.

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