Effects of d-amphetamine sulfate and UCS-levels on one-way avoidance behaviour of two selectively bred strains of rat

by

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THESIS

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ABSTRACT

Two experiments were carried out involving 40 animals of RHA/Lu and RLA/Lu strains in a one-way active avoidance situation. Subjects were tested for avoidance conditioning and activity with seven behavioural measurements under training for three days and, under the effect of d-amphetamine sulfate for 5 days. In the first experiment, subjects were selected to form strain-sex groups to ascertain strain and sex differences. Sex differences emerged only on activity scores. In the second experiment, subjects were all female and were tested under two levels of UCS footshock. Shock-differences demonstrated a consistent effect with the higher shock value evoking a larger number, and faster, responses. Activity was shown to be a qualified indicator and to yield different results varying with the nature of the task (i.e. 'step-up' as opposed to 'step-down' behaviour). The 'drug session' had a dominant effect on performance, statistically eliminating strain differences in both experiments. U-shape dose dependant curves were shown with most measurements. Sex and shock level factors emerged as significant, but only in the RHA/Lu strain; presenting evidence for differential stimuli sensitivities between strains. A placebo effect with the RLA/Lu strain was demonstrated. Strain difference continued to be evident despite the equalization of UCS footshock given to subjects.

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INTRODUCTION

Recent emphasis on psychogenetic, rather than phylogenic, research in comparative psychology has served to emphasize the question of research on intra-species behaviour, which in comparison with inter-species study, had previously been relatively neglected (Wilcock, 1972). This distinction, between the phylogeny of a species and the process by which evolution in species comes about, is focussing the attention of present research on the means of occurrence of adaptation, and specifically adaptive behaviour, within species. To this end, the study of differences in psychological processes within species using selectively bred strains for comparison - rather than inter-species comparison of similar processes - permits analyses of species behaviour and potentially, an understanding of how these differences evolve.

The adoption of the view that behaviour, in most biological systems, is largely genetically determined (Broadhurst 1966; Broadhurst 1960) provided psychogenetic research with an opportunity to demonstrate that there exists a significant heredity variation in both innate and acquired behaviour (Bignami 1965). Just as a number of studies have indicated that there are marked behavioural differences among strains of rats and mice which have not been selectively bred (Carr and Williams, 1957; Davidson and Walk, 1969; Routtenberg and Gluckman, 1964; Paré, 1969) so too the application of the classical genetic techniques of selection and cross-breeding have yielded research (Broadhurst 1962; Broadhurst and Levine 1963) which demonstrated success in controlled selection breeding, thereby producing, from a single original source, strains of animals with characteristically different patterns of behaviour. Bignami (1965) applied controlled selective breeding to a single population source of Wistar strain rats and after five generations established two strains (Roman High Avoidance; Roman Low Avoidance) differing widely on shock avoidance conditioning.

In the following pages, comment is offered reviewing research done with Roman strains of rats, particularly with administration of various drugs. As well, some discussion will be offered about various experimental conditions used in rat studies (i.e. d-amphetamine sulfate; shuttlebox). The following discussion notes some areas recommended for study and integrates a number of research objectives into a two part study.

I - Roman Strains

As indicated by Bignami (1965) psychogenetic research is particularly important both for the investigation of the genetic mechanisms underlying behavioural traits, as well as for the purpose of providing stable biological material for further psychological and pharmacological investigations. For example, Tryon's "maze bright" and "maze dull" rats (Tryon, 1940) have been demonstrated to have a stable behaviour, effective for some time after withdrawal of the selective breeding process. Stable bidirectional selection over five generations was reported by Bignami (1965) using high and low rates of avoidance conditioning as selection criteria. With a parental generation of 62 albino Wistar strain rats, initial mating was assigned on the basis of speed of acquisition of conditioned avoidance response and on high or low retention rate between testing sessions in an automatic, two-way, escape-avoidance shuttlebox, which had light as the conditioned stimulus (CS), and foot-shock of 1.6 ma as the unconditioned stimulus (UCS). When the rate of avoidance acquisition of the selectively bred animals was compared, the first five generations of Roman High Avoidance (RHA) subjects demonstrated a steady upward advance of avoidance scores from a common parental rate of 105 mean number of avoidances, out of 250 trials, to a value of 171. The Roman Low Avoidance (RLA) strain score decreased from 105 to a rate of 51 mean number of avoidances. Bignami demonstrated the stable nature of this bidirectional selection process.

After the transfer of part of the Roman strains from Rome to Birmingham (Broadhurst and Bignami 1965), the animals were retested for stability of acquisition of conditioned avoidance response in an automatic two-way shuttlebox, using a buzzer as the conditioned stimulus (CS) and a foot-shock of 0.25 ma as the unconditioned stimulus (Levine and Broadhurst 1963). At this point the precaution of preventing inter-trial crossings, by maintaining continual shock in the vacated compartment of the two-way shuttlebox, was eliminated. Results of testing on the basis of defecation and avoidance conditioning rates distinguished the Roman strains from the Maudsley strains, the latter being selected on the criteria of high and low defecation in an open-field test (Broadhurst 1958). Results also demonstrated that the RHA strain was significantly more active in exploratory movements and in inter-trial crossing than the RLA strain. Results also affirmed that RHA demonstrated a significantly greater number, and faster rate, of conditioned avoidance responses, as well as shorter latency in escape responses, than the RLA strain. In addition, it was shown that the RLA strain proved to weigh more than the RHA strain, and that escape latency scores demonstrated a reversal in the effect of the sex factor within strain. Male RHA rats escaped faster than did females, whereas female RLA animals escaped faster than male RLA, thereby yielding a significant strain by sex interaction.

In research on the genetic basis of various behaviours observed in avoidance conditioning, Wilcock and Broadhurst (1967) tested five strains of rats in an open field for 4 days and then gave 50 trials of escape-avoidance conditioning to all subjects in a two-way shuttlebox. Both experiments confirmed strain differences. A principal component factor analysis of correlation scores identified an emotionality factor and a factor concerned with avoidance learning. This latter contained an activity component represented by intertrial crossing and ambulation

measurements. In discussion, Wilcock and Broadhurst suggest that the positive association of ambulation and number of avoidances was similar to that observed in the Roman strains (Broadhurst and Bignami 1965), where the RHA and RLA strains typically ambulated 8.1 and 1.0 metres per day and avoided 19.6 and 2.2 times in fifty trials respectively.

Testing of the eighth generation of Roman strains by Holland and Gupta (1966a) was done to investigate differences between RHA and RLA strains with regard to two factors: reactivity or emotionality and spontaneous activity (arousal). Measurements were taken of frequency of defecation and ambulation in an open-field and activity cage as indicators of the first factor; frequency and duration of rearing as indicators of the second, along with number of avoidance and intertrial crossings in an automatic two-way shuttle system previously described. Results indicated that the significant differences between RHA and RLA groups lay primarily in differences of activity level, whereas the reactivity (emotionality) factor weights did not serve to differentiate the two Roman strains.

A further study on Roman strains at the 17th generation was done (Imada 1972) to investigate emotional reactivity and conditionability of these animals in comparison with Maudsley Reactive (MR) and Non-reactive (MNR) strains. Initially, subjects, after 23 hours of thirst, were allowed to drink water freely for 5 minutes in a test cage. After 15 days of this condition, the level of water consumption during the 5 minutes reached an asymptote. Thereafter, identical unsignaled .5ma electric shocks of .7 seconds duration were given to subjects in a random pattern five times daily for 7 days. This caused a suppression in water drinking which was relative to the strain, and was therefore regarded as a measure of emotionality. Using this latter as an index, variable shock was administered to strain groups so as to evoke an equal

amount in quantity of suppressed drinking by all strain groups (i.e. in this case set at 50-60% of the asymptotic level reached in the unshocked freely drinking situation.) This proportional equivalence of suppression was considered to be a matched basal emotional level (BEL) with the strain differences in emotionality thereby being considered as a controlled variable in the conditioning procedure which followed. Results of this experiment, which thereby separate emotionality from conditionability, indicated that the RLA strain was more emotionally responsive than RHA, which, it was suggested, may have been occurring through its being less active in ambulation; and, that the RLA strain demonstrated poorer conditionability than RHA. Defecation scores between the two Roman strains did not differ significantly. In absolute quantity, the RLA strain drank significantly less water than all other tested strains.

In an examination of spontaneous activity as distinguished from 'stressed activity' by Holland and Gupta, (1967a) defined in terms of pre-testing free intertrial crossings in a two-way shuttlebox, Satinder and Hill (1974) examined the thesis that the criterion for selection of Roman strains, although thought to be conditionability, might in fact be attributable to differences in activity among subjects. However, results indicated there were no significant differences between strains in activity, although RLA was slightly more active than RHA.

II - Chemical Studies on Roman strains

Soon after the Roman strains were shown to offer a stable avoidance conditioning behaviour, these animals were utilized in a number of pharmacological research projects with depressant and stimulant drugs, as well as with two enzyme studies.

Rick, Morris and Kerkut (1968), using fifteen male subjects from the Roman strains, along with Tryon maze bright (TMB) and Tryon maze dull (TMD)

subjects, attempted to correlate γ-aminobutyric acid (GABA) from the cerebral cortex with the activity of cholinesterase (ChE) which may serve to enhance learning, and the activity of cholineacetyltransferase (ChAc). GABA and ChE were tested for correlation since GABA production was previously shown to vary in rats bred for high and low defecation under mild stress, while Broadhurst and Watson (1964) had showed a similar relationship between reaction to stress and ChE activity. However since ChAc did not vary between strains there was no correlation between GABA and ChAc. Experimental results however did indicate that the production of GABA in the cerebral cortex of the five tested strains correlated with the activity of ChE of the same brain area. This relationship held both for individual measures and strain means.

Jordan and Satinder (1971), using 16th generation Roman High Avoidance subjects (redesignated RHA/Lu as the Lakehead University colony (Satinder 1971) in a two-way avoidance conditioning shuttlebox researched the effect of ribonuclease enzyme (RNase), which is known to bring about amnesia in pigeons and mice. Animals injected with 0.01 gm/kg RNase in saline for seven days before behavioural testing did not show any appreciable acquisition of the conditioned response. Subjects injected with the same dosage seven days before testing as well as during seven days of training acquired the response beginning on the 4 day of training. On the 7 day, these animals were not any different from the control groups which went through the same procedure receiving only saline injections.

Brewster (1969), following on several studies which have demonstrated the effect of strain differences on ethanol preference in several strains of mice and rats, performed three experiments in which preference for various concentrations of ethanol was investigated in five strains, three

of which were RHA, RLA and Roman Control Avoidance (RCA). Sixty subjects of both sexes, from the seventh generation, were used. Subjects were provided with four drinking bottles containing ethanol mixtures of .01, .1 , 1.0, 10.0% concentration, and were allowed to drink freely twenty-four hours per day, for seven days. Two principle measures were taken: a) preference ratio, of ethanol as a percentage of total fluid intake, and, b) absolute quantity of ethanol intake, corrected for body weight and expressed in mg./kg. Results indicated that there was no strain preference for an absolute intake of ethanol, except for the ten percent ethanol mixture. At this concentration, RHA gave significantly higher scores on both measurements than either of the other two strains, between which there was no statistical difference. Analysis of variance revealed a significant sex difference, with females showing the higher preference for ethanol. This statistical difference was entirely attributable to a highly significant sex difference for 10 percent ethanol mixture. Brewster suggests, following Erikson and Malmstrom (1967), who observed similar sex differences in albino rats, that this effect could be accounted for by the higher rate of metabolism of ethanol in females.

Satinder (1972a) reported a further study to that of Brewster (1969) to analyse some of the factors involved in differential responding to self-selection of alcohol by bidirectionally selectively bred strains of rats. Five strains of subjects were used, three of which were RHA/Lu, RLA/Lu and RCA/Lu. In the first part of the study, 12 subjects of each strain (18th generation), after an adaptation procedure, were given a choice of three liquids (distilled water, alcohol solution, glucose solution) ad lib, for fifteen days. This procedure was repeated to include alcohol of three concentrations:

5%, 10%, 20%. Taking measurements of absolute alcohol intake, and, proportion of each specific liquid to total fluid intake, the results indicated that of the Roman strains, RHA/Lu consumed significantly more than RLA/Lu in the 5% and 10% levels of concentration, but this relationship reversed, although statistically insignificant, with the 20% alcohol mixture. Females, of all strains, consumed larger absolute amounts of alcohol under all three levels of mixture. In the latter part of the study, Satinder investigated the effects of caloric restriction on self-selection of 10% alcohol using the same three bottle situation, with the earlier glucose bottle simply remaining empty. The caloric restriction was achieved by food deprivation on two occasions for forty-eight hours. Whereas the RCA/Lu group did not show an increased alcohol consumption, because of food deprivation, both RHA/Lu and RLA/Lu did demonstrate a significantly increased consumption with the RLA/Lu strain being affected to a greater extent than the RHA/Lu. Satinder suggested that the effects of food deprivation on alcohol consumption werere related to the phenotype of emotional reactivity and in the Roman strains, to a certain extent, to avoidance conditionability. Interpreting emotional reactivity as an index of the sensitivity of the organism to environmental change (i.e. increased susceptibility to stress situations), high emotional animals are considered to respond to stress and therefore may select more alcohol solutions as a learned adaptive response. Satinder suggests that a similar relationship to tension may exist for the RHA/Lu strain, thereby explaining its higher alcohol consumption rate than RLA/Lu.

Satinder (1973), using eight subjects of four selectively bred strains of rats (two of which were 20th generation RHA/Lu and RLA/Lu) examined the effects of age, sex and experimentally induced stress on self-selection of nine levels of alcohol mixture ranging incrementally from

.25% to 64% concentration. The procedure was identical to that used in Satinder (1972a) exposing all nine alcohol concentrations to 28 day old subjects for seven days each.

Using proportional and absolute measures, results indicated that the RHA/Lu and RLA/Lu strains differed significantly from each other on the proportions consumed of 2% alcohol concentration. RHA/Lu consumed higher proportions of alcohol solutions under .25, 1, 2, 4, 8 and 32% concentrations, while RLA/Lu consumed higher proportions under .5, 16, and 64% concentrations. There were no significant sex differences between strains on any of the nine concentrations.

In terms of absolute amounts of alcohol consumed, the RLA/Lu subjects consumed significantly larger amounts of alcohol under the 64% level of concentration. No significant sex differences were found, although female subjects consumed larger amounts of alcohol than males under all the concentrations. Although the Roman strains did not differ in body weight the RLA/Lu consumed significantly larger amounts of total fluid (ml./100 gms.) than the RHA/Lu.

The above testing procedure, with the same subjects, was repeated when the animals had reached 105 days of age (Experiment 2). The RHA/Lu subjects consumed higher proportions of alcohol solutions than RLA/Lu, under all the concentrations. However, the differences were statistically significant only under 4, 8, 16% concentration. There were no significant sex differences with proportional scoring measures.

In terms of the absolute quantity of alcohol consumed, the RHA/Lu consumed significantly more than RLA/Lu under 8% concentration. The females again consumed larger quantities under all concentrations than the males, although statistical significance appeared only under .25, .5 and 1% concentrations.

Results therefore indicated that in RHA/Lu, between the experiments at

28 days and that at 105 days, the proportions in the latter were significantly higher than in the first experiment at 1, 8, 16 and 64% concentration levels. This was also true of RLA/Lu with significant differences between experiments occurring at the .25% concentration. Between experiment comparison of absolute alcohol intake showed that the RHA/Lu consumed less than the RLA/Lu under .25, .5, 1 and 2% levels; and more than RLA/Lu under 4, 8, 16, 32 and 64% concentration in the 105 day as compared to the 28 day experiment. In RLA/Lu the amounts of absolute alcohol intake was smaller except at 3% in the 105 day experiment, however, the significant differences between experiments was demonstrated under .25, .5, 1, and 2% concentrations. All tested strains consumed smaller amounts of total fluid under the 105 day experiment as compared with the 28 day experiment. There was a clear trend that, with increase in age and body weight, the total fluid intake decreased.

Results on sex differences confirm previous findings (Satinder 1972a) that there were no significant differences in the proportion of alcohol solutions consumed. Under lower concentration levels there were no significant sex differences in the consumption of absolute amounts of alcohol when the body weight differences were minimal (as in the 28 day experiment), but sex differences appeared only when the body weight differences became obvious (as in the 105 day experiment). It would also appear that higher alcohol concentration levels obscured the sex differences in the consumption of the absolute amounts of alcohol even when body weight differences were obvious and the consumption was calculated per unit of body weight. This was demonstrated by the absence of significant sex differences under higher alcohol concentration levels in both experiments.

Gregory (1967) using the tranquilizing methylpentynol carbamate on

11th generation Roman strain subjects, showed that this drug reduced the difference in general activity of the RHA and RLA strains in that it increased the rearing frequency of RLA subjects, while decreasing the rearing frequency of RHA subjects, given a dosage of 25 mg/kg of methylpentynol carbamate intraperitoneally (ip) fifteen minutes before retesting of rearing. However, post-avoidance conditioning injections appeared to have no effect either on rearing itself or on its suppression in indicating whether the shock experience, given 40 trials in a two-way shuttlebox, resulted in greater stress in either of the two Roman strains.

Using only RHA subjects in a two-way shuttle box, Gregory (1968) tested the effects of two depressant drugs, which have both been shown to deplete catecholamine (CA) stores - reserpine and prenolymine - the latter acting on CA below an injection level of 50 mg/kg, while acting on serotonin (5HT) above this injection level. Both sexes of RHA were examined for rearing frequency and performance, out of twenty-five trials, of avoidance conditioning behaviour under three dosage levels of the drugs: reserpine 0.5, 2.0, 4.0 mg/kg; and, prenolymine 5.0, 20.0 and 40.0 mg/kg. Results indicated that performance on both measures was depressed at the highest dosage of each of the drugs employed. Since this effect was not observed with prenolymine above the 50 mg/kg dosage, these findings seem to suggest that the catecholamine levels of the subjects may be responsible for these effects. Gregory put forward two theories for depression of the conditioned avoidance response: (a) that the drugs alleviate fear and therefore reduce the subjects characteristic motivation to respond, and, (b), that the sedative action disrupts motor performance. By an analysis of covariance of rearing scores with avoidance scores, and then conducting an analysis of

variance on the adjusted scores Gregory demonstrated results which, lending support to the latter thesis, suggested that the drugs were affecting the performance of the conditioned avoidance response.

In the area of research on the effects of stimulant drug dosages on Roman strains, Garg and Holland (1969) reported a study on the behaviour of four strains, two of which were Roman in the eighth generation. Eight RHA and RLA subjects were tested in a Hebb-Williams closed field maze having been given an interperitoneal injection of 0.8 mg/kg of nicotine bi-tartrate solution 2 min. after the subject successfully fed at the maze goal box. Two types of measurement were taken of behaviour - (a) the number of false entry errors made each day; and, (b) the time taken to traverse the maze from the start position to the goal box - in order to determine if the dosage administration had an effect on post-trial consolidation of learning, and, if such an effect was in any way different between strains. Results indicated that post-trial dosages of nicotine improved learning in all strains tested, and that the 0.8 mg/kg dose of nicotine bi-tartrate served to improve this performance more in the RHA than RLA strain. This suggested that strain differences in conditionability may be attributable to correlated differences in the transmission of sensory information, or neural events, as will shortly be noted in a discussion by Holland and Gupta (1967b). This theoretical position was chosen by Garg and Holland over the theory that subjects differed in emotionality, and thereby in rate of performance, because of the failure to clearly demonstrate that there were significant differences between RHA and RLA in performance on criteria of emotionality. The authors, therefore, suggest that the differential performances in the two Roman strains may be attributable to a difference between strains of ACh/ChE balance in the brain mechanism. Additionally, results of this

experiment demonstrated a superior learning, with 'time scores' performance, of Roman female subjects over that of Roman male subjects, although there was no significant differentiation between sexes on 'error scores'.

A further paper by Garg (1969) reported the effects of 0.8 mg/kg dose of nicotine bi-tartrate on the rearing frequency of four strains of rats, including RHA and RLA strains. Using 16 subjects of the 7th and 8th generation in a rearing cage, subjects were injected with a dosage in volume 1.0 c.c. per 250 grams of body weight, 15 minutes before trial. The rearing cage allowed two measurements: (a) the frequency of occasions in which the subject reared on its hind legs within $\frac{1}{2}$ inch of the top of the cage, and (b) the length of time during rearing that each subject presented itself in the top space of the apparatus. Results indicated that the nicotine bi-tartrate significantly facilitated the rearing frequency, with the RHA strain responding more to dosages than the RLA strain, on which the mixture failed to produce any significant effects when compared to a control group receiving placebo injections. In addition to strain differences, the females reared more frequently, with both placebo and nicotine bi-tartrate injections, than males. Garg suggested that strain differences in rearing activity may be due to differences in the 'excitability level of the central nervous system (CNS)', which is not correlated with emotionality as evidenced by the absence of significant differential defecation rates between Roman strains. The author also suggested that the greater rearing frequency of females supports previous findings (Levine & Broadhurst, 1965; Garg 1969) which suggest that females are more active in exploration and are therefore more greatly affected by nicotine-bi-tartrate injections than males.

Gupta and Holland (1969), following earlier formulations (Holland and Gupta 1966b) examined the theory that individual and strain differences in rats, as observed in investigations of the characteristics of conditioned avoidance responses, are due in part to reactivity or emotionality - (as inherited differences between strains in autonomic system response to identical stimuli); and, activation or arousal - an inherited difference between strains in functioning (i.e. excitability) of the central nervous system (CNS), pa ·ticularly of the reticular formation.

Gupta and Holland (1969) suggested that avoidance responding may be determined by the interaction of the genetically determined arousal level of the CNS, and/or emotionality along with a level of drive or motivation which acts through an external source provoking the autonomic system. Emotionality has a drive property which multiplies with the existing level of CNS excitation to produce overt responses.

Gupta and Holland (1969) suggested that one of the most effective ways of controlling the impinging environment on subjects is through the administration of drugs. Using Maudsley strains, selectively bred for defecation scores, and two central nervous system drugs (1) the stimulant d-amphetamine sulfate, and, (2) the depressant sodium amytal , along with two autonomic nervous system (ANS) drugs ((1) the stimulant adrenaline, and, (2) the depressant methylpentynol), the authors report a wide number of conclusions. With Maudsley strains, results indicated that all the main effects (treatment, strain, dose, but not sex) operated significantly to yield statistical differences between groups. t-test comparisons indicated that the amphetamine group was significantly more different from all others as a treatment effect, with the exception of the ANS depressant methylpentynol. The central stimulant and autonomic

depressant drugs facilitated, while the central depressant and autonomic stimulant drugs blocked, the acquisition of conditioned avoidance responses. Overall results of this experiment with Maudsley rats therefore indicated that conditioned responses in a two-way shuttlebox were affected by the selectively bred, emotional reactivity level of the subjects. As well as the drugs having a differential effect, there was also a strain specificity demonstrated, in that the MR strain proved to be influenced only by ANS drugs whereas MNR strain was affected by all drugs used.

Although dose-response relations of the drugs were not influenced significantly either by emotionality or sex, both central stimulant and autonomic depressant drugs did yield a characteristic inverted U-curve, increasing the avoidance conditioning response, in relation to dosage, up to a limit, with further increases in dosages causing a decrease in performance. Increasing dosages of the central depressant and autonomic stimulant drugs yielded consistently decreasing performance. Since the general results indicate that MNR is more conditionable than MR, this lends support to the theory that the higher emotionality of MR produces a characteristically observed freezing and crouching posture which effectively interferes in subject's acquisition of an avoidance response. On the other hand, stimulant drugs increased psychomotor activity thereby, seemingly, breaking up this freezing posture in Maudsley strain subjects.

Satinder (1971) examined strain differences as one of the experimental conditions which may be influencing differential responding to similar d-amphetamine conditions. Using four selectively bred strains of rat, including RHA/Lu and RLA/Lu of the 16#generation, in two CNS stimulant drug conditions, differential responses for strain groups were demonstrated in a two-way shuttlebox. This indicated that in the case of caffeine

and d-amphetamine sulfate, escape-avoidance behaviour was dependant on the strain of animals used. RHA/Lu was superior to RLA/Lu in having a greater mean number of avoidances, and, faster avoidance and escape latencies. RHA/Lu did not show any significant improvement in performance under either stimulant, with the mean number of avoidances and avoidance latency deteriorating markedly under 3.0 and 4.0 mg/kg of d-amphetamine sulfate. The RLA/Lu strain showed a significant facilitation of escape-avoidance conditioning under all, except the highest dosages of the two stimulant drugs. Satinder noted that a placebo effect was noticed in the RLA/Lu performance on mean number of avoidances and escape latency scores. Of interest too was the indication that general activity, measured by intertrial crossings (ITC) was selectively changed by the drugs used. Although frequency of ITC increased in all strains, the MNR/Har/Lu and RHA/Lu animals were affected by both CNS drugs, whereas the MR/Har/Lu and RLA/Lu strains were affected only by d-amphetamine sulfate. In addition RHA/Lu had significantly more ITC than RLA/Lu under both stimulant drugs. Satinder also indicated that improvement of escape-avoidance behaviour under drugs was correlated with intertrial crossings, indicating that general activity partly confounds improved performance under both stimulant drugs.

In a follow-up on this latter point, Satinder (1972b) investigated the correspondence between avoidance performance and intertrial activity by permitting or punishing intertrial crossings (ITC) in a two-way shuttlebox, both without, and under, dosages of d-amphetamine sulfate. Using four strains of rats, two of which were RHA/Lu and RLA/Lu of the 20th generation, it was shown that, without drug, in RHA/Lu avoidance responses were not affected by ITC punishment. However ITC of this strain were

significantly inhibited by the "ITC punishment condition", as opposed to the "ITC permissable condition." Since in 50 training trials, the RLA/Lu did not show an increment from the baseline of performance, no effect from ITC punishment was demonstrated.

Under d-amphetamine sulphate, in RHA/Lu, the avoidance response in both ITC permissable and punishment groups were significantly suppressed. However, the drug caused a significant ITC increase in the ITC permissable group, and no change in the ITC punishment group.

In RLA/Lu, d-amphetamine sulfate facilitated the number of avoidances and intertrial crossings in the ITC permissable group, without affecting any changes in the ITC punishment group. This confirmed previous findings (Satinder 1971) that in RLA/Lu, the facilitation of avoidance behaviour under d-amphetamine sulfate was confounded with an increase in general activity.

Overall, intertrial crossing punishment (i.e. shock) can therefore produce strain dependent dissociation between avoidances and intertrial responses, a result which is also differentially influenced by d-amphetamine sulfate.

In view of the fact that d-amphetamine sulfate was chosen as the stimulant drug used in this thesis research, the following is offered as an additional discussion of the multivarious and at times contradictory findings available with research using amphetamine on rat and other categories of subjects.

Carlton and Didamo (1961), Sidley and Schoenfeld (1963), Verhave (1958), Verhave, Owen and Slater (1958), have all indicated that certain stimulants, such as d-amphetamine sulfate enhance some avoidance conditioning behaviour.

Hearst and Whalen (1963) showed that amphetamine treated subjects

in comparison to untreated subjects were much more likely to show efficient avoidance behaviour specific to the CS, occurring without stimulus generalization. Increased activity and motor movements are caused by d-amphetamine but do not transfer to subsequent non-drugged states.

Krieckhaus, Miller and Zimmerman (1965) in a re-examination of the freezing and crouching hypothesis demonstrated that amphetamine tends to affect a quicker break-up of the fear-freezing behaviour induced by a CS, both in an operant and classical conditioning situation. In a further experiment, it was demonstrated that all three dosage levels of amphetamine injected into Sprague-Dawley subjects, although not significantly different from each other, resulted in improvement over a control group in avoidance acquisition. Withdrawal of d-amphetamine sulfate showed the performance of the larger prior-drug-injection group (5 mg/kg) deteriorating most in avoidance conditioning. In conclusion Krieckhaus et al. (1965) suggested that an animal's tendency to freeze is one of the most important variables in avoidance conditioning, and that d-amphetamine, because it breaks up, or artificially suppresses, freezing thereby produces enhanced avoidance behaviour.

Despite the above evidence, Powell, Martin and Kamano (1965) in a study designed to test the effects of d-amphetamine sulfate on acquisition by rats over eight sessions, disagreed with previous findings and indicated that there were no significant differences between drug and non-drug group shown in the shuttlebox avoidance situation. However, Powell et al. (1965) did agree that gross activity results, measured by a crossing of a hurdle, indicated that drugged subjects performed at a significantly higher rate, consistent with the theory that amphetamine breaks up freezing behaviour.

Since amphetamine has been observed to increase gross activity, and to affect food consumption (Cole 1963, 1965, 1968), as well as to interact with shock conditions (Teitelbaum and Derks 1958), Cole (1966) suggested that other experimental conditions in the conditioning of the avoidance task must also be studied. Emphasizing that more research needs to be done on conflicting findings, he suggests closer controls on the interaction of amphetamine with experimental conditions. Barry and Buckley (1966) point out the importance of seemingly minor procedural differences which produce substantially different effects of drugs on avoidance conditioning.

In a later paper Cole (1967) reviews many of the known experimental effects of amphetamine including its depressant effect on food consumption and food-motivated behaviour, as well as its facilitating effects on motor performance, bodily activity, avoidance conditioning and escape behaviour. The diverse effects of amphetamine are due to the fact that it is one of several psychotropic drugs having both a central and peripheral action on behaviour, increasing the complexity of predicting behaviours resulting from such treatment. As a supplement to this paper, Cole (1970a, 1972) emphasized that experimental evidence about amphetamine to date lends itself to a number of generalizations, if the limitations and parameters of such generalizations are recognized. For example, the depressant effect of amphetamine on food motivated behaviour, under a variety of specified reinforcement programmes, suggests an inverse relation between operant response output and drug dose - under a fairly wide dose range. This relationship, however, must be qualified by inconsistent findings with lower doses, tests using complex discrete trial tasks, and by the necessity to establish control levels of behaviour.

Similarly, within limitations, the general facilitating effect of

the conditioned avoidance response by amphetamine, has been well established (Bovet and Oliverio 1967; Cicala and Kremer 1969; Efron, 1968; Hanson, 1967; Krieckhaus, 1965; Powell and Hopper 1971; Sansone and Bovet, 1969), while recent studies have further outlined some of the qualifying factors to this effect. For example Lal (1968, 1969), Powell (1970) have presented evidence suggesting that facilitation by amphetamine of the conditioned avoidance response is a drug controlled state, unable to cause an improvement that will last longer than the drug. Gupta and Holland (1969) and Pradham and Dutta (1970) have demonstrated that the facilitating effect of amphetamine is dose-dependent. For example, smaller doses of amphetamine, such as 1.0, 2.0, 3.0 and 4.0 mg/kg facilitated the acquisition of conditioned avoidance response, whereas a 5.0 mg/kg dose reversed this facilitating effect. Along with these qualifying factors to any generalization about the effects of amphetamine, Kamano, Powell and Martin (1967) point to the necessity of recognizing differences in the performance levels of subjects.

Findings from research on activity also suggests that the generalization about increased activity as the result of amphetamine must also be qualified, not only by a drug-dose consideration, but also by task characteristics (i.e. motor requirements or reinforcement schedule format (MacPhail 1971); novelty versus the absence of novelty; as well as subject and test condition variability (Glick, 1971). Kulkarni (1968) had distinguished between amphetamine affecting the rate of responding in "performance" of avoidance behaviour, and, the facilitation of avoidance acquisition. Amphetamine differentially affects the time course of changes in motor-activity, from that of changes in avoidance responses during acquisition. Cicala, Ulm and Drews (1971), using chlorpromazine and d-amphetamine on 64 male Wistar rats, reported an assessment that

while chlorpromazine impaired learning, and, the performance of escape responding, d-amphetamine facilitated only performance. Schirring (1971), studying various components of locomotion and grooming in the rat given d-amphetamine sulfate, showed that some behavioural items increased in frequency while others decreased, and thereby concluded that amphetamine cannot be characterized as a general stimulant since it selectively stimulates only some behaviours, while selectively inhibiting others.

Despite the limitations which must be applied to any generalized comment on the effect of amphetamine, Cole (1972) suggests that a generalizing methodological approach is both useful and necessary. Generalizations force a specifying of the drug's unexpected effects, and offer hypotheses for further research. Indeed the process of generalization offers an analytical basis for further understanding the complex interaction of the drug with subjects. Cole suggests, (p. 100) that "since the drug affects a wide variety of experimentally observed behaviours, there is a need for comparing and distinguishing the effects of amphetamine on different behaviours as well as defining its action on a single behaviour."

III Footshock As a Variable in Conditioning

Although there are no studies available specifically testing the conditioning response of Roman strain subjects under comparable, and differential UCS conditions, there is substantial evidence available, following Reiss (1970 p.482), that "the UCS intensity variable (i.e. footshock intensity) is considered to have achieved an enduring status as possibly the single most potent parameter in the aversive control of behaviour. UCS intensity has been shown to relate monotonically to behaviour within the paradigms of aversive classical conditioning, conditioned acceleration, conditioned suppression, pain elicited aggression, passive avoidance, and punishment of both positively and negatively reinforced instrumental processes."

Studies on the effects of shock intensity on aversive learning which have used rats as subjects originally were thought to show that learning simply increases as a function of UCS shock intensity increases (Boren, Sidman, Herrnstein, 1959; Denenberg, 1959; Dunlap, Gentry and Zeigler, 1931; Kimble, 1955; Moyer and Korn, 1966; Williams and Eichelman, 1971). However, this relationship has often been questioned (Reiss, 1970) within the paradigms of : unsignaled escape, unsignaled avoidance, unsignaled escape-avoidance and notably signaled escape-avoidance. Here the effects of intensity of UCS are sufficiently interacting with other variables that no uniform functional relationship has been agreed upon. For example, Moyer and Korn (1964), using 123 female albino rats under 0.5, 1.0, 1.5, 2.5, 3.0, 3.5 and 4.5 ma of shock in avoidance training, for 30 trials per day for four days, found that the curve relating avoidance learning to shock intensity was not simply monotonic but complex, with deflections. Relatively intense shock interfered with acquisition of both escape and avoidance responses. Learning rates fell off rapidly after 1.0 ma and seemed to be maximally disrupted at about 2.5 ma, with higher intensities up to 4.5 ma having relatively limited additional effect. Observation indicated that 0.5 ma shock disturbed subjects but did not activate them into intense running activity. Middle range shock tended to elicit a running behaviour, while the highest levels of shock resulted in considerable disorganized behaviour including bar biting, jumping, falling and bumping into walls. In suggesting that the middle shock range generally produces optimum behaviour for quickly escaping from shock, Moyer and Korn carefully indicated that different shock levels might be optimal in other situations where different types of escape responses are required. In this experiment, Moyer and Korn, later supported by others (Bauer, 1972; Bolles and Warren, 1965; Cicala and Kremer, 1969;

D'Amato, Fazzaro and Etkin, 1967; Johnson and Church, 1965; Kurtz and Shafer, 1967), suggested that over a rather substantial rate of values, shock-intensity and rate of avoidance learning are inversely related. For example, Levine (1966), working with generally smaller shock levels (0.20 - 0.80 ma) confirmed Moyer and Korn's finding that the general function is linear and inverse. Levine also suggests that whether shock increases or decreases the rate of avoidance conditioning will always depend on many factors, including the nature of training, of responses, and the relative motivating characteristic of the shock in the paradigm.

In an attempt to reconcile the evidence between monotonic and inverse relation generalizations, McAllister, McAllister and Douglass (1971), using 120 female hooded rats in a two-way shuttle apparatus, factorially combined two levels of shock (.3 and 1.6 ma) with three durations of intertrial intervals (15, 30 and 45 sec.). They investigated the notion that the amount of effective reinforcement for an avoidance response is: (1) positively related to the amount of fear reduction occurring with CS termination, and, (2) negatively related to the amount of fear presented by situational cues following response. The authors suggested that the inverse relationship between shock and learning is not due simply to the presence of a 'staying' or 'freezing' response. Rather it is also due to a decrease in the amount of effective reinforcement for the shuttle response, as a result of an increase in fear of situational cues associated with strong shock. One of the implications of this reinforcement interpretation is that any procedure which decreases the amount of fear elicited by the discrete CS, should facilitate avoidance conditioning by increasing effective reinforcement.

Reiss (1970) and Herrnstein (1970) however, have shown that the

relationship between intensity of UCS shock and behaviour for signaled escape avoidance paradigms, when studied during terminal performance, were without exception positive, and, that the function of response to shock intensities was monotonic. As well, Reiss (1970) showed that his rat subjects demonstrated a point of discontinuity of increasing sensitivity to increasing shock at roughly the 1.0 ma point. Between 1.0 and 4.0 ma the response function was almost horizontal, which suggests that about 1.0 ma represented an intensity threshold for subjects. The author also showed that the effect of response to variations in duration was nearly identical to that of intensity, except that the rise in the curve does not level off as abruptly at higher levels. The similarity of the effects of duration and intensity are in agreement with findings for these two variables in other aversion paradigms. Reiss (1970) emphasized that the effects of intensity of UCS footshock are complicated with other variables such as apparatus differences, response topography, procedural detail, as well as strain and species differences.

For example, Theios, Lynch and Lowe (1966) found that shock settings between 1.0 ma and 2.5 ma, did not result in systematically different escape latencies. This was the case even though different shock intensities did result in different learning rates in a two-way shuttle situation. Results seem to indicate therefore, that in the optimal shock range 1.0 - 2.5 ma (Moyer and Korn, 1964), different intensities of shock do not result in differentially disrupted escape responses.

Satinder and Hill (1974) investigating the effect of postnatal experiences (i.e. handling and 3 min. of shock for 15 days after birth) found a significant difference in shock thresholds between strains, but not as a result of postnatal handling and shock. The RHA/Lu strain had a significantly lower flinch threshold than the RLA/Lu, with females having significantly lower flinch thresholds than the males of

each respective strain. Satinder and Hill therefore suggest that differences in their subjects shuttlebox avoidance conditioning may be affected by the rats' differential shock sensitivity.

Cicala, Masterson and Kubitsky (1971) recently have attributed differential response to shock threshold as being centered in different initial probability, or operant response levels of subjects. The authors demonstrated that responding persists throughout an extended series of shocks in the absence of reinforcement from either escape or avoidance, and suggested that this operant level of response may be one of the most important sources of behaviour available for reinforcement in avoidance learning situations.

The importance of the variable of apparatus differences has been reflected not only by Moyer and Korn (1964) and by Reiss (1970), but by a large number of other experimentalists. (Cassady, Cole, Hall and Williams, 1971; Henderson, 1970; Krivanek, 1971; Marquis, 1971). This is particularly true when research on escape-avoidance conditioning digresses from the traditional two-way shuttle situation in favour of other paradigms, as for example, are offered by the one-way shuttle system. This point is made by D'Amato, Fazzaro and Etkin (1967), who suggest that the generalization, in which an acquisition of a discriminated avoidance response is inversely related to shock intensity, does not extend to one-way shuttlebox avoidance conditioning. In this manner, the use of the one-way shuttle situation presents a basis for examining the generalizations attained from performance in other paradigms (i.e. two-way shuttle box situations). For example, Moyer and Korn (1966), having shown that intense shock interferes with avoidance acquisition in a two-way shuttlebox, examined the question of whether this relationship would hold in a one-way shuttle situation.

Using 41 female rats, subjects were given 50 trials of acquisition in a one-way shuttlebox with UCS at 0.5, 1.5, 2.5, 3.5 ma. The 0.5 ma group made significantly fewer avoidances and had longer response latencies than other groups in acquistion. The highest shock level produced significantly longer escape latencies on early trials, but did not retard avoidance latency. Although further evidence with different UCS levels in a one-way avoidance situation is not yet available, these results indicated the merit of testing escape-avoidance conditioning under various levels of UCS, and, in different conditioning paradigms in order to examine if any qualifications must be made to established behaviour generalizations; and, as will be described next in the case of one-way shuttle system, to establish initial research using d-amphetamine sulfate and selectively bred strains of rats.

IV Experimental Apparatus as a Variable

The foregoing review of research done to date on Roman strain rats (Section I), including all chemical studies (Section II), indicates that the testing of behavioural performance in avoidance conditioning situations has been done almost exclusively in two-way shuttleboxes. Indeed most of the research done on Roman strain escape avoidance conditioning was done in an adapted Miller-Mowrer shuttlebox, having a buzzer as a CS and footshock as the UCS, required subjects to pass through an opening, bottom centre, of a partition which divided the apparatus into two compartments. The use of this basic two-way shuttlebox in conditioning experiments was first reported by Levine and England (1960) and was then used repeatedly, with some adaptations (i.e. automatic control via floor tilting) throughout the history of research on Roman strains.

Theios and Dunway (1964) suggested that the use of the shuttle procedure in avoidance conditioning became popular primarily because of the convenience it offered in automation. This equipment however has always demonstrated the difficulty of not being able to train subjects to 100% avoidance criterion in any reasonable length of time. For example, with optimal shock intensities, Moyer and Korn (1964) took an average of about 90 trials to reach 90% avoidance criterion. By contrast Theios (1963) has reported that when rats were required to run in only one direction (rather than returning as in a two-way shuttle-box), the 90% avoidance criterion was reached in 11 trials. Potts (1970) indicated that his rat subjects in a one-way shuttlebox all reached 90% avoidance criterion in less than 30 trials. Theios and Dunway (1964) comparing these two procedures showed that subjects reached criterion in 10 trials in a one way shuttlebox as opposed to 55 trials required in a two-way shuttlebox, The authors suggested two factors make the two-way learning condition, a complex task: (1) that, in a two-way shuttlebox, subjects must learn to reorient themselves and turn around (supported by Olton and Isaacson, 1968; Wedeking 1967); and, (2) that subjects must return to a location in which they had been shocked on the previous trial.

Levis, Bouska, Eron and McIlhon (1970) modified the Miller-Mowrer apparatus and, using it as a one-way shuttlebox, noted the marked dissimilarity of their results to those previously obtained in a two-way shuttlebox. Differences were particularly observed in the time characteristics of the avoidance response, trials to acquisition criterion, and resistance to change. In a two-way shuttlebox, subjects exposed to serial (light and sound) CS conditions tended to delay responding until after onset of the last stimulus introduced

into the CS sequence. This tendency was noticeably absent in the one-way situation. Subjects in both serial and non-serial conditions produced latency distributions that peaked close to CS onset. As well, in the one-way shuttlebox, there was a much faster rate of avoidance acquisition, and there was a marked superiority, in comparison to the two-way condition, in the subjects' persistance in responding in the absence of shock.

Levis et al. (1970) suggest that the difference in performance in the two situations may occur because of relative differences in contextual or apparatus cues between the situation preceeding the response and the situation following the response. In the two-way situation, both ends of the apparatus are identical with CS being the only external change in the stimulus complex. In the one-way situation the apparatus and subject transport cues are subject to differential reinforcement. This view is supported by other research Biederman, 1969; Seegal and Isaac, 1971) which emphasizes the differential effects of apparatus stimuli. Owen (1970) using kHA, RLA and RCA strains in a manual one-way shuttlebox showed that the difference between strains was smaller than that observed in a two-way shuttlebox. Owen suggested that the amount of handling the subjects received (necessitated by non-automatic procedure) may have affected the strains' individual rate of conditioning (Ashe and McCain, 1972). With this emphasis on apparatus-determined stimuli, and with the suggestion that further research needs to be done utilizing the one-way conditioning procedure, Levis et al. (1970) join others (Cole, 1972 re amphetamine; Potts 1970 re strains; Reiss 1970 re apparatus) in suggesting that variables such as equipment specificity, i.e. foot-shock, and strain differences, as well as amphetamine effects--be highlighted as central experimental variables in further research. Such research would also concur with Wahlsten's (1972a) emphasis on investigating the genetic correlates to learning, particularly as to motivation and the generality of learning differences.

Rationale and Objectives of the Present Research

It was precisely with the intention of bringing together the above conditions that the following experiments were conceived. Since the literature reveals that the RHA/Lu strains have demonstrated reliable differences in two-way active avoidance learning, along with the fact that there has been a relatively small amount of work done with Roman rats, it was decided to use these strains in an avoidance conditioning paradigm. However, the experiment was to be attempted in apparatus not previously used with the Roman strains--the one-way shuttle system-- and, after training, with various dosages of the stimulant drug, d-amphetamine sulfate. A question existed if the characteristic avoidance conditioning of the Roman strains, and their behaviour under equivalent dosages of d-amphetamine sulfate, would be generalizable to the one-way shuttle-system from the results previously demonstrated in two-way shuttlebox. (Satinder, 1971, 1972b) By determining the generality of learning differences between strains over different paradigms, information may be gained about general learning ability which transcends specific task trials (Wahlsten 1972 a, p.155).

Finally, in view of the recently demonstrated finding that the RHA/Lu is more responsive to unconditioned electric shock than is the RLA/Lu strain, it was decided to observe the effect on strain performance of the administration of an equal UCS set relative to each subject's individual shock threshold level in both strains tested. This procedure standardized the subjects' UCS making any continued significant strain differences in performance the result of factors other than simply different strain responsiveness to shock levels. The usage of a subject-relative UCS was also continued as a condition under which strain performance could be noted in the 'drug sessions' of Experiment 2, the design of which was equivalent to the 'drug sessions' of Experiment 1.

With the rationale of bringing together these experimental

variables, the following four objectives for this research project were set:

EXPERIMENT 1

(1) Roman strain (RHA/Lu and RLA/Lu) subjects were used for training in a one-way shuttle system. As well as determining strain performance in an apparatus never before used in conjunction with Roman strains, subjects were also chosen in terms of sex groups, in order to test for the emergence of sex as a significant factor in escape/avoidance conditioning using the one-way shuttle system.

(2) Given that strains and/or sex performance indicate a response to conditioning in the one-way shuttle system consistent with the above literature already discussed, subjects were then tested, in 'drug sessions' for general and specific responses to d-amphetamine sulfate (placebo and four dosage levels) injected interperitoneally following Gupta and Holland (1969) and Satinder (1971).

EXPERIMENT 2

(3) In a second experiment, using only naive female RHA/Lu and RLA/Lu strains, subjects were tested, in training, for conditioning in a one-way avoidance system using two distinct UCS footshock levels ('Equal' shock, the same as in Experiment 1; and, 'Differential' shock set in relation to each subject's shock threshold level).

(4) In the second half of Experiment 2 ('drug sessions'), subjects were tested for performance in the one-way shuttle system utilizing the two conditions of UCS, given also a placebo and four dosage levels of d-amphetamine sulfate, in a general design identical to that of Experiment I.

METHOD

Experiment 1

The purpose of Experiment 1 was to test whether the differential behaviour of Roman High Avoidance (RHA/Lu) and Roman Low Avoidance (RLA/Lu) strains of rats, previously tested in a two-way shuttle system, would prove to be a general phenomenon and yield strain differences in a one-way shuttle system. In addition, the animals tested of both strains were of both sexes in order to investigate any possible sex differences in performance.

The investigation was conducted in two parts: a three day 'training' session followed by a five day 'drug session' to test the effects of d-amphetamine sulfate dosages. The difference between the 'training' and 'drug sessions' lay in the fact that in the latter, d-amphetamine sulfate was administered to all subjects, with a placebo and four dosage levels, to determine the drug and dosage effect on behaviour.

Shock threshold levels for each subject were ascertained after the completion of Experiment 1.

General Design

The design of this experiment, following an analysis of variance format, utilized RHA/Lu and RLA/Lu strains of rat, with both sexes, in five animals per strain-sex group. The testing situation for the 20 subjects lasted 8 days, divided into 1) three day 'training', and, 2) five day 'drug session'. Each subject received one warm-up trial and ten scored trials of the conditioning task on each of the 8 experimental days. The general design of Experiment 1 may be schematized as follows:

Table 1
General Design of Experiment 1

	Three Day 'Training Session' t,1-10	t,1-10	t,1-10	Five Day 'Drug Session' t,1-10	t,1-10	t,1-10	t,1-10	t,1-10
Group 1 RHA/Lu 5 S's Male								
Group 2 RHA/Lu 5 S's Female								
Group 3 RLA/Lu 5 S's Male								
Group 4 RLA/Lu 5 S's Female								

Prior to the initiation of the experimental procedure, subjects were selected from the experimental animal breeding colony and transported from their original cages to a housing unit, next to the experimental room. There, each animal was code numbered and caged separately in a randomly selected cage on the housing rack, 2 days prior to the commencement of the 8 day experimental procedure.

The subjects' experimental room was dimly lit, measured with a Gossen lightmeter at less than one foot candle at the single light source kept in a position to the side of the one-way shuttle system throughout the experiment. Noise levels were taken inside the experimental room with a General Radio Type 1551-C sound level meter. It was found that external noise at 10 db were not of sufficient consequences to affect animals during the experiment, since a constant white noise was provided at 40 db from an internal building airconditioning unit functioning continually throughout the experiment. The sound intensities were averages taken at the floor level above the standard reference level of .000 2μbar. Temperature and humidity did not appreciably vary at any time during experimentation.

Injection Room - The injection room, normally a multi-purpose experimental room, was lighted by neon lamps and was maintained at 72 ± 2 °F,

with humidity at 40% and had its air changed by a York (Borg-Warner) air-conditioning unit.

The injection procedure required 26G. $\frac{3}{8}$" size, disposable needles and a Becton, Dickinson D-5238 injectors which were sterilized daily before injection in a Wilmot Castle sterilizer.

Throughout experimentation a double blind technique was used. The person recording the responses of the animals did not know anything about the strain of the animal, or dosages administered.

Subjects

Twenty naive rats, ten each from RHA/Lu (S_{22}, 236 days old) and RLA/Lu (S_{22}, 210 days old) strains, equally represented by both sexes, were selected as subjects. All the animals were bred, reared and weaned at 28 days in the Psychology Laboratory at Lakehead University.

Before experimentation the animals were housed in groups of two of the same sex. The two strains were housed on separate cage racks. Before transfer from the housing colony to the experimental housing room, the animals were code numbered using a double blind technique, so that the experimenter was unable to identify subjects by strain. During the course of experimentation the subjects were housed in individual cages measuring 10 x 7 x 7 in. on a mobile conveyor. In both pre-experimental and experimental housing, water and Purina Rat Chow food were always freely available. Defecation trays under each of the five levels of cages were cleaned daily. The laboratory temperature was thermostatically controlled within the range of $72 \pm 2^{\circ}$ F, and the humidity level was maintained at 40%. Fluorescent lights were on from 9 : 00 a.m. to 9 : 00 p.m.

Apparatus

One-Way Shuttle System. Experiment 1 was run in an A-586 one-way

shuttle system, prepared by the Lafayette Instrument Company of Indiana. Operated manually, this unidirectional system was a one-way active avoidance conditioning box for rats. The conditioned stimulus (CS) was multiple, having both 6 w. light illumination, and, noise from the light switching on and off. The UCS was a shock, in the presence of the CS illumination, of 90 volts, alternating current 60 c.p.s., standardized over a resistance of 47 K ohms in series with the 18 rod grid. This shock henceforth will be known as an Equal Shock (ES). The 6 mm thick Plexiglas grid-box measured 265 x 200 x 200 mm, the floor formed of anodized aluminium bars, 5 mm in diameter and 10 mm apart. The light CS grid electrification was controlled from the control box which was located behind the light (CS) fixture. The conditioning task required the experimental animal to exhibit escape behaviour by jumping up to a resting platform located at the opposite end from the light-CS. The resting platform box, elevated 80 mm from the floor level of the grid was made entirely of aluminium and was characterized by the fact that the box's most distant wall from the light fixture was a sliding unit 200 mm wide and 125 mm high. This was operated manually and could be withdrawn or pushed inward towards the Plexiglas-grid-box forming its back wall and thereby a closure to the opening of the resting platform. The floor of the resting platform, when fully opened, measures 137 x 200 mm of space. Animals were not handled between trials.

Drug

Previous research with d-amphetamine sulfate on Roman strains (Satinder, 1971, 1972 b) revealed the most effective dosage levels for obtaining relatively optimal performance.

D-amphetamine sulfate was used in Experiment 1 (drug sessions) in four dosage levels along with a placebo. The drug was administered

intraperitoneally (ip) in saline in the volume of 2 ml/kg in the following doses: 0.5, 1.0, 2.0 and 4.0 mg/kg. Each subject received all four dosages and the placebo on five different sequential days, in different orders assigned at random.

Each of the five consecutive 'drug session' days, with 10 trials per day, were begun 30 minutes after subjects had been administered the ascribed dosage, at approximately the same time of day for each subject.

Procedure

One-way shuttle system: Three day 'training sessions'

Experiment 1 began the 8-day experimental cycle with 3 training days. Previous experimentation (Potts, 1970; Theios, 1963; Satinder, 1973) showed that 10 training trials per day, for 3 days is generally sufficient to elicit a stable conditioned avoidance response pattern. Three days of 'training sessions' without drugs was given prior to the 5 days of 'drug sessions' in the avoidance conditioning paradigm under varying dosages of d-amphetamine sulfate.

The training procedure was as follows for each animal. Every animal prior to training was removed from its cage and weighed. Both the weight and the time of commencement of training were noted on the aninal's record sheet. The animal was then carried into the dimmed experimental room, placed on the grid of the one-way shuttle system and the top was closed.

Each animal was given 20 sec. to adapt and one trial before results of the next 10 cycles were noted on the record sheet. This complete procedure constituted 1 day of training per animal.

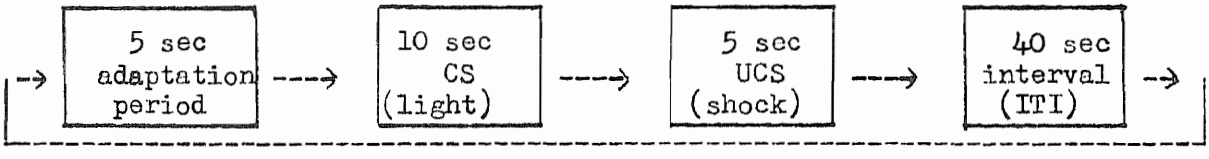
In each trial, after a 5 sec. adaptation period the CS (light) preceded the onset of the UCS (shock) by 10 sec. A

response during the CS terminated the CS and avoided the UCS which in Experiment 1 was an invariable Equal Shock. An unconditioned response (UCR) after the onset of the UCS shock terminated both the UCS and the CS simultaneously. If there was no UCR, the grid would remain electrified for 5 sec.

Following the 15 sec CS/UCS cycle the one-way shuttle system would remain inactive for 40 sec whether the animal was resting on the grid if there had been no response, or whether it rested in the resting platform box after having made either a CR or an UCR.

At the completion of this 1-minute cycle, the animal would receive 5 sec. of adaptation before second trial would commence. If the animal was on the resting platform, the experimenter would utilize the sliding back wall of the resting platform box to push the animal back onto the grid where it would remain and be given the 5 sec. adaptation period before the onset of the CS. The sliding wall would be withdrawn to have the resting platform box open before the beginning of the 5 sec. adaptation period.

One trial of the avoidance conditioning paradigm may be schematized as follows:



The experimenter recorded the animal's behaviour according to the following code:

A - Conditioned avoidance response, yielding both number of avoidances, and, by stopwatch timing-avoidance latency

E - Unconditioned avoidance response (i.e., escape), yielding both number of escapes, and by stopwatch timing-escape latency

↑ - Voluntary 'step-up' to the resting platform box, neither as an UCR nor CR, but at any period during 5 sec. adaptation period, or 40 sec. intertrial interval period. A voluntary within trial crossing-up was defined as a 'step-up'

↓ - Voluntary 'step-down' to the grid from the resting platform without the experimenter using the sliding wall at any time during the 40 sec. intertrial interval period. A voluntary within trial crossing-down was defined as a 'step-down'.

NNE or 15.0 - With a stopwatch the experimenter recorded the length of elapsed between the onset of the CS and the UCR or CR. The "15.0" represented an animal which has taken full 10 sec. of light (CS) and full 5 sec. of UCS (shock) and had not left the grid of the one-way shuttle system. Note that only this particular case of timing is also referred to as NNE - Number of No Escapes. This term was not applied to response latencies less than 15.0 sec.

Measurements

As indicated by the previous discussion of coding procedure, in the 'training session' both Experiment 1 and 2 measured a number of distinct behaviours made by the experimental subjects:

Avoidances - the number of acquired conditioned responses by which the subject, on being presented with the CS, would leave the grid and move to the resting platform of the one-way system

Avoidance latency - the length of time, to a maximum of 10 sec. that the animal took to make an avoidance while the conditioned stimulus (light) was on.

Escapes - the number of times the subject fled the UCS (shock) and moved from the grid to the resting platform of the one-way shuttle system

Escape latency - the length of time the subject took to escape the UCS. The shock onset began 10 sec. after CS (light) has been on, and lasted until the subject left the grid, or, until the maximum of five sec. of shock has elapsed.

Step-up - the number of voluntary movements made by the subjects from the grid onto the resting platform during the 5 sec. adaptation period and/or the 40 sec. "intertrial interval" period. As a voluntary within-trial movement, the "step-up" may be considered to be a gauge of body movements, similar to general activity (Cole 1970 a), somatic motor activity (SMA) as described by Kulkarni and Job (1967), or, intertrial crossing (Satinder 1971, 1972 b).

The step-up behaviour was an activity predetermined by the nature of the one-way system (i.e. the resting platform) and was therefore a body movement specific to this piece of apparatus, yet is an activity which is included within the general category of "body movement".

Step-down - the number of voluntary movements made by the subjects from the resting platform onto the unelectrified grid during the 40 second "intertrial interval" period. Similar to the "step-up" as an indication of body movement, the "step-down" is an activity measure unique to the one-way shuttle system (i.e. a body movement specific to the existence of the resting platform in the experimental apparatus).

The procedure for measurements under 5 days of differing d-amphetamine sulfate replicated that procedure used for the 3 training days, with the following exceptions:

(a) After weighing and recording the weight and time for each animal, the subject was taken into an injection room and there, utilizing a double blind technique, was injected interperitoneally (ip) with one of four possible dosages of d-amphetamine sulfate or a placebo according to a randomised order chart. A notation of time was made on the recording sheet, to test the subject precisely 30 min. after the injection. The animal was returned to its individual cage to await the noted time after which it was taken into the experimental room by experimenter for its daily trials. The person who injected all animals did not observe the animals in the one-way avoidance box.

The administration of a placebo and four levels of d-amphetamine sulfate to each subject during the five days of the 'drug session' resulted in a number of distinct behaviours. Measurements of performance were identical with those used during the training period, with the addition of two further analyses:

Avoidance by days - avoidances, computed as previously described, analysed to determine the days effect, as distinct from the dosages effect on avoidance over days.

Avoidance latency by days - avoidance latencies, computed as previously described, and analysed to determine the days effect on avoidance latency, as distinct from the dosages effect on avoidance latency over days

METHOD

Experiment 2

The purpose of Experiment 2, was to determine how RHA/Lu and RLA/Lu female subjects would respond under two distinct conditions of UCS shock. These conditions were: (1) an 'Equal' and invariable footshock of the same intensity given in each trial for all the subjects in Experiment 1; and, (2) a 'Differential' and relative shock set by the criterion of : twice the value of each subject's mean score attained in individual flinch threshold testing.

As in Experiment 1, this investigation was also done in two parts, having both 'training session' and 'drug session', along with the same general design in which d-amphetamine sulfate was administered to all subjects only on the 5 day 'drug sessions'.

All subjects were female, thereby eliminating the possibility of sex dependent behaviour, as was tested in Experiment 1. Also unlike Experiment 1, the procedure of Experiment 2 required that flinch threshold levels be determined before, rather than after, commencement of the eight day experimental procedure.

General Design

The general design of Experiment 2 was identical with that used in Experiment 1, with the following differences. All the subjects were female (rather than of both sexes, as in Experiment 1); and, two levels (Equal and Differential) were used as UCS conditions, rather than just the one level (Equal) of footshock used in Experiment 1. As a result, and in analogy with Experiment 1, the general design of Experiment 2 may be schematized as follows:

Table 2
General Design of Experiment 2

	3 Day 'Training Session'				5 Day 'Drug Session'			
	t,1-10	t,1-10	t,1-10	t,1-10,	t,1-10	t,1-10	t,1-10	t,1-10
Group 1 - RHA/Lu 5 S's Equal Shock UCS								
Group 2 - RHA/Lu 5 S's Differential Shock UCS								
Group 3 - RLA/Lu Equal Shock UCS								
Group 4 - RLA/Lu Differential Shock UCS								

In a manner similar to Experiment 1, two days prior to experimentation subjects were transferred from their colony to the experimental housing unit and assigned randomly to their housing rack. In Experiment 2, however, the S's flinch thresholds were established two days prior to the experimental session's beginning.

Subjects: Twenty naive female rats, ten each from RHA/Lu (S_{23}, 123 days old) and RLA/Lu (S_{23}, 117 days old). All the animals were bred, reared and weaned at Lakehead University. Animal care procedure, as well as pre-experimental and experimental procedures described in Experiment 1 apply to the subjects of Experiment 2.

Apparatus:

One-Way Shuttle System

The same one-way system, described in the Method to Experiment 1, was also used to test the 20 subjects in Experiment 2, with one exception.

In order to meet the experimental requirements of the

Differential shock condition for 10 animals in Experiment 2, the grid electrical system was adapted so that it had an optional flexible cord connector. The use of this connector enabled application of the shock-UCS from the one-way system control box both with the Equal shock input previously described above, or, from a package capable of discharging Differential, or variable shock. The package was comprised of a powerstat Variable autotransformer Type 116B; a Hunter timer automatically controlling the length of time of variable UCS shock discharge; and, a Phillips PM 3230 oscilloscope indicating whether or not shock was being received, the degree of shock being received during UCS application, as well, an indication of the individual rat resistance (compared with the 47 K ohms setting), and resistance changes during the 5 sec UCS.

Except for this difference in application of Differential shock as compared with Equal UCS, all parts of the one-way system apparatus, including manual control of the CS and resting platform, were used identically as in Experiment 1.

Drugs:

D-amphetamine sulfate was used in Experiment 2, in a manner identical with that described in Experiment 1.

Room Conditions

The housing, experimental and injection room for Experiment 2 were the same as described in Experiment 1.

Flinch Threshold Box. Constructed at Lakehead University the flinch threshold box, measuring 300 mm x 295 x 270 mm had three sides and the open-door top made of Plexiglas. The fourth wall of the box was blackened, while the floor was constructed of 23 stainless steel grids, 10 mm apart and 2 mm in diameter. The grid electrical

system was hooked up in series and connected to a variable shock-package which included a powerstat variable autotransformer, type 116B, produced by the Bristol Electric Co. of Bristol, Connecticut; a .5 sec Hunter timer automatically controlling the length of shock applied; and a Phillip's PM 3230 oscilloscope. The apparatus offered the user ten shock levels ranging from .1 ma to 1.0 ma in steps of .1 ma. This apparatus has been described previously by Satinder and Hill (1974).

Miscellaneous Apparatus. In addition to the previously mentioned apparatus, experimentation required the use of two stop-watches, plastic animal carrying boxes, weight scale, electrical timers, and a Gossen light meter.

Procedure:

The procedure described for Experiment 1, including weighing the subject, trial cycles, and coding were all identically utilized in the procedure for Experiment 2--with one exception.

It was necessary to obtain individual flinch threshold data to be used to set up a "Differential UCS" level for each of the ten subjects categorized in the "Differential Shock" groups of the experimental design. The procedure used was to multiply, by a factor of two, each of the individual mean shock levels recorded by the flinch threshold procedure. The advantages accrued were therefore two fold: (1) since the mean shock threshold level was doubled to define the 'Differential UCS', each subject would be assuredly sensitive to the application of the UCS; yet, (2) since the base figure for the establishment of the 'Differential UCS' was obtained

by individual shock threshold testing, it represents a UCS established to the individual sensitivities of the subject.

One Way Shuttle System - Three Day Training Session.

The procedure for Experiment 2 was identical with that described in the Method for using the one-way shuttle system, as described in Experiment 1.

Five day 'Drug Sessions' Under Different Dosages

Procedures for the conducting of experimentation with the five-day 'drug sessions' was identical for that described in Experiment 1. However since ten of the subjects in Experiment 2 received 'Differential' rather than 'Equal' shock (as in Experiment 1) the experimenter was obliged to modify the source of power for the UCS before 'Differential shock' subjects were tested. This was done by disconnecting the 'Equal Shock' UCS power system and attaching the flexible connector from the grid to the variable shock package. When this procedure was being followed, the experimenter set the UCS level before subjects were tested. (in accord with Table 9). Along with all previous observation and recording duties, described in Experiment 1, the experimenter also took oscilloscope readings.

Establishing Flinch Threshold

Previous comments about the general design of both sections in this study indicated one additional procedural difference between Experiments 1 and 2, i.e. testing subjects of Experiment 2 for flinch threshold to determine differential UCS level before one-way avoidance testing. However, to determine the effect of prior shock experience on one-way avoidance the subjects of Experiment 1

were tested for flinch threshold after the one-way avoidance testing. This provided data for the comparison of both avoidance and shock threshold between the experiments.

The procedure for establishing flinch threshold began with the weighing of the animal. The subject was carried in an open container into the normally lighted experimental room and placed on the table near the flinch threshold box for 1 minute. During this time the grid of the box was wiped first with steel wool to remove any particles left from the previous animal testing, and with tissue paper to clear any moisture which could serve to short the electrical system.

The testing procedure was run using a double blind technique with two experimenters. Experimenter number one placed the animal in the flinch threshold box, observed and reported the animal's response to experimenter number two after hearing experimenter number two announce the trial number and administer the shock level. Experimenter two observed the oscilloscope to assure himself that the shock was being received and recorded the response told him by experimenter one, but did not watch the animal's response. Flinch response was defined as a mild startle response, made by lifting only one paw to the shock stimulus. The flinch threshold score of each animal tested was determined by method of limits based on ten shock values at which a flinch response was observed.

Each animal was given a number of shocks in ascending order, at approximately five second intervals, lasting .5 sec, the levels of which begin with 0.0 ma, .1 ma, .2 ma, and so on, with the range

possibility reaching 1.0 ma. Each trial was terminated when experimenter one observed a flinch response. Each animal received 10 such trials, beginning with 0.0 ma in the first trial, and in following trials at a randomly selected shock levels below the animal's demonstrated flinch threshold. Since the presentation of shocks, although in an ascending series, are begun randomly at different levels, no time/sequence clue, or expectation cue, was available.

RESULTS

Experiment 1

Training

Despite a difference in the avoidance task used, as contrasted with those offered by Bignami (1965) and Satinder (1971), results of the three day training sessions of Experiment I indicated that RHA/Lu and RLA/Lu strains differed significantly in the training period on: number of avoidances (F=21.9, df=1/16, $p<.01$) (See Figure 1), as well as on avoidance latency (F=23.6, $p<.01$) (Figure 2), and escape latency (F=19.9 $p<.01$) (Note: For brevity, the absence of df in further quoted results indicate a df value similar to preceeding scores.)

Mean number of avoidance responses averaged over days indicated that the RHA/Lu strain (Mean 6.8) made a higher number of avoidances than the RLA/Lu strain (2.7). Mean scores also indicated that RHA/Lu had a shorter mean escape latency (RHA/Lu = 0.7 secs. RLA/Lu = 3.0 secs.)

The RHA/Lu strain's faster acquisition, than the RLA/Lu strain, of the conditioned response over the three training days was proven statistically significant on: number of avoidance responses (F=47.67, df=2/32, $p<01$), and number of escapes (F=26.4, $p<.01$). The number of avoidance responses by RHA/Lu (3.50, 7.60, 9.40), when compared with RLA/Lu (0.90, 3.00, 4.10) confirmed the superior rate of acquisition by the RHA/Lu strain.

The mean number of escapes occurring over the three training days by the RHA/Lu strain were 4.7, 2.4, and 0.6. In this case, a diminishment of the number of escapes occurring over three days reflects a conditioning in avoidance responses. This performance may be compared with the RLA/Lu strain's 1.6, 2.6, and 1.3 mean number of escapes.

The RLA/Lu strain's slower rate of improvement of escape scores must be considered in conjunction with results of the Number of No Response (NNR) scores. The nature of the 'escape score' was such that its measurement was dependant on subjects not leaving the grid until the shock was presented. This measurement was pre-empted by an avoidance. Rapid avoidance conditioning (as by the RHA/Lu strain) did not therefore present sufficient 'escape scores' to allow strain to be proven statistically different, using this measurement.

Avoidance response latency (F=35.69, df=2/32, $p < .01$) and escape response latency (F=25.20, $p < .01$) over days indicated a significant difference between strains as to their rate of conditioned response (CR) and unconditioned response (UCR). Avoidance latency scores demonstrated that the RHA/Lu subjects (Means 8.16, 5.70, 4.00) were conditioned to the CS at a faster rate than the RLA/Lu subjects (Means : 9.71, 8.30, 7.63) and that this same effect was also demonstrated with escape latencies (RHA/Lu 1.78, 0.39, 0.07 compared to RLA/Lu 4.29, 2.73, 2.04 seconds).

The performance of strains interacted with training days indicated statistical significance using data on the number of avoidance responses (F=4.33, df=2/32 $p < .05$) and number of escapes (F=22.05, $p < .01$). Results therefore indicated that strains differed over days and that the degree of change shown by the RHA/Lu strain over the three training days was greater (See Figure 1) than the degree of change demonstrated by the RLA/Lu strain.

The avoidance latency scores also yielded significant statistical results (F=3.87, df=2/32; $p < .05$) in the strain by days interaction, indicating that the RHA/Lu strain over the three training days improved its speed of avoidance faster than did the RLA/Lu strain.

Although the mean escape latency scores of the RHA/Lu strain (1.8, 0.39, 0.07 seconds) and the RLA/Lu strain (4.29, 2.73, 2.04 seconds) also showed RHA/Lu to have a faster escape latency than RLA/Lu, the escape latency scores did not indicate significant strain by days interaction. This demonstrated that the strain effect was independent of the days effect.

Analysis of the activity scores: (1) step-up, and, (2) step-down for strain differences in training, in Experiment 1, indicated that RHA/Lu performed significantly more actively than RLA/Lu in both cases (1) $F=7.36$, $df=1/16$, $p < .05$; and, (2) $F=7.07$, $p < .05$. Mean frequency scores averaged over days for RHA/Lu in (1) step-up and (2) step-down, in Experiment 1 respectively were 4.87 and 0.83, whereas the RLA/Lu mean scores were 1.23 and 0.03.

Too few step-up (Mean score: female 2.67; male 3.43) or step-down (Mean score: female 0.43; male 0.43) movements were made to be able to ascertain which sex of each strain was more active in the training period. Means indicated that the step-up activity (Mean 3.05) was more predominant than step-down behaviour (Mean 0.43). The RHA/Lu subjects were more active (Means over three days: 8.00, 14.20, 7.00) than the RLA/Lu subjects (Means 2.40, 2.60, 2.40) in the three day training period.

In the training sessions of Experiment 1, none of the statistical tests, run on any of the experimental measurements indicated the two-groups of animals in either strain to have demonstrated any significant sex differences. Only the interaction of the sex by day variables, using frequency of escape scores, proved significant ($F=22.05$, $df=2/32$, $p < .01$). In this case the RHA/Lu females (with mean escape scores of 6.00, 2.20 and 0.60) and RLA/Lu females (Mean escape scores 1.80, 2.40 and 1.00) over the three training days, improved their rate of number of

escapes more than did the male animals over days, thereby yielding the significant interaction effect (RHA/Lu males 2.40, 2.60, 0.60; RLA/Lu males 1.4, 2.8, 1.6 mean number of escapes.

In view of the nature of the strains used (bred for avoidance conditioning) particular note was made of the subjects which did not respond to the UCS at all, thereby experiencing a full five seconds of shock. As previously noted this situation is described as "number of no escapes" (NNE). In the training sessions of Experiment 1, the two strains demonstrated a differential occurrence of this condition (F=8.53, df=1/16 p <.01) with the RHA/Lu averaging 0.60 mean number of NNE and RLA/Lu 5.50. Days effect was also statistically significant (F=17.15, df=2/32, p <.01) with the mean scores of the RHA/Lu strain at 1.80, 0.00, 0.00, while RLA/Lu had 7.5, 4.4, and 4.6 mean number of NNE during the three training days.

Effect of d-amphetamine sulfate on one-way active avoidance

Despite the evident differentiation of strains in the training period of Experiment I, administration of d-amphetamine sulfate in the second part of the experiment resulted in all measurements with the exception of step-down, showing strain differences non-significant. As will later be discussed however, avoidance latency, escapes, step-up and step-down did demonstrate a dosage effect. Only step-down measurements indicated that the RHA/Lu strain had a significantly larger mean (Mean: 6.34) than the RLA/Lu strain (Mean: 0.40) (F= 6.61, df=1/16, p <.05). Examination of the step-down behaviour demonstrated that the females RHA/Lu (Mean 9.96) were more active than the males RHA/Lu (Mean 2.72),

while the male RLA/Lu (Mean 0.56) was slightly more active than the female group (Mean 0.24) of the RLA/Lu strain.

Although not showing statistical significance on any of the measurements in training, the sex variable did show a statistically significant sex difference with the step-up performance (Table 3) during drug testing ($F=4.80$, $df=1/16$, $p < .05$). The RLA/Lu strain with a mean of 8.26 demonstrated a more frequent step-up behaviour than the RHA/Lu (Mean 7.50). Review of the sex groupings indicated that females in both RLA/Lu (Mean 10.52) and RHA/Lu (Mean 11.24) performed at a higher rate than males in RLA/Lu (Mean 6.00 and RHA/Lu (3.76) strains.

In all other measures of performance under dosages, the sex differences did not prove significant as a main variable, however, sex by strain did yield a significant interaction effect on avoidance latency scores ($F=9.27$, $df=1/16$ $p < .01$), and number of escape responses ($F=9.18$, $p<.01$). Avoidance latency scores indicated the male RHA/Lu (Mean 2.96) and female RLA/Lu (Mean 3.51) were performing with a shorter avoidance latency than their strain group, sex counterparts: female RHA/Lu (Mean 4.04) and male RLA/Lu (Mean 4.78). However results of the number of escape responses showed that the female RHA/Lu (Mean 1.24) and male RLA/Lu (Mean 1.32) scored more of escape responses than the male RHA/Lu (Mean 0.40) and the female RLA/Lu (Mean 0.76). Also, although not statistically significant, the mean of step-down measures on strain by sex interactions were consistent with the above findings indicating that female RHA/Lu (Mean 9.96) performed better than the male group (Mean 2.72), and, that the male RLA/Lu had more step-downs (Mean 0.56) than the female group (Mean 0.24) under the d-amphetamine dosage condition.

Analysis within strain of avoidance scores indicated that it was the significant sex differences within the RHA/Lu strain (F=13.79, df= 1/8, $p < .01$) that was yielding strain by sex significance, with males (Mean 9.60) having more avoidances than females (Mean 8.44).

Analyses of the effect of d-amphetamine sulfate on measures of behaviour of experimental subjects indicated that dosages had a differential effect on avoidance latency (F=2.64, df=4/64, $p < .05$), number of escapes (F=3.00, $p < .05$), and on both step-up (F=4.46, $p < .01$) and step-down performances (F=4.85, $p < .01$). Means of both (1) avoidance latency and (2) number of escape responses were higher with the RLA/Lu strain ((1) 4.12 (2) 1.04) than the RHA/Lu strain ((1) 3.50 (2) 0.82). This indicates that the RLA/Lu strain avoided the UCS slower and experienced the UCS more often than the RHA/Lu strain under dosage conditions. Step-up behaviour was demonstrated more frequently by the RLA/Lu strain (Mean 8.26) under dosages (RHA/Lu Mean 7.50) whereas, the opposite effect was seen with the step-down behaviour (RHA/Lu:Mean 6.34; RLA/Lu:Mean 0.40). Females performed at a higher rate than the males on step-up and, with RHA/Lu strain, in step-downs movements. In this latter case females (Mean 9.96) in RHA/Lu performed better than males (Mean 2.72). However, with RLA/Lu step-downs, males (Mean 0.56) had a more frequent step-down behaviour than females (Mean 0.24).

In addition Table 3 and Table 4 demonstrate the activity level of the strain by sex groups, for each of the administered level of drug. For RHA/Lu and RLA/Lu females the maximal step-up activity occurred with 1.0 mg/kg, 2.0 mg/kg, the dosage level which was also optimal for performance in male groups of both RHA/Lu and RLA/Lu strains.

In step-down activity 1.0 mg/kg produced maximal performance in females of both strains as well as for males of the RLA/Lu strain, while 2.0 mg/kg remained the dosage which gave the greatest mean frequency of activity in the RHA/Lu males.

Both Tables (3, 4) indicate that strain by sex groups react to the various levels of drug dosage in different ways, with the peak level of activity for RHA/Lu females being a mean step-up of 19.6, RHA/Lu male mean 7.8; RLA/Lu female mean 16.8 and RLA/Lu male mean 12.6. The peak levels of the strain by sex mean step-down activity were as follows: RHA/Lu females 21.2, RHA/Lu males 5.8, RLA/Lu females, 1.0, RLA/Lu males 0.8.

In addition to the behavioural performances which indicated that dosage levels of d-amphetamine were working as an independent variable, a number of measurements indicated that dosages interacted with the strain characteristics of the subjects to give significantly different behaviours.

The dosages by strain interaction proved significant both with the number of avoidance responses ($F=3.10$, $df=4/64$, $p < .05$) and number of escape responses ($F=4.65$, $p < .01$) data, as well as with avoidance latency ($F=3.80$, $p < .01$) and the step-down activity measurements ($F=3.82$, $p < .01$).

Within strain analysis of (1) avoidance responses and (2) avoidance latency means scores indicated the RHA/Lu strain (1) ($F=7.83$, $df=4/32$, $p < .01$) and (2) ($F=7.91$, $p < .01$) contributed the greater amount of dosages variability in comparison with RLA/Lu strain. The male RHA/Lu exhibited the most number of avoidance responses (Mean 9.60) as compared to female RHA/Lu (Mean 8.44), and had a shorter avoidance latency (Mean 2.96 sec.) than the females of the RHA/Lu strain (Mean 4.04 sec.)

The number of escapes, as mentioned earlier, indicated that the RLA/Lu strain experienced the UCS more often than the RHA/Lu strain under dosage conditions. Within, or by, strain analysis indicated that 0.5 mg/kg of d-amphetamine was the dosage level which produced optimum escape behaviour (i.e. 0.0 escapes) for both the male and the female groups of the RHA/Lu strains. The same optimum level of behaviour was achieved by 2.0 mg/kg dosage for the male and female of the RLA/Lu strain. Because of the nature of the escape measurements (i.e. dependent on the subject not avoiding) this comparison may not have been entirely reliable, however, it did indicate the RLA/Lu strain required a higher dosage level to eliminate behaviour--as occurred to RHA/Lu at a lower dosage level.

The highest dosage level, 4 mg/kg, demonstrated a consistent decrement in performance on escapes for all strain/sex groups, with females RHA/Lu being affected most, 4.0 mean escapes. This may be compared to the mean scores of the male RHA/Lu (Mean 0.6); with, the males and females of the RLA/Lu group having 0.6 and 0.8 mean number of escapes.

The effects of dosage on strain behaviour for RHA/Lu females, RHA/Lu males, and RLA/Lu females behaviour patterns indicated dosage specific performances, when avoidance latency measures were used. All three demonstrated U-curves which, with increased drug levels, first increased then decreased performance. The RHA/Lu strain, both females and males show that 0.5 mg/kg of d-amphetamine sulfate produced the shortest avoidance latency for their strain/sex group, with female means at 2.60 sec. and male means at 1.99 sec. The female RLA/Lu strain demonstrated its fastest mean avoidance latency at the 2.0 mg/kg dosage level with a mean latency of 1.75 sec.

After each of these three strain/sex groups achieved its maximum avoidance latency performance with dosage level, an increase in the level of d-amphetamine sulfate dosages rather than continue to improve performance, lengthened the avoidance latency performance. At 4.0 mg/kg the mean avoidance latency for each group were: RHA/Lu females - 7.23 sec.; RHA/Lu males -3.52 sec.; RLA/Lu females 3.74 sec. Unlike the performance of any of the three previous groups, RLA/Lu males under dosages did not appear to have reached its maximal speed of avoidance latency. Increasing dosages from 0.5 to 4.0 mg/kg appeared to consistently improve group avoidance latency performance, with the final mean being 3.14 sec. A reversal of improved avoidance latency with increased dosage level was not observed.

A review of the step-up (Table 3) and step-down (Table 4) performances under d-amphetamine sulfate dosages indicated that the activity level of most of the strain/sex groups were specific to the dosage level of drug administered. All groups in the step-down activity and the RHA/Lu strain, of both sexes, clearly demonstrated that their placebo level of activity increased with dosage level, to a maximum (means previously given) whereupon further administration of increased dosage level, decreased activity, in some cases below the initial placebo level of activity (RHA/Lu strain in both step-up and step-down). Again similar to avoidance latency scores the RLA/Lu strain proved to be an exception to the rule, having demonstrated a variable response to dosage levels on the step-up measurement of activity, ending with females (improvement) and males (decrement) of the RLA/Lu strain having reacted to the final dosage level with opposite behavioural responses.

An analysis by days of the avoidance and avoidance latency scores made in the 'drug session' indicated that there was a significant result with both measurements (1) $F=6.98$, $df=4/64$, $p < .01$ (2) $F=4.96$, $p < .01$. This indicated that both the number of avoidances made and the avoidance latencies were affected not only by the dosage level, but by continued differential conditioning of the strain/sex groups over the five days of testing.

A strain analysis of avoidance responses by day scores indicated that the day effect was significant only in the RLA/Lu strain ($F=8.02$, $df=4/32$, $p < .05$) and that RLA/Lu, not the RHA/Lu strain, experienced an ongoing statistically significant conditioning, independent of administered drug dosages.

A strain analysis of the avoidance latency by day scores did not indicate the days effect to be statistically significant in either of the strains. However, the mean avoidance latency by day scores indicated that in both RHA/Lu and RLA/Lu strains the female group displayed the greater and more systematic on going behaviour improvement of scores, demonstrating that sex group's continuing conditioning independent of the dosages effect.

EXPERIMENT 2

Training

Similar to the major results of Experiment 1, training sessions in Experiment 2 demonstrated both strains and days to be statistically significant variables. Differential shock as a main variable in training sessions of Experiment 2 did not prove to be a significant variable in training session. The measurements of behaviour used in both 'training' and 'drug sessions' of Experiment 2 were identical with those used in Experiment 1, and, have been previously discussed.

In the three training days of Experiment 2, the strains differed significantly in avoidance ($F=11.47$, $df=1/16$, $p < .01$), avoidance latency ($F=6.72$, $p < .05$), escape latency ($F=14.64$, $p < .01$), step-down $F=14.40$, $p < .01$) and on the number of no escapes (NNE) exhibited ($F=13.37$, $p < .01$). Similar to Experiment 1, mean scores indicated that the (1) RHA/Lu strain had: more avoidances (Means (I) 6.70 (2) RLA/Lu=3.23); a shorter avoidance latency under both Equal and Differential shock ((I) RHA/Lu means under Equal shock 6.12 whereas (2) RLA/Lu mean was 7.11; and, under a Differential shock (I) RHA/Lu mean was 6.4, whereas (2) RLA/Lu mean was 9.00) ; a faster escape latency ((I) Mean 0.72 sec. (2) RLA/Lu 2.88 sec.; more step-downs (RHA/Lu Mean 4.43; RLA/Lu 0.57); and fewer NNE ((I) Mean 0.60 (2) Mean 5.00) - than RLA/Lu.

Unlike Experiment I however, the 'training sessions' of Experiment 2 did not differentiate strains on the basis of step-up behaviour. (Table 3)

The effect of conditioning over days demonstrated statistically significant differences using all experimental measurements: avoidance responses, ($F=36.44$, $df=2/32$, $p < .01$), number of escape responses ($F=4.53$, $p < .05$), avoidance response latency ($F=24.53$, $p < .01$) escape response latency ($F=39.24$, $p < .01$), step-up ($F=6.13$, $p < .01$), and

step-down (F=12.65, p<.01). Mean scores indicated that the RHA/Lu strain was conditioned over the three training days making: more avoidances (Means 3.90, 7.70, 8.50) than the RLA/Lu strain (Means 1.10, 3.70, 4.90); fewer escapes (Means 3.40, 1.60, 1.30) than the RLA/Lu strain (Means 2.70, 2.40, 2.00) (See Table 6); a shorter rate of avoidance latency (Mean 6.27) than the RLA/Lu strain (Mean 8.05 sec.); a faster rate of escape latency over the training days (Means 2.39, 1.06, 0.83 sec.) than the RLA/Lu mean escape latencies (3.29, 1.84, 1.40 sec.); more step-ups (Means 2.70, 6.10, 6.80) than the RLA/Lu strain (Means 1.20, 2.70, 5.80); and, more step-downs over the three training days (Means 0.60, 5.00, 7.70) than the RLA/Lu strain (Means 0.00, 0.60, 1.10).

Of the possible interaction effects in the 'training session', day by strain (F=6.83, df=2/32, p<.01) and day by shock by strain (F=4.36, p<.05) proved significant with step-down measurements. A review of the means of both (1) RHA/Lu and (2) RLA/Lu strains, in both Equal and Differential shock conditions, over days, with mean step-downs indicated that strains did differ, and, that the degree of change demonstrated by the RHA/Lu strain over three training days was greater (Means 0.60, 5.00, 7.70) than the degree of change demonstrated by the RLA/Lu strain (Means 0.00, 0.60, 1.10).

As was done previously in Experiment 1, the performance by strains of the NNE behaviour was noted (See Table 8). Analysis indicated that strains differed significantly (F=13.37, df=1/16, p<.01) with the RLA/Lu having displayed a larger mean number (5.00) of NNE than the RHA/Lu strain (Mean 0.60). A further review of mean scores indicated that those groups receiving the Differential shock (Mean 3.40), although statistically non-significant, made more 'no escapes'

(NNE) than the strain under Equal shock (Mean 7.20) condition. RLA/Lu had more NNE (Means 7.1, 4.60, 3.30) as compared with the RHA/Lu (Means 1.80, 0.00, 0.00). Analysis of the days effect indicated it to be a significant (F=27.49, df=2/32, $p < .01$) difference.

In conjunction with strain differences, and day effects as main variables, the days by strain interaction also proved statistically significant (F=3.30, df=2/32, $p < .05$). This indicated that strains differed over days and that the degree of change exhibited by the RLA/Lu strain was statistically greater than the degree of change over days demonstrated by the RHA/Lu strain.

Effects of d-amphetamine sulfate on one-way active avoidance.

In the second part of Experiment 2, dosages of d-amphetamine sulfate were administered to the subjects, all females, in a manner identical with that used in Experiment 1.

Analysis of measurement scores under dosages for strain differences indicated that the strains, which demonstrated significant differences on three behavioural measurements in training, proved significant only on the step-down measurements (F=11.21, df=1/16, $p < .01$) Mean scores indicated that the RHA/Lu strain had a higher mean frequency of step-downs (9.76) than RLA/Lu (2.94), but that the majority of this activity came from RHA/Lu subjects in the Differential shock condition. (Mean RHA/Lu 12.32, whereas RLA/Lu 0.56). A greater frequency of step-downs was also maintained by the RHA/Lu strain in the Equal shock groups with a mean of 7.20, whereas the RLA/Lu Equal shock group had a mean frequency of 5.32.

Consistent with the above relationship, step-down measurements indicated that the shock by strain interaction under dosages was significant (F=5.88, df=1/16, $p < .05$).

By strain analysis of avoidance scores indicated a significantly different response under the two shock conditions in subjects of the RHA/Lu strain (F=8.87, df=1/8, $p<.05$) and no statistically significant response difference in the RLA/Lu strain. Perusal of the means showed that the Equal shock group in the RHA/Lu (Mean 8.84) avoided the shock more often than RHA/Lu subjects receiving the Differential shock (Mean 6.60).

By strain analysis of avoidance latency scores indicated that the subjects (all female) in each of the strains responded differently to the two shock conditions. Results of scores in RHA/Lu strain indicated a significant difference (F=6.80, df=1/8, $p<.05$) in response to the two shock groups, with the Equal shock group (Mean 3.70 sec.) avoiding faster than the Differential shock RHA/Lu group (Mean 5.65 sec.) Although the same relationship existed with shock groups of the RLA/Lu strain, results of by strain analysis of variance did not prove significant.

Escape scores (See Table 6), when analysed by strain, indicated that the RHA/Lu experimental animals reacted to the shock conditions significantly differently (F=8.37, df=1/8, $p<.05$). This did not occur with the RLA/Lu strain. Examination of means in the RHA/Lu strain indicated that the Equal shock group (Mean 0.92) had fewer escapes than the Differential shock group (Mean 2.08).

Administration of d-amphetamine sulfate to subjects was statistically demonstrated to be a significant independent variable having affected behaviour of subject groups differentially on all experimental measures: number of avoidances (F=13.12, df=4/64, $p<.01$), number of escapes (F=3.55, $p<.05$) avoidance latency (F=16.55, $p<.01$), escape latency (F=12.51, $p<.01$), number of step-ups (F=5.96, $p<.01$)

and, number of step-downs ($F=10.19$, $p<.01$).

Means of number of avoidance responses indicated that the dosage group with Equal shock (Mean 7.72) had more avoidances than the dosage group with the Differential shock (Mean 5.34).

Mean scores on the number of escapes however, showed the dosage group with Differential shock to have a greater mean frequency of escapes (Mean 2.00) than the dosage group with the Equal shock (Mean 1.14) condition.

Means of the avoidance latency scores indicated that the dosages groups with Equal shock (Means 3.47, 3.00, 3.35, 5.26, 8.32) performed with a shorter rate of avoidance than the dosage groups with Differential shock (Mean latencies 5.80, 5.72, 5.76, 6.27, 8.03).

Means of the escape latency scores (See Table 7) show, as in avoidance latency, that the dosage groups with Equal shock scored an overall mean of 0.68 sec., and have a lower latency time in escaping shock than did the dosage groups with Differential shock.

As previously mentioned, both step-up and step-down measurements, under drug, demonstrated significant statistical dosage differences. It was noted that the maximum step-up activity for the RHA/Lu strain under both shock conditions was at 0.5 mg/kg (although RHA/Lu continued equal maximum activity under 1.0 mg/kg.) The RLA/Lu strain demonstrated its maximum step-up activity under 1.0 mg/kg with the Equal shock condition, and, at 2.0 mg/kg with the Differential shock condition.

With the step-down measurements, maximum activity for the RHA/Lu strain was at 0.5 mg/kg with the Equal shock condition, and, at 1.0 mg/kg with Differential shock. RLA/Lu strain performed its most frequent step-down behaviour at 0.5 mg/kg under the Equal shock

condition, and, at 2.0 mg/kg under the Differential shock condition.

Review of both step-up and step-down means demonstrated that the shock by strain groups performed to dissimilar peak activity levels. In both (I) step-up, and, (2) step-down behaviour, the RHA/Lu strains, under both shock conditions, was more active than the RLA/Lu strains. RHA/Lu peak mean scores are: (I) 18.8 at the Equal shock, and, 14.2 with the Differential shock condition; and in (2) reversing position, with a mean score 14.0 under Equal shock, and, 18.6 with Differential shock. The peak scores of RLA/Lu for both step-up and step-down measurements, under both shock conditions, were less than those attained by the RHA/Lu strain. Indeed the strain difference with step-down scores, as previously noted, proved statistically significant. With step-up scores, although not statistically significant at $p < .05$ ($F=4.17$ df 1/16) strain performances over shock categories (Mean scores: RHA/Lu 10.6; RLA/Lu 5.68) were consistent with that found in the step-down activity, and supported the evidence showing strain types to be an important factor of activity, under various shock levels and d-amphetamine sulfate dosages.

In contrast to Experiment 1, NNE scores did indicate significant differences under dosages ($F=5.7$, $df=4/64$, $p < .01$). Mean scores indicated that the RLA/Lu strain both in Equal shock condition (Mean 2.4 where RHA/Lu mean is 0.24) and in the Differential shock condition (Mean 4.32 where RHA/Lu mean is 1.36) had a greater number of no escapes (NNE) than the RHA/Lu strain.

Strain by dosage analysis proved to be a statistically significant interaction with: number of avoidances ($F=3.97$, $df=4/64$, $p < .05$), step-up ($F=3.57$, $p < .05$) and step-down ($F=3.28$, $p < .05$), and avoidance latency measurements ($F=2.61$, $p < .05$).

Strain by dosages mean scores indicated that the RHA/Lu by

dosage means (8.1, 8.4, 8.9, 7.8, 6.5) demonstrated an interaction effect yielding more avoidances than the RLA/Lu by dosages interaction (Means 7.3, 6.8, 6.2, 4.7, 0.60). The same relationship continued to exist for the (I) RHA/Lu by dosages interaction over the (2) RLA/Lu by dosages interaction in the cases of: Mean step-ups (I) 10.7, 16.5, 15.4, 8.7, 1.7 over (2) 3.9, 6.5, 6.8, 6.7, 4.5; as well as Mean step-downs (I) 9.5, 16.1, 14.1, 9.0, 0.10 over (2) 1.6, 4.8, 3.9, 4.4, 0.00.

Strain by dosage mean avoidance latency scores indicated that RHA/Lu strain (Means 3.47, 2.98, 3.35, 5.26, 8.32 sec.) performed with a faster avoidance latency than did the RLA/Lu strain (Means 5.80, 5.72, 5.76, 6.27, 8.03 sec.) over dosages.

By strain analysis of avoidance scores showed that subjects in the two tested strains receiving similar dosages of d-amphetamine sulfate, performed differently. The RHA/Lu strain (F=16.22, df= 4/32, $p < .01$) demonstrated a statistically significant dosages effect that was not significant for the RLA/Lu strain. This statistically significant dosages effect was also indicated for the RHA/Lu strain with avoidance latencies (F=16.57, $p < .01$), escape latencies (F=9.53, $p < .05$), and step-up (F=5.95, $p < .05$) measurements. Similar statistical significance did not occur within the RLA/Lu strain for these measurements. In both avoidance and escape latencies those subjects of the RHA/Lu strain receiving Equal shock had both shorter avoidances and escape latencies than those RHA/Lu subjects receiving Differential shock. Similarly, the Equal shock groups in the RHA/Lu had both more avoidances and step-ups than the RHA/Lu subjects receiving Differential shock.

Analysis of variance in Experiment 2 demonstrated that the application of Equal shock, as contrasted with Differential shock,

yielded statistically significant differences with avoidance and avoidance latency behavioural measurements. In the case of number of avoidances ($F=5.82$, $df=1/16$ $p<.05$), mean scores indicated that the subjects receiving Equal shock had a significantly greater number of avoidances (Mean 7.72) than those subjects receiving Differential shock (Mean 5.34).

Avoidance latency scores ($F=6.55$, $df=1/16$, $p<.05$) indicated that the subjects under Equal shock (with a mean latency time of 4.31 sec.) performed significantly faster in avoiding shock than those subjects receiving Differential shock (Mean 6.68 sec.)

The analysis of the effect of Equal and Differential shock also statistically demonstrated different results when the effect of the shock was examined over the days sequence. Both (I) avoidance and (2) avoidance latency scores showed that the type of shock applied over 5 consecutive days was having a significant effect, independent of the dosages or strain effect ((I) $F=4.76$, $df=1/16$, $p<.05$ and (2) $F=6.55$, $p<.05$). Examination of mean scores confirmed that the groups receiving Equal shock had more avoidances and a shorter avoidance latency than those groups receiving the Differential shock. In both categories of shock, the RHA/Lu performed at a faster avoidance latency than the RLA/Lu strain (RHA/Lu: Equal shock condition, Mean 3.70; Differential shock condition, Mean 5.65 sec. This is compared with RLA/Lu mean latencies of 5.65 sec. under Equal shock conditions, and, 7.71 sec. under Differential shock condition.)

Similar to the performance on avoidance latency, although not statistically significant, Table 7 confirms this tendency and demonstrates that (I) RHA/Lu subjects receiving Equal shock escaped at a faster rate (Mean (I) 0.64 sec.) than the (2) RLA/Lu subjects receiving Differential shock under varying dosage conditions (Mean

(2) 1.86 sec.)

Dosage by shock interaction proved statistically significant on measurements of number of avoidances ($F=3.97$, $df=4/64$, $p<.05$) and escape latency ($F=5.29$, $p<.01$) Means of Equal shock groups under dosages (Means: 9.2, 9.2, 9.3, 7.1, 3.6) demonstrated a greater mean number of avoidances than did the Differential shock group under dosages (Means 6.2, 5.8, 5.8, 5.4, 3.5). The escape latency scores of the Equal shock group under dosages (Means 0.55, 0.59, 0.53, 0.58, 1.15) were statistically significantly shorter than the Differential shock group under dosages (Means 0.94, 1.24, 1.26, 1.75, 3.94 sec.)

When avoidance and avoidance latency scores were analysed by day to note if any significant learning effect was occurring in the 'drug session' and contaminating scores under the dosages condition, statistical testing with both measurements did not show this effect to be occurring to any significant degree.

Flinch Thresholds

As was noted in the Method, flinch thresholds tests were given to subjects of Experiment I after the 'drug session'. Results of analysis of variance demonstrated that subjects' flinch thresholds were statistically significantly different, both in terms of strain differences ($F=38.85$, $df=1/16$, $p<.01$) and in terms of sex differences ($F=5.67$, $p<.05$). Means scores (See Table 5) show the RHA/Lu (Mean 0.30 ma) had a lower flinch threshold than the RLA/Lu strain (Mean 0.49 ma).

Analysis by strain indicated that the RHA/Lu, within strain, contributed the greatest variation in flinch thresholds ($F=29.90$, $df=1/8$, $p<.01$), and, that RHA/Lu females (Mean 0.26 ma) had flinch thresholds consistently lower than males (Mean 0.34 ma). RLA/Lu

females mean was 0.46 ma while RLA/Lu males mean was 0.52 ma. No interaction results proved statistically significant.

In Experiment 2, subjects were run through the flinch threshold tests, before they were subjected to the three day training and five trial days of drug testing. Results of an analysis of variance on flinch thresholds show the subjects to have had significantly different response during testing only on the basis of strain differences (F=38.82, df=1/16, $p < .01$). Mean scores demonstrated that the RHA/Lu (0.34 ma) strain had a lower shock threshold than the RLA/Lu strain (Mean 0.50 ma). By strain analysis also indicated that the RLA/Lu strain exhibited a significant trials (F=2.27, df=9/72, $p < .05$) and a significant shock by trials (F=2.88, $p < .05$) effect. This result did not occur with analysis of flinch threshold testing for the RHA/Lu strain, and indicated a greater within strain variability with the RLA/Lu strain.

DISCUSSION

Although significant work has already been done in establishing many behavioural characteristics of Roman strain rats. (Bignami, 1965; Broadhurst and Bignami, 1965; Holland and Gupta, 1966(a); Satinder, 1971, 1972a) most of the research reported has been done using two-way conditioning paradigms. Following Wahlsten (1972(a)) in order to demonstrate that the differential conditionability of RHA/Lu and RLA/Lu strains is a generalizable phenomenon, and not specific to the two-way avoidance box, a one-way shuttle system was used.

First, it was noted that results reported earlier (Theios and Dunway, 1964; Potts, 1970), about the rapid rate of conditioning that occurs with the one-way as opposed to the two-way shuttle system, were confirmed in the training period of these experiments. Statistical differences between strains reported on avoidance, avoidance and escape latencies scores were achieved with the 30 trials subjects received in three training days. On each of these three measures the RHA/Lu strain proved superior to the RLA/Lu strain, in that RHA/Lu, showed a significantly greater number of avoidances and faster avoidance and escape latencies. Examination of the subjects' performance over three days also confirmed results, previously known from the two-way shuttlebox paradigm, that the RHA/Lu strain had a faster rate of avoidance acquisition than the RLA/Lu strain (Figure 1). Except for one interaction effect, no statistical significane was obtained in the training session of Experiment 1 demonstrating sex-group differences. This was equally true for the sex variable in measures of acquisition of conditioning, or in response latencies, both for avoidance and escape behaviour. However step-up and step-down behaviour, both activity measures, did demonstrate sex differences in that females were more active than males with both measurements.

In addition to thereby providing answers to the experimental objectives set for the training period in Experiment 1, some additional information on Roman strain activity scores may be noted from research results of (1) NNE and (2) st p-up and step-down. Although NNE, like escape scores must, as previously noted, be considered a qualified measurement, results indicate a significantly greater 'number of no escape(NNE) were scored by the RLA/Lu strain in comparison to RHA/Lu. This behaviour characterized by Krieckhaus, Miller and Zimmerman (1965) as 'freezing', can therefore be seen to be affected by strain characteristics of the experimental animals used.

A second form of activity of the Roman strains in training is that described earlier as 'step-up' and 'step-down', and is specific to the one way shuttle system. Results from the training session show that in both measurements the RHA/Lu strain was more active. This finding would support Holland and Gupta's (1966a) view that these strains differ in arousal, perhaps stemming from functional differences in central nervous system mechanisms such as the reticular formation. More interestingly, it generally appeared that subjects of both strains favoured the 'step-up' activity over the 'step-down' activity. This could be explained by the fact that (1) stepping up represented a move away from the grid; whereas stepping-down meant that subjects had to go to a location where they had previously been shocked; (2) stepping down meant that subjects would have to reorient their direction, as described by Theios and Dunway (1964) in a manner analogous to a two-way avoidance box; and (3) moving up onto the platform meant moving away from the CS, which had been paired with the UCS. Stepping-down meant facing the light (CS) installation which may have served as a negative environmental cue in the manner suggested by Reis (1970) and by Anisman (1973) who suggests differing compounded response

hierarchies as a model.

An overall view of the effect of the administration of d-amphetamine sulfate to subjects, both in Experiments 1 and 2, indicates that the dosages had a dominant effect on performance. Strain differences, which had emerged as a statistically significant factor in training, disappeared statistically under all measurements taken in the 'drug sessions' (with the exception of step-down scores in Experiment 1; and, step-down scores in Experiment 2.) This patterned disappearance, between training and drug sessions, of statistically significant strains effect, indicates that the strain factor generally came under the influence of the administered dosages of d-amphetamine sulfate. This is statistically evident when it is observed that the 'dosage factor' proved statistically significant with a number of avoidance responses, latency and activity scores in the trial sessions of both Experiment 1 and 2. That the effect of d-amphetamine sulfate on behaviour is general in this study, supports the variety of findings previously reported by Cole (1970 a). In both Experiments 1 and 2, the drug increased activity of both step-up and step-down measures, and shortened avoidance and escape latencies of both strain shock and sex groups. In all cases mentioned, behaviour demonstrated a dose-dependent inverted U-Curve, with the facilitation of responding generally being increased by d-amphetamine sulfate at 0.5 and 1.0 mg/kg. Larger doses of the drug often at 2.0 mg/kg and certainly at 4.0 mg/kg inhibited previously improved performance. The finding in the 'drug session' of d-amphetamine sulfate U-dose curves with Roman strains, generally supports Satinder's (1971) results, where performance of Roman strain subjects also demonstrated an initial facilitation, followed by a depression of the performance curve to increased drug dosages. This phenomenon is more clearly evident in the present study, and is marked by the crossover in

superiority of the performance curve (i.e. from the RHA/Lu strain to the RLA/Lu strain under the 4.0 mg/kg dosage) with avoidance and avoidance latency scores in Experiment 1. The appearance of these results, in such a clear manner is attributable to the use of the one-way shuttle system instead of the two-way shuttlebox. Evidence for this thesis may be taken from the fact that the RLA/Lu strain showed acquisition of avoidance conditioning within three training days in the one-way shuttle system, whereas in a two-way shuttlebox (Satinder 1971), the RLA/Lu strain failed to show acquisition of avoidance behaviour given five training days.

The occurrence of a dose-dependent curve with d-amphetamine sulfate dosage, is consistent with the findings of Cole (1970, 1967) who suggests that amphetamines have both a central activating, or arousal, effect as well as a general depressant effect (excessive arousal) the latter being more specifically defined as an inverse relation between operant response and drug dose. Results also confirmed Cole's comment (1970) that a demonstration, by amphetamine, of depression of performance requires a moderately high level of responding prior to drug administration. For example, that the level of responding under drugs is related to the strain/sex groups activity level before administration may be seen clearly in Table 4.

The general stimulating effect of amphetamine on bodily activity is well established, with Yagi (1963) also having shown that larger doses of amphetamine (6 mg/kg) decreases general activity. As well as this qualification, evidence in both Experiments 1 and 2 demonstrated that general activity of rats under dosages of d-amphetamine sulfate, here measured in 'step-up' and 'step-down' behaviour, must also be qualified in terms of strain differences, sex differences, UCS foot-shock levels (Table 5), and in terms of the nature of the activity task itself (Table 3 as compared with Table 4).

The use of d-amphetamine sulfate in the 'drug sessions' of Experiment 1 and 2 in both cases had effects on the second test factor of each experiment--i.e. 'sex' in Experiment 1; and, 'shock group' in Experiment 2. In the former case, d-amphetamine dosages resulted in the emergence of significant sex differences within the RHA/Lu strain. In Experiment 2, difference between shock groups, in training proved significant within RHA/Lu only on latency scores, and on RLA/Lu only on step-down scores. However, in 'drug session' the Equal and Differential shock groups proved significantly different on number of avoidances, number of escapes and avoidance latency with RLA/Lu not yielding any significant shock-group differences. Thus in both cases, these differences emerged with d-amphetamine sulfate dosages only in the RHA/Lu strain. This finding suggests that responses may be specific to the strain tested with RHA/Lu responding more to environmental conditions than the RLA/Lu strain--with the male RHA/Lu group in Experiment 1 and the Equal shock-RHA/Lu group in Experiment 2 yielding the highest performance. It is the effect of the higher doses of d-amphetamine on these strain groups that caused the performance curve cross-overs in Experiment 1, and, the meeting of performance curves in Experiment 2 with both avoidance and avoidance response latency scores. Of course these results must be taken within the limitation of the finding that, despite the 30 trials given in the training period, the RLA/Lu strain (particularly females in Experiment 1) continued to demonstrate acquisition of avoidance behaviour and improved avoidance latency behaviour over days in the 'drug session'. This served to confound the performance scores attributable to injection of the stimulant drug. The fact that (1) in training there was a difference in both strain-sex (activity measures) and strain-UCS behavioural base lines, supports (2) prior evidence (Satinder 1971; Gupta and Holland, 1969) that behavioural base lines

for subject groups are selectively sensitive to avoidance conditioning in the first instance, and administered drug in the second instance. Results of this study confirm that the RHA/Lu and RLA/Lu strains respond to avoidance conditioning with strain-specific, differential rates. As well under d-amphetamine sulfate the differences between strains decreased to the point of disappearing with administration of higher drug dosages. This is demonstrated with avoidance scores by the cross-over of response curves (Figure 1) in Experiment 1, and a meeting of strains avoidance response curves in Experiment 2 (Figure 3). The fact that this pattern of behaviour was more evident in the current study than previously shown by Satinder, (1971; 1972 b) may be attributable to the use of the one-way shuttle system, as opposed to the two-way shuttlebox.

Initially reported in Satinder's (1971) study using Roman strain subjects, this current study also demonstrated the occurrence of a placebo effect in the performance of the RLA/Lu strain in both Experiments 1 and 2. Analysis by strain indicated that the larger portion of this effect was contributed by the RLA/Lu female, as opposed to male, subjects, and, by the RLA/Lu Differential, rather than the Equal, shock group. Existing literature on placebo effects with drug injections is contradictory. Schnitzer and Ross (1960, 1961) using locomotion as an index originally suggested that needle injections depressed activity, while later (Herrnstein, 1962; Ross and Schnitzer 1963) they found no results, and suggested that other factors (age, room temperature) may be responsible. Phil and Altman (1971) using rat subjects also found a placebo effect which is specific to d-amphetamine sulfate (AMP) and suggested that the strength of the response was related to the pairing procedure between an active drug and the circumstances associated with giving the drug. The results of this present experiment, confirms

a placebo effect in rats with d-amphetamine and demonstrated that the effect is partially a function of strain, and may thereby be influenced by differential strain conditioning patterns.

Results of training sessions in Experiment 2, despite differences in subject age and sex from subjects in the training session of Experiment 1, again generally confirmed the previous original findings of Experiment 1 of Roman strain performance in the one-way shuttlesystem. Conditioning of subjects in the one-way system, in comparison to the two-way shuttlebox, was rapid and demonstrated significant differences between strains. The RHA/Lu strain responded with a greater number of avoidance responses (Figure 3) and a shorter avoidance response latency (Figure 4) both to Equal and Differential shock levels than did the RLA/Lu strain. The differential response by strains for the Equal shock condition in training confirms the findings of Experiment 1 discussed earlier. However the continued significant difference in performance between RHA/Lu and RLA/Lu strains under the Differential shock condition in Experiment 2 indicated that the characteristic strain-specific performance is to be attributable to factors other than simply the footshock ampere value of UCS given to subjects. This result is evident in the training session of Experiment 2 since the RHA/Lu strain continued to perform better than the RLA/Lu strain despite the procedure taken to standardize the UCS by making it relative to the subject's mean flinch threshold. Differential Roman strain performance is therefore clearly a response more complex than simply a correlation of response to the degree of a given motivating UCS stimulus.

However, the experimental formula defining 'Differential UCS' - although ensuring that the Differential UCS (RHA/Lu = .68 ma mean; RLA/Lu = 1.00 ma mean) was always smaller in magnitude than the Equal

shock and allowing for a general comparison of shock levels - was not structured to allow for a resolution of the question concerning the nature of the UCS - response function. This was a research limitation which would require two changes to the experimental design: (1) a minimum of three levels of shock for each strain would have to be used to indicate any linear UCS-response function, and, (2) such a comparison could not safely include additional variables (such as: differential subject conditioning rates) as well as differential rates of responding to drug dosages.

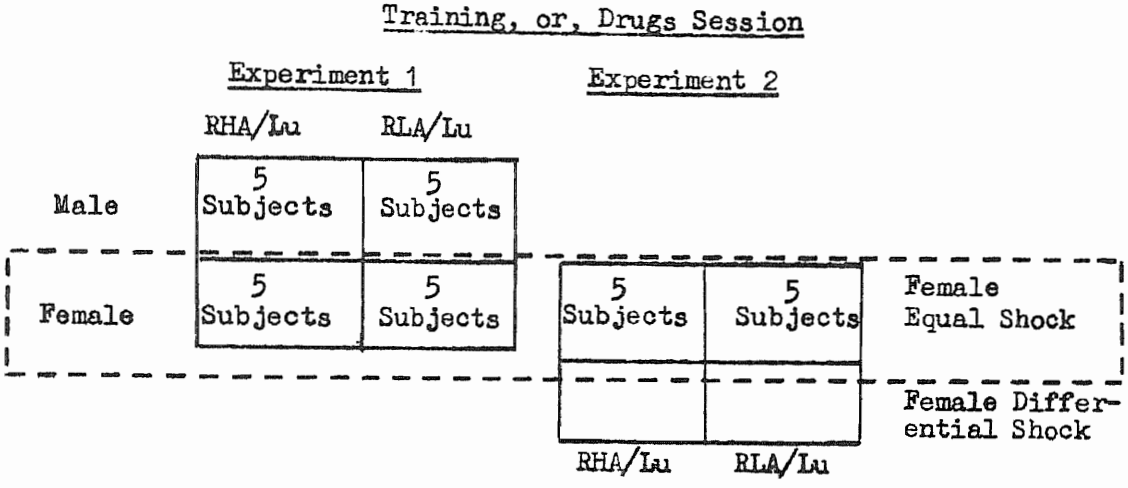
Despite design constraints, both shock levels of UCS were demonstrated to be sufficient both in training and 'drug sessions' to serve as a sufficient UCS allowing differential conditioning and strain differences, in Roman strains, to appear. The effect of shock, although statistically significant in training within RHA/Lu strain only with avoidance and escape latency scores; and, within the RLA/Lu strain with step-down measures did clearly demonstrate in a number of measures that the two administered shock levels result in separate response magnitudes. The fact that these results in training session did not prove statistically significant suggests support for Reiss' (1970) finding that subjects have a point of discontinuity of increasing sensitivity, after which the response to shock by groups is an almost horizontal function. This phenomenon may account for the absence of statistical significance between shock groups. Additionally, the fact that the significant difference between shock groups, within strain, vary and are not identical in the RHA/Lu strains suggests that each point of intensity threshold of sensitivity is specific with a characteristic level for each strain group.

Results of the training session in Experiment 2 also indicate that both RHA/Lu and RLA/Lu groups, which were given identical shock

conditions (i.e. twice the flinch threshold level) continue to perform at different levels of response (i.e. Figures 3, 4). This would indicate that differential conditioning rates between Roman strains is not simply a different (i.e. specific) strain response to shock level of UCS. In Experiment 2, the UCS was set relative to the subjects' individual flinch threshold, and yet, strains continue to perform differently. Strain differences, in a manner analogous to the finding of Satinder and Hill (1974) with regard to activity, can not therefore be attributable to different strain-specific responses to UCS shock level. This result perhaps may suggest further research in the direction of Cicala, Masterson and Kubitsky's (1971) contention that different innate operant levels of response may be one of the sources of different levels of performance.

This study is the first available in the literature which tests rat subjects (Roman strains, in this case) for behaviour under d-amphetamine sulfate in a one-way avoidance conditioning paradigm. The general dominant effect of the drug on behaviour (facilitant and depressant) over the effect of the strain factor--and the statistical disappearance of the strain effect--has already been discussed. As well, comment has already been made about the emergence of a statistically significant shock effect within the RHA/Lu, and not the RLA/Lu strain. These results indicated firstly, that dosages are the most significant factor in 'drug sessions', and secondly, that the RHA/Lu subjects, particularly the Equal shock group, responds most to the dosage condition (Figure 3, 4). This is consistent with results from the training trials. Performance after the administration of d-amphetamine sulfate confirmed observations in the training trials that each group responded with different but with characteristic strain-shock levels of operant response. Generally it may be said that RHA/Lu performs more responses and faster than RLA/Lu, and, that the Equal shock condition elicited more responses and faster than the Differential shock condition.

In view of this study's use of identical statistical designs and test procedure in Experiments 1 and 2, a comparison of performance scores of identical strain-sex-shock groups is possible between Experiments in both training and drug sessions. The inter-Experiment equivalence of design cells may be characterized as follows:



Generally, inter-experimental statistical testing of comparable cells indicated that, in spite of standardized conditions between compared groups, results showed differential responding. This variation in behaviour must therefore have been due to factors other than those which were controlled between experiments, perhaps having to do with some systematic characteristic of the subjects themselves. It is suggested that this variability may have arisen from the distinct age differences between subjects in each of the two Experiments. Further evidence for the non-equivalence of subject groups between experiments, may be found in groups flinch threshold scores which also showed that subjects differed significantly. Subjects of Experiment 2 showed that their flinch thresholds of both female strain groups (RHA/Lu Mean 0.34 ma; RLA/Lu Mean 0.50 ma) were significantly higher than those of strain groups in Experiment 1 (RHA/Lu Mean 0.26 ma; RLA/Lu Mean 0.46 ma.)

This difference in flinch thresholds between female subjects may be attributable to age, with the older female RHA/Lu subjects having a lower flinch threshold. This may have been the basis of inter-experiment variability.

A second source of systematic error may have arisen because of the non-identical experimental procedures used (i.e. the testing of flinch threshold before training in Experiment 2, and after the 'drug session' in Experiment 1.) Anisman and Waller (1972) have reported that signalled, inescapable, prior shock exposure (PSE of 1.0 ma. facilitated subsequent one-way avoidance learning. Anisman and Waller (1971) in similarly discussing unsignalled prior shock exposure, have suggested that such experience facilitate responding when PSE is coincident with the nature of the stimulus and response requirements of the following experiment. (i.e. flight as a response to prior shock coincides with flight requirements in a one-way avoidance situation). In the present experiment, the procedure assumed that flinch threshold testing for subjects of Experiment 2 would give subjects a shock considerably lower than 1.0 ma (Table 9) and that this experience would not significantly affect performance. Inter-experiment statistical tests, of comparable female subject groups for both training and drug sessions, were done using avoidance and avoidance latency data. Both scores indicate that in training, female subjects of both strains in the Equal shock condition, performed significantly differently between Experiments 1 and 2. Mean scores (Figures 1, 2, 3, 4) indicate that subjects of Experiment 1 performed fewer avoidances, and, avoid less quickly than do subjects of Experiment 2. A similar comparison of subjects in the 'drug session' of both Experiments revealed that these two subject groups also responded to

dosages significantly differently both in terms of avoidance ($F = 6.88$, $df = 4/64$, $p < .01$) and avoidance latency ($F = 7.83$, $p < .01$). Mean scores indicated that subjects of Experiment 1 had a greater number of mean avoidances and a shorter avoidance latency. These results, however, must be qualified by the observation made above, that these subject groups may not be comparable (as to the effects of prior shock exposure) since they may also/or/either be affected by differences in subject-group age. It is not clear whether the significant differences discussed are differences as a result of PSE, difference in age between subject-groups, or a combination of the two. This question could only be resolved by an independent study which, by controlling for one factor could test the other (i.e. by controlling for age, would test if PSE of 0.5 ma in a flinch testing situation, facilitated responding in a one-way shuttle system.)

Both of the above reasons--differential group mean flinch threshold, perhaps-arising from unequal subjects' age; and, dissimilar PSE experiences--indicate qualifications within which the general results of this study must be placed.

Despite these qualifications however, the questions which formed the original rationale of this study - about RHA/Lu, RLA/Lu performance in a one-way shuttle system; subjects' behaviour in this apparatus under d-amphetamine dosages; and, subjects' behaviour under two levels of UCS, and the effects of amphetamine dosages on performance in this situation - now have the foregoing evidence offered in their resolution.

SUGGESTIONS FOR FURTHER RESEARCH.

A number of shortcomings in the procedure of this study, along with suggestions coming out of this research suggest the direction in which further research in this area might proceed.

Shortcomings of the research include the following:

(1) the apparent lack of a fully stabilized behavioural base line in the conditioning of the RLA/Lu strain.

> This may be overcome by extending the training period, for perhaps another two days. Using a fixed ratio, rather than a fixed interval, schedule may also aid in stabilizing the behavioral base line.

(2) the potential difference in environmental cues.

> Here the solution would involve modification in the one-way apparatus for comparative experiments. For example a sound CS could replace the light and its fixture; the resting platform could be constructed of plexiglas in a manner identical with that of the grid box, and so on.

(3) the apparently different frequency of times each of the strains was forced off the resting platform. This occurred because subjects would not move off the resting platform in time for the next trial cycle, and had to be pushed off by the sliding back wall of the resting platform.

> This procedure, theoretically, could represent a form of aversive conditioning. Its use is necessitated by the very construction of the one-way shuttle system. Whether it had a significant effect can only be ascertained through experimentation.

In addition, a number of questions arose from the results of this study and might be posed as questions for future research.

(4) Since statistically significant strain differences disappeared under the dosages condition, would they reappear if the subjects were run in a further series under non-drug conditions?

(5) If neither response to UCS-shock, nor activity rates determined strain differences, what other UCS or CS variations could clarify the relationship of the subjects' response to cues in the conditioning paradigm?

(6) Would a series of three or more shock levels over a broad shock range demonstrate the functional relationship of behaviour to shock levels, and possibly demonstrate variations between strains?

(7) Would control for the factor of the oestrus cycle in female subjects affect strain performance differentially?

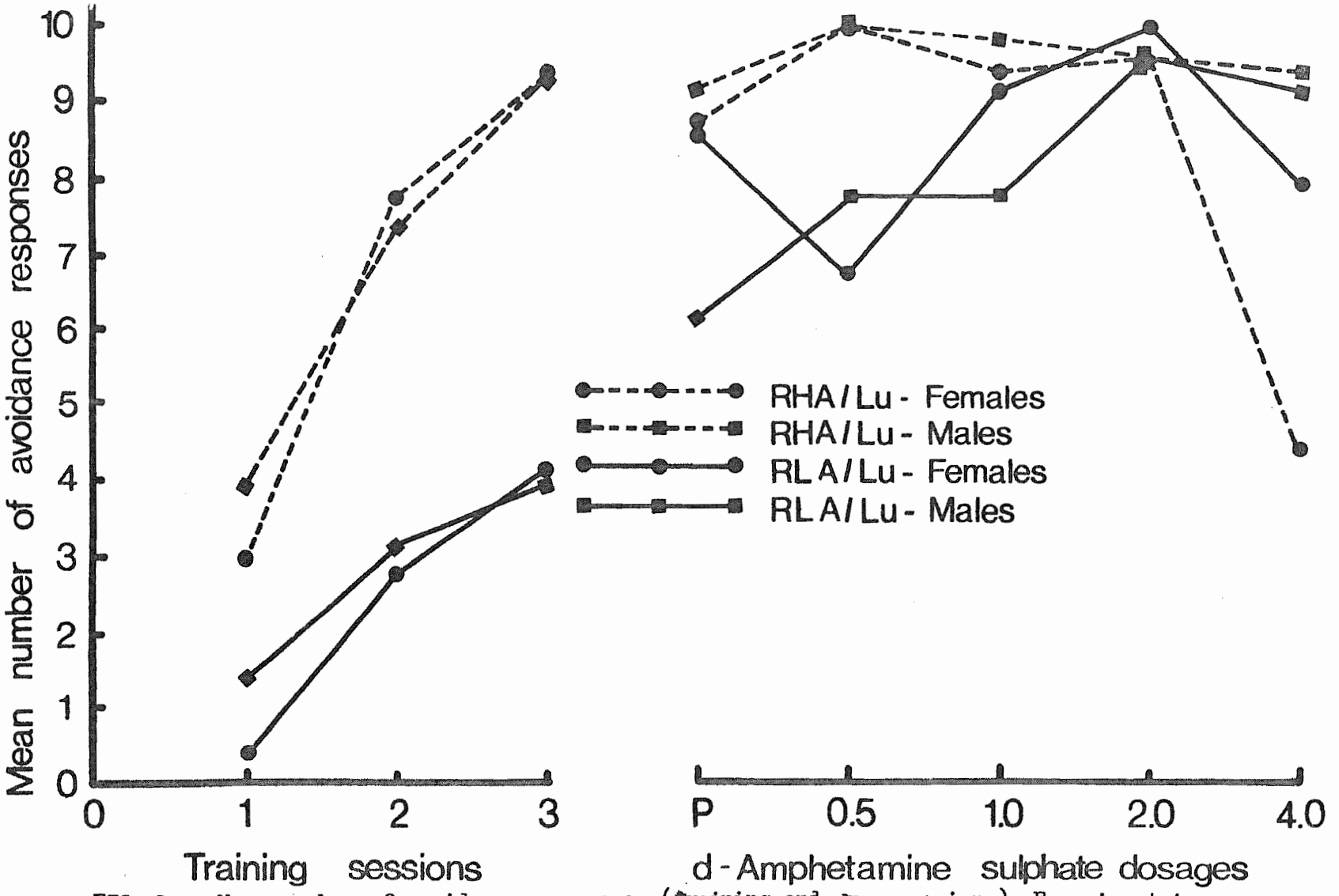


FIG. 1. Mean number of avoidance responses (training and drug sessions) Experiment 1

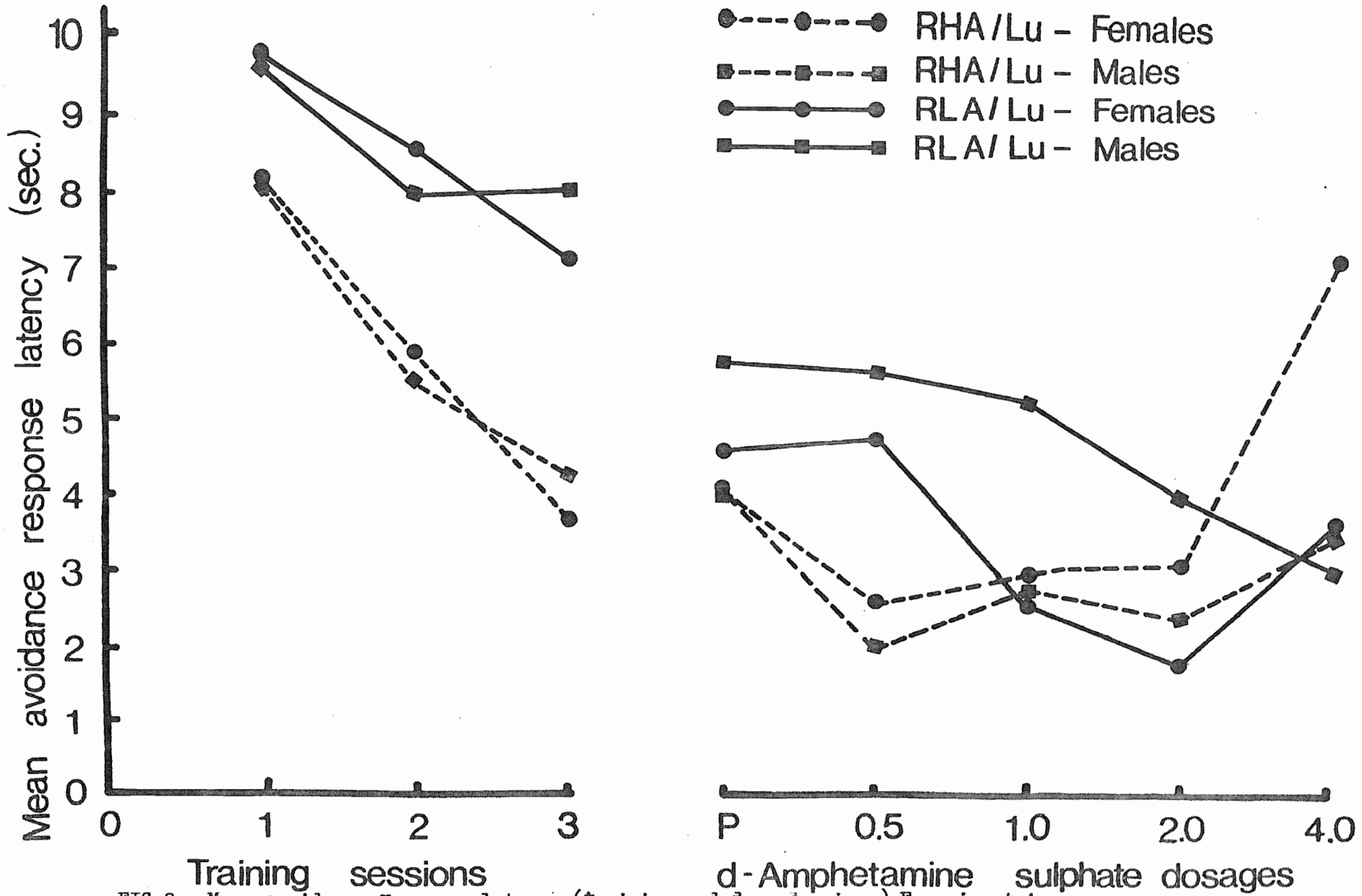


FIG.2 Mean avoidance response latency (training and drug sessions) Experiment 1.

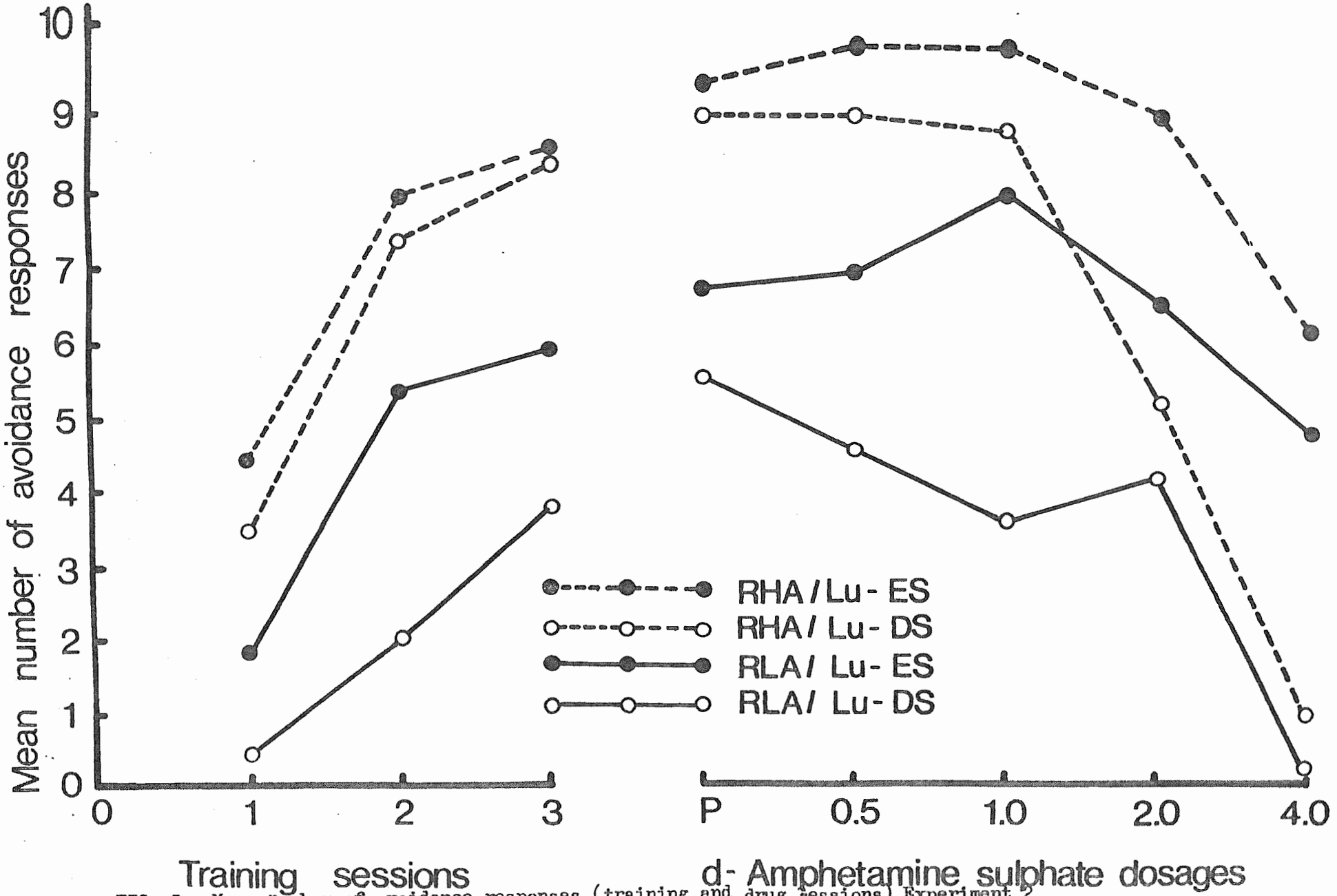


FIG. 3 Mean number of avoidance responses (training and drug sessions) Experiment 2

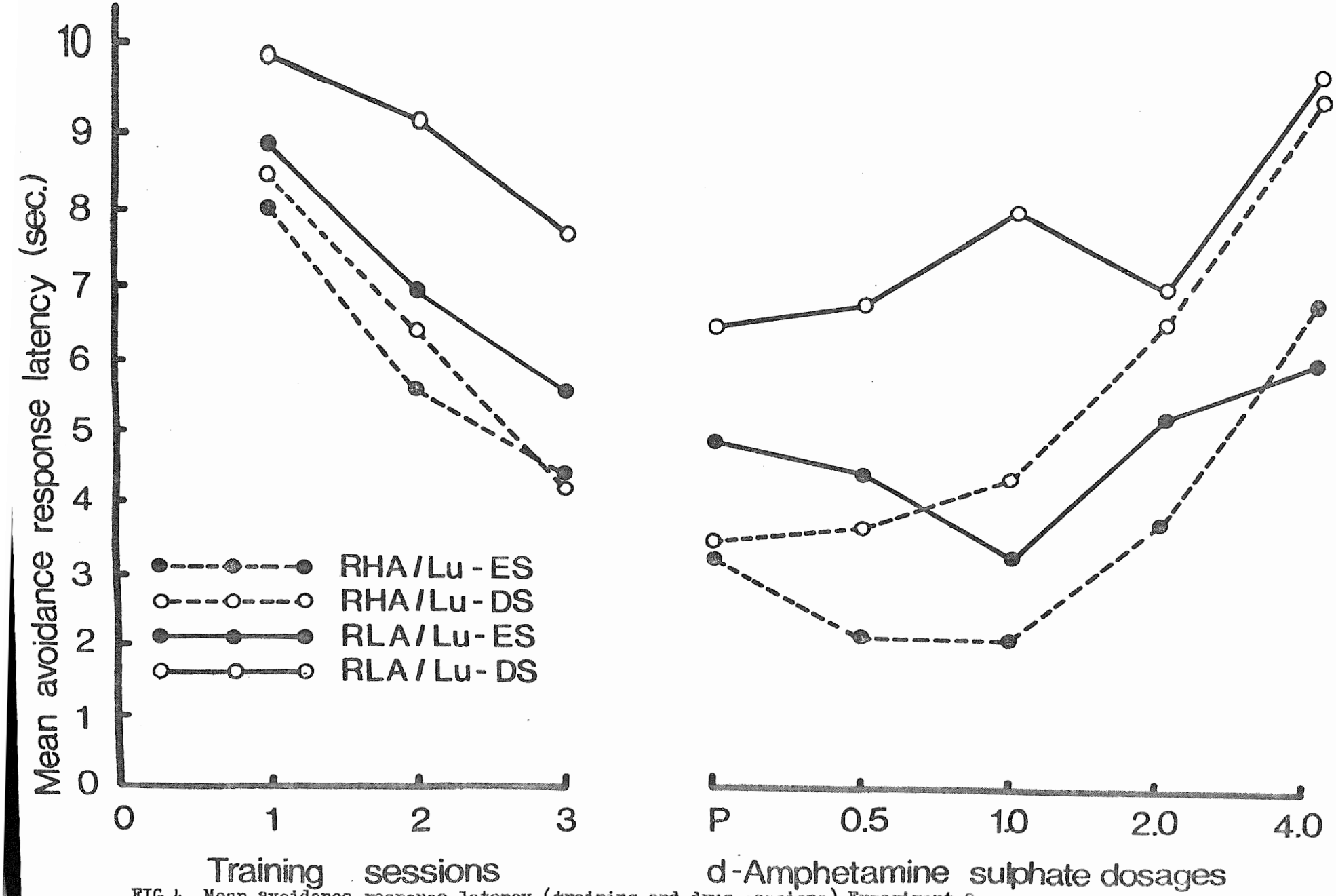


FIG.4 Mean avoidance response latency (training and drug sessions) Experiment 2.

Mean Number of Step-ups (Training and Drug Sessions) Experiment 1.

Session	Strain	Sex	Days 1	2	3	Dosages(mg./kg.)d-amphetamine sulfate p	0.5	1.0	2.0	4.0
Training	RHA/Lu	Female	3.60	5.60	2.60					
		Male	4.40	8.60	4.40					
	RLA/Lu	Female	1.00	1.20	2.00					
		Male	1.40	1.40	0.40					
Drug Session	RHA/Lu	Female				6.80	11.20	19.60	15.40	3.20
		Male				0.80	3.60	5.60	7.80	1.00
	RLA/Lu	Female				5.80	3.60	16.80	11.20	15.20
		Male				2.40	5.80	2.80	12.60	6.40

TABLE 4

Mean Number of Step-downs (Training and Drug Sessions) Experiment 1.

Session	Strain	Sex	Days 1	2	3	Dosages(mg./kg.)d-amphetamine sulfate p	0.5	1.0	2.0	4.0
Training	RHA/Lu	Female	0.0	0.80	1.60					
		Male	0.0	1.20	1.40					
	RLA/Lu	Female	0.20	0.0	0.0					
		Male	0.0	0.0	0.0					
Drug Session	RHA/Lu	Female				6.40	8.60	21.20	12.80	0.80
		Male				0.80	1.80	5.20	5.80	0.0
	RLA/Lu	Female				0.0	0.20	0.80	0.20	0.0
		Male				0.60	0.20	1.00	0.80	0.20

TABLE 5

Mean Flinch Thresholds Experiment 1

Strain/Sex Group	Trials 1	2	3	4	5	6	7	8	9	10	Mean
RHA/Lu - Female	0.29	0.23	0.33	0.21	0.23	0.29	0.23	0.29	0.29	0.21	0.26
RHA/Lu - Male	0.35	0.33	0.37	0.39	0.35	0.37	0.35	0.31	0.31	0.31	0.34
RLA/Lu - Female	0.39	0.41	0.39	0.45	0.55	0.53	0.45	0.45	0.51	0.49	0.46
RLA/Lu - Male	0.63	0.51	0.57	0.59	0.55	0.45	0.45	0.43	0.53	0.53	0.52

TABLE 6

Mean Number of Escapes (Training and Drug Sessions) Experiment 2.

Session	Strain	Days 1	2	3	Dosages(mg./kg.)d-amphetamine sulfate p	0.5	1.0	2.0	4.0
Training									
Equal Shock	RHA/Lu	4.60	2.00	1.40					
	RLA/Lu	2.20	1.20	1.20					
Differential Shock	RHA/Lu	4.00	2.60	1.60					
	RLA/Lu	1.40	2.20	2.40					
Drug Session									
Equal Shock	RHA/Lu				0.60	0.20	0.20	1.00	2.60
	RLA/Lu				1.20	1.00	000	1.40	3.20
Differential Shock	RHA/Lu				1.00	1.00	1.00	3.60	3.80
	RLA/Lu				1.60	1.60	3.00	2.80	0.60

TABLE 7

Mean Escape Response Latencies (Training and Drug Sessions) Experiment 2.

Session	Strain	Days 1	2	3	Dosages(mg/kg.)d-amphetamine sulfate p	0.5	1.0	2.0	4.0
Training									
Equal Shock	RHA/Lu	1.20	0.19	0.11					
	RLA/Lu	3.58	1.93	1.55					
Differential Shock	RHA/Lu	2.13	0.41	0.28					
	RLA/Lu	4.46	3.26	2.51					
Drug Session									
Equal Shock	RHA/Lu				0.03	0.04	0.05	0.05	1.02
	RLA/Lu				1.08	1.14	1.00	1.11	1.28
Differential Shock	RHA/Lu				0.22	0.21	0.22	1.47	3.12
	RLA/Lu				1.65	2.27	2.29	2.03	4.75

TABLE 8

Mean Number of No Responses (NNE) Training and Drug Sessions Experiment 2

Session	Strain	Days 1	2	3	Dosages(mg/kg.)d-amphetamine sulfate p	0.5	1.0	2.0	4.0
Training									
Equal Shock	RHA/Lu	1.00	0.0	0.0					
	RLA/Lu	6.00	3.40	2.80					
Differential Shock	RHA/Lu	2.60	0.0	0.0					
	RLA/Lu	8.20	5.80	3.80					
Drug Session									
Equal Shock	RHA/Lu				0.0	0.0	0.0	0.0	1.20
	RLA/Lu				2.00	2.00	2.00	2.00	2.00
Differential Shock	RHA/Lu				0.20	0.0	0.20	1.20	5.20
	RLA/Lu				2.80	3.80	3.40	3.00	8.60

Table 9

UCS (Shock) Administered in Experiment 2

No.	Strain	Sex	Flinch Threshold	UCS- Shock Level
1	RHA/Lu	F	.35	Equal Shock
2	↓	↓	.35	↓
3			.37	
4			.35	
5			.29	
6	RLA/Lu		.43	
7	↓		.48	
8			.50	
9			.54	
10			.55	
11**	RHA/Lu	F	.35	.70 mA
12	↓	↓	.33	.66
13			.25	.50
14			.33	.66
15			.44	.88
16	RLA/Lu		.57	1.14
17	↓		.52	1.04
18			.54	1.08
19			.50	1.00
20			.38	.76

M_x=.68

M_x=1.00

**No. 11-20 received "Differential UCS"

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