# Effects of postnatal taurine administration upon inhibitory-facilitatory behaviour of selectively bred strains of rats

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# EFFECTS OF POSTNATAL TAURINE ADMINISTRATION UPON INHIBITORY-FACILITATORY BEHAVIOUR OF SELECTIVELY BRED STRAINS OF RATS

by

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ABSTRACT

The present experiment was conducted to test the effect of taurine, a putative inhibition modulator. Maudsley reactive (MR), Maudsley non-reactive (MNR) and Roman control avoidance (RCA) rats, including both sexes were used in this experiment. Rats were further divided into taurine and physiological saline groups and injected intraperitoneally with taurine (62.5 µg/g (0.5M) of animal body weight) or a comparable strength of physiological saline (0.5M) every second day between postnatal days 8 and 20. Specific measures (inhibitory response failure, mean number of avoidance responses, avoidance response latency, mean number of escapes and escape response latency) used to test inhibitory-facilitatory behaviour revealed clear cut significant strain, sex and test-order differences. There were no significant differences between taurine or saline injected rats for inhibitory response failures. Open-field behaviour (sections crossed, defecatory behaviour) was recorded. There were significant strain and sex differences for sections traversed in the open-field over a five day period. In addition, there were no significant differences in defecation between taurine and saline injected rats. Analysis of endocrine glands using both an absolute weight and a corrected weight measure revealed that the saline injected animals had larger thyroids and adrenals than the taurine injected rats. However, these differences were not significant. In conclusion taurine administration displayed no clear-cut signif-

icant differences on any of the behaviours tested. The present results provide no behavioural support for taurine's suggested role as an inhibitory neurotransmitter.

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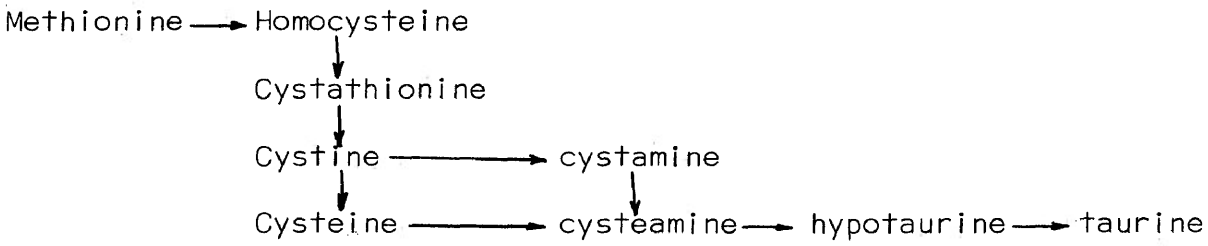
# CHAPTER I

## INTRODUCTION

The relationship of brain-biochemistry to behaviour is presently being investigated by many researchers. Taurine, a sulphur amino acid, has drawn much attention because it is one of the most concentrated chemicals in the free amino acid pool in the rat brain (Davison, 1956). Almost no information has been collected on the behavioural effects of taurine. However, in the recent past there has been chemical investigation of taurine (Read & Welty, 1962; Peck & Awapara, 1967). At the biochemical level taurine has enticed many researchers to investigate its properties in an attempt to understand its function in the organism.

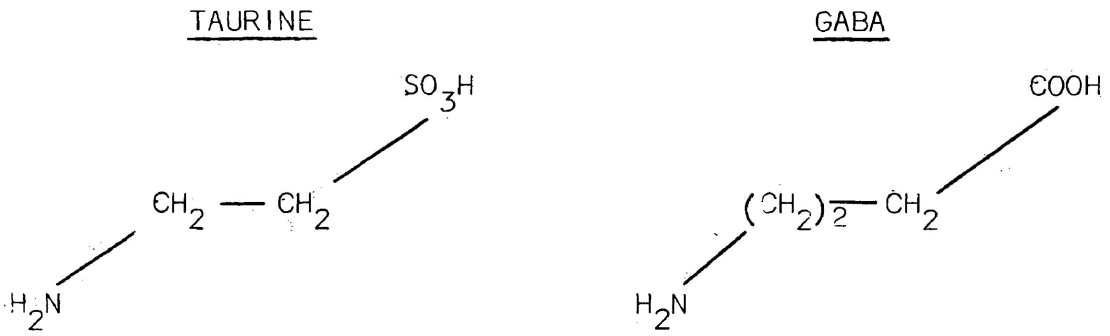
### Neurochemical Properties of Taurine and Its Similarity to Y-Amino Butyric Acid (GABA)

Taurine is not one of the twenty essential amino acids in the body, but it is synthesized from one of the essentials, methionine. A schematic of possible synthesis routes can be drawn as follows (Gaitonde, 1970):



The synthesizing enzyme of taurine is known as cysteine sulfinate decarboxylase. Furthermore, metabolites of taurine are significant because of their potential biochemical-behavioural properties (Gaitonde, 1970). One of these metabolites, isetheonic acid, is located in large concentrations in the heart and axoplasm of squid neurons. Comparatively little is known of taurine or its metabolite's functions.

In 1971 Davison and Kaczmarek remarked on the interesting structural similarities between taurine and the well known inhibitor transmitter candidate, GABA. A schematic of the structural similarity is as follows:




GABA is presumably formed by the decomposition of glutamic acid by the synthesizing enzyme glutamic acid decarboxylase (Baxter & Roberts, 1960). Glutamic acid and its metabolites are also found in high concentrations throughout an organism. It is interesting to note that taurine concentrations decrease with age and are paralleled by a similar increase of glutamic acid in the free amino acid pool. A similarity between the synthesizing enzymes

of taurine and GABA has been suggested by Davison (1956). Experimenters have stated that these may be the same enzymes (Davison, 1956).

Initial studies with taurine involved isolating properties that would qualify it as a neurotransmitter candidate. Werman (1966) has suggested that neurotransmitter substances should have the following properties:

1. the compound should be present in nerve endings;
2. the corresponding synthesizing enzyme should be present in the brain;
3. there should be a mechanism for the termination of the action of the compound on the postsynaptic membrane;
4. stimulation of the neurons should lead to its release into the extracellular fluid;
5. the action of the suspected transmitter should be identical in every way to that of the natural transmitter.

Davison and Kaczmarek (1971) state that the first two criteria for a neurotransmitter are met by taurine. Taurine, together with its synthesizing enzyme, is present in isolated nerve ending fractions of adult rat brain. The distribution of glutamate decarboxylase and GABA follow a similar pattern (Ryall, 1964). Indeed, the parameters for taurine and GABA uptake in the rat cortex are very similar (Iversen and Neal, 1968).

When electrical impulses are applied to tissue slices perfused with Krebbs Ringer medium as described by Srinivasan, Neal and Mitchell (1969), taurine is released. Preliminary experiments demonstrate uptake of low concentrations of taurine into slices of rat brain cortex, with no detectable metabolism of taurine (Kaczmarek & Davison, 1972). The similarities regarding release and uptake mechanisms between GABA and taurine, and the marked resemblances in localization and biosynthesis, suggest a similar function.

Differences in characteristics between GABA and taurine should be noted. One example is taurine's high concentration in non-neural tissue, a property which does not typify GABA or other neurotransmitter candidates. In addition, taurine's uptake and turnover is relatively slow in contrast to other chemicals and the presence of a quick catabolizing enzyme at the synapse is not yet evident. Consequently, taurine and GABA may be similar in inhibitory effect yet differ in the time period of the effect. The existence of inhibitory transmitters for short-termed neural processes and inhibitory modulators for longer-termed processes has been considered an important possibility (Hebb, 1970).

## Taurine Distribution

Taurine injected into young animals is absorbed into the blood stream and transported to the brain as well as other organs (Spaeth & Schneider, 1974). Due to the fact that taurine is

water soluble it will gain access into the brain by active transport and simple diffusion (Jacobsen & Smith, 1968). This process is possible in the young organism (Chanda & Himwich, 1970; Jacobsen & Smith, 1968) since the lumenal endothelial cell membrane, a layer of cytoplasm, and an outer cell membrane of the CNS capillary wall is not fully developed in the neonate (Olendorf, 1974). This allows for easy penetration of administered drugs. Conversely, the blood brain barrier (BBB) is fully developed in mature animals and does not allow for easy molecule penetration (Jacobsen & Smith, 1968).

Taurine levels in the brain obtain maximum values between the first to the seventh postnatal day. The initial high concentration is followed by a steady fall until the organ-dependent levels asymptote during adulthood (Chanda & Himwich, 1970; Cutler & Dudzinski, 1974). A concomittant decrease in liver taurine levels also occurs between the postpartum days 1 - 5. Suggestions have been made that taurine synthesized in the liver is transferred from blood to brain during this period (Chanda & Himwich, 1970). Yet Federici, Silvestro, Rosei and Granata (1974) have suggested that taurine is metabolized only in part in the liver of the rat and such findings should be reinvestigated. Indeed, it has been suggested that decrements in taurine content in the brain after seven days may be due to the development of an effective blood brain barrier and the consequent inhibition of transport (Chanda & Himwich, 1970).

Approximately 24 hours after intraperitoneal injection, taurine was found to be 111 μmoles/g in the heart and 21 μmoles/g in the brain of the rat (Peck & Awapara, 1967). Yet, Dietrich and Diacono (1971) have suggested that the rat heart has a low sensitivity to taurine, which seems to suggest that some of the effects of taurine on the heart are related to cellular calcium transport. The turnover of taurine in the rat was found to correspond to a half life of 12 - 13 days and to an amount of 35 μmoles of taurine synthesized endogeneously in 24 hr./100 g body weight of the rat (Bouquet & Fromageot, 1965). This value is in good agreement with the value of 22 - 52 μmoles of taurine/ 24 hrs./100 g body weight of the rat, calculated for the endogenous synthesis of taurine. This calculation assumes that 13 - 31 percent of the daily requirment (Eidjarn, 1954) of the total sulphur amino acids (cysteine: 42 μmoles and methionine: 335 μmoles) for a 250-g rat are converted into taurine (Lajtha, 1970). Taurine, once considered an end-product with no further metabolism, has been shown to give rise to isethionic acid (2-hydroxyethane sulfonic acid) in the dog heart in vitro (Read & Welty, 1962), and in the rat heart and brain in vitro and in vivo (Lajtha, 1970).

Indeed, some differences in the regional distribution of taurine and GABA have been observed in the rat brain as well as other organisms (Lajtha, 1970). Since many studies have been undertaken concerning regional distribution, these will be

mentioned.

The highest concentrations of taurine have been regionally located in the neurohypophysis (109.71 - 17.39 μmole/g), adenohypophysis (17.87 - 3.2 μmole/g), pineal gland (60.26 - 8.10 μmole/g) and the cerebral cortex (11.07 - 1.05 μmole/g) in the rat (Crabai, Sitzia & Pepeu, 1974; Neuhoff & Tonge, 1973). This seems to confirm that taurine is essential to the central nervous system. Other researchers investigating taurine in humans have found the highest concentration of taurine in the frontal lobes (Okumura, Otsuki & Kameyama, 1960), whereas further research with cats by Battistin, Grynbaum and Lajtha (1969) revealed high concentrations of taurine in the cerebral hemispheres (5.34 μmole/g of body weight) and cerebellum (4.9 μmole/g). Similar concentrations are reflected in the newborn rat brain where the cerebral hemispheres contain 21.6 μmole/g, the cerebellum 14.1 μmole/g, while the pons medulla and spinal cord contain 12.6 μmole/g and 11.0 μmole/g respectively (Cutler & Dudzinski, 1974). The decrease in taurine brain levels is quite obvious if this data is compared to that reported by Davies and Johnston (1974). These authors state that by 10 days of age the cerebellar hemispheres contain 14.7 μmole/g, the cerebellum contains 9.2 μmole/g, while the pons medulla and spinal cord contain 6.6 μmole/g and 4.9 μmole/g respectively (Davies & Johnston, 1974). These data seem to support earlier results by Chanda and Himwich (1970), Cutler and Dudzinski (1974) that brain taurine levels decreased with

age.

The lowest concentrations of taurine in the human adult brain have been found in the thalamus (Okumura et al., 1960), whereas in the rat lowest concentration was in the pons medulla (Piha, Oja & Uustalo, 1962). The cell density of a certain region of the brain is not likely to be the main determinant of regional differences in uptake (Battistin et al., 1960). Regions of high neuronal density (the midbrain, cortical areas and the cerebellum) take up amino acids such as taurine and GABA to a higher level than highly myelinated regions do (Battistin et al., 1969). Since neurons appear to show a greater capacity to accumulate amino acids against a concentration gradient than do glial cells, the type of cells of the various areas rather than the cell density may determine regional difference in uptake (Battistin et al., 1969). However, recent investigation by Ehinger (1973) refutes this idea since taurine has been found to be taken up by glial cells in rabbit retina.

Taurine is present in high levels in the visual systems of many species of animals. In the cat's visual system, particularly the retina, a high concentration of this amino acid is maintained throughout embryonic and postnatal life (Guidotti, Badiani & Pepin, 1972). A higher amount of taurine is present in the retina of dark-reared chicks as compared with those of chicks reared under normal light conditions (Kubicek & Dolcnek, 1958; Pasantes-Morales, Ledig, Klethi & Mandel, 1972; Pasantes-Morales, Urban,

Klethi & Mandel, 1973b; & Pasantes-Morales, Klethi, Urban & Mandel, 1974). Light-induced taurine efflux appears to be related to changes in light intensity. The total amount of taurine released and the rate of the taurine released increased significantly with increasing stimulus intensity (Pasantes-Morales et al., 1974). Conversely, light stimuli failed to modify GABA efflux in perfused rat retinae. GABA and taurine are influenced in different ways by differential light conditions in chick retinae (Pasantes-Morales et al., 1973a, 1974). GABA levels increased in the retinae of continuously light-exposed animals, whereas taurine content was not affected. Taurine seemed to exert its effect by causing a depressant action on ganglion cells (Pasantes-Morales et al., 1973b). Bonaventure, Wioland and Mandel (1974) have suggested that former results have led to the conclusion that taurine and GABA are putative inhibitory transmitters or modulators in the retina, but seem to have different mechanisms and sites of action.

## Physiological Correlates of Taurine

A considerable amount of taurine is consumed in foods of both animal and organic origin (Roe & Weston, 1965). Taurine is excreted in large amounts in the urine when administered to rats or man, orally or intravenously (Awapara, 1956; Lajtha, 1970). Federici et al., (1974) have demonstrated that up to 40% of the taurine injected intraperitoneally to adult rats was collected in urine samples.

A study by Sturman and Cohen (1971) has shown that rats deficient in Vitamin $B_6$ develop a number of physical and biochemical abnormalities and have a reduced excretion of taurine. They report that the mammalian transsulfuration pathway normally utilized 80 - 90% of the ingested essential amino acid methionine, much of which goes to produce cysteine, an important constituent of protein. However, with impaired transsulfuration the rate of conversion of methionine to cysteine is reduced, resulting in the accumulation of various other metabolites. In such cases the body is dependent on the diet for cysteine since little or none can be produced from methionine. Amino acid analysis of urine from various groups of animals revealed no changes in excretion of cysteine or cystathionine, but excretion of taurine increased progressively by increasing amounts of cysteine in the diet. It appears that excess cysteine is converted largely to taurine and inorganic sulphate even in Vitamin $B_6$ deficient rats. In addition, these researchers have suggested that cysteine is metabolized differently in Vitamin $B_6$ deficient rats compared to control rats not deficient in Vitamin $B_6$. Tissue extracts from groups of animals contained S-cysteic acid, particularly in the liver and kidney (Sturman & Cohen, 1971). Extracts from these vitamin -deficient rats contained more of this acid than those of the control rats, suggesting that the conversion of cysteic acid to taurine had been impaired. Animals maintained on a diet deficient in pyridoxine soon start to excrete cystathionine in the urine

associated with a decreased excretion of taurine in the urine (Hope, 1957). These disturbances are caused by a reduction of the cystathionase activity in various organs and the concurrent loss of activity of cysteinesulfinic acid decarboxylase, the enzyme immediately responsible for taurine formation (Sturman & Cohen, 1971).

Spaeth and Schneider (1974) have suggested that a slow uptake but high concentration of taurine in the heart and other muscles further suggested that taurine may have a function in the contractile process. Furthermore, taurine tended to cause changes in parameters of electrocardiogram (ECG) that represent the rates of repolarization of the ventricles of the isolated guinea pig heart (Chazov, Malchikova, Lipina, Asafov & Smirnov, 1974). Investigators believe this is a result of the ability of taurine to regulate the excitability of the myocardium, perhaps through a membrane impermeability effect caused by the action of taurine on calcium shifts in the heart (Huxtable & Bressler, 1973; Laborit & Thuret, 1974).

## Behavioural Correlates of Taurine

Changes in taurine concentration have been reported in a number of central nervous system (CNS) abnormalities such as cell damage, seizures of various origins and certain types of mental retardation (Barbeau & Donaldson, 1974; Bergamini, Mutani, Delsedime & Durelli, 1974; Goodman, Kind & Thomas, 1964; Mutani,

Bergamini, Fariello & Delsedime, 1974; Perry, Hansen, Bratty, & Dolman, 1973; Piez & Eagle, 1958). Determinations of amino acid content in epileptogenic human cerebral cortex indicated a high glycine level combined with a low concentration of taurine in the focus of maximal epileptic activity (Van Gelder, 1972). Below normal concentrations of GABA, aspartic acid and glutamic acid also were found throughout the cortex of patient and animals with chronic focal epilepsy (Derouaux, Puil & Naquet, 1973; Mutani et al., 1974a).

Recent investigation of taurine in epileptic patients has shown a decreased level of this chemical in cerebrospinal fluid (Mutani, Monaco, Durelli & Delsedime, 1974b). Furthermore, replacement therapy whereby taurine was administered intravenously to humans (Barbeau & Donaldson, 1974; Bergamini et al., 1974) and intraperitoneally to animals (Adembri, Bartolini, Bartolini, Giotti &Ziletti, 1974) resulted in a reduction in epileptic-like seizures. Recent investigation by Gaito (1976) demonstrated that intraperitoneal administration of taurine in rats had an obvious retarding effect on simulated epileptic convulsions only at the initial stage (normal exploration) of brain stimulation.

Bergamini et al., (1974) and Perry, Bratty, Hansen, Kennedy, Urquhart and Dolman (1975) have speculated that taurine may permeate the brain and modify the amino acid-impaired metabolism in

organic epileptic cases, particularly in young patients. Indeed, taurine deficiency may be a key factor not only in epileptic-like seizures but also in another clinical syndrome which emulates mental depression and Parkinsonian symptoms (Perry et al., 1973, 1975). These investigators state that a marked decrease of taurine in blood plasma and cerebrospinal fluid typify this classical syndrome (Perry et al., 1973). It is quite feasible that an enzymatic failure in taurine synthesis may explain the modulating symptoms of depression, steatorrhea, weight loss and tremor (Perry et al., 1973). Even if the action of taurine is confined to a catalyst role in the normal recovery processes of the CNS, administration of this non-toxic amino acid in cases of acute brain damage may be helpful in decreasing the symptoms (Van Gelder, 1972).

Although considerable research has dealt with taurine from the biochemical perspective, there are only two known studies involving the behavioural effects of taurine on the rat.

Baskin, Hincamp, Marquis and Tilson (1974) investigated the effects of taurine on spontaneous motor activity in the rat. Male adult rats' motor activity measurements were taken daily. In a first experiment intraperitoneal injections of taurine were administered preceding seven consecutive daily habituation sessions (Baskin et al., 1974). Taurine caused a dose-dependent depression of psychomotor activity. In a further experiment these investigators noted that taurine administered intraventricularly to adult

rats, following seven consecutive daily habituation sessions, caused a dose and time-dependent depression effect on psychomotor activity. In fact, the largest dosage (62.5 µg) of taurine intraventricularly administered produced significant decreases in motor activity for the entire testing session (Baskin et al., 1974).

An investigation by Persinger, Valliant and Falter (1976) indicated that rats injected once every two days between postnatal days 4 and 20 with 62.5 µg/g or 125.0 µg/g (body weight) of taurine did not differ significantly from physiological saline injected controls tested in the open-field for ambulatory activity. There was a strong but non-significant tendency for taurine injected rats to run faster than their controls in an alley speed test for food reinforcement. Taurine injected rats ran significantly less in the running wheel test and displayed lower response reinforcement ratios following step-like changes in differential reinforcement of low rates of responding (DRL) reinforcement schedules. Quicker adjustments to the changes in DRL schedules were noted to not occur immediately but during sessions following the change. Persinger et al. (1976) concluded that taurine administration during early juvenile development could weakly influence adult inhibitory behaviour.

## Rationale for the Proposed Research

The present investigation was initiated on the assumption that taurine injections during development might increase this

amino acid in the neonatal rat's brain. Taurine is notably taken up in the rat's brain until postnatal day 20 (Chanda & Himwich, 1970). Furthermore, taurine levels in the rat's brain obtain maximum values between the first and seventh postnatal days, a period noted for a decrease in liver taurine levels (Chanda & Himwich, 1970). Taurine synthesized in the liver is transferred from blood to brain during this period (Chanda & Himwich, 1970). Hence, injections of taurine between days 8 and 20, when a decrease of this chemical begins, might compensate for the decrease by means of continually restoring this suspected modulator to brain cells. That taurine would be taken up into the rat's brain for CNS use is substantiated by evidence that taurine administered intraperitoneally or intravenously to animals (Adembri et al., 1970) and humans (Barbeau & Donaldson, 1974; and Bergamini et al., 1974), was beneficial in reducing epileptic-like seizures. This seems to imply that taurine uptake in brain cells has the ability to interfere with transmitter modulating properties in either pre- or postsynaptic areas. Hence, taurine might interact at the cellular level by facilitating neuronal cells of the CNS to develop modulating properties. Indeed, this might allow animals greater adaptibility for required inhibitory behavioural responses.

Consequently, this thesis examines the effects of manipulating brain taurine levels on adult behaviour. Three strains of rats were chosen as subjects: a Maudsley reactive (MR), Maudsley non-

reactive (MNR) and a control strain of rats, Roman Control Avoidance (RCA). The MR and MNR strain respectively (Jay's nomenclature, 1963) were originally bred for extremes of emotional elimination in Hall's (1938) open-field test (Broadhurst, 1960). The RCA strain has been included mainly as a control to examine differences in behaviour in the MR and MNR animals because of selection traits.

There was a specific reason for interest in the MR and MNR strains. In bioassay measurement MR animals displayed a greater concentration of GABA than the MNR strain (Rick, Tunnicliff, Kerkut, Fulker, Wilcock & Broadhurst, 1971). Because of the aforementioned similarity between GABA and taurine, it is possible that taurine administration may differentially affect the two strains.

To assess the effects of taurine on behaviour, the animals were tested in two situations, open-field and one-way active avoidance delayed response. The open-field task requiring no specific type of responses should reveal general defecatory and ambulatory behaviour. Additionally the one-way active avoidance delayed response will examine the rats' ability to inhibit responses.

# CHAPTER II

# METHOD

## Subjects

Ninety-eight rats were used as subjects in this experiment. Strains were MNR/Har/Lu (n = 19), MR/Har/Lu (n = 24) and RCA/Lu (n = 24). Both sexes were tested. Results were analyzed for missing N (Refer to Table 1). Of the ninety-eight animals tested in this experiment only the first seventy-two were used for data analysis since some cells contained more animals of a particular strain than were needed. Details of the development of the strains are reported in Satinder (1971, 1972).

All subjects were bred and reared in the Lakehead University Behaviour Genetics Laboratory and given food and water ad libitum. Prior to experimentation the three strains were housed on separate cage racks, two animals per cage according to sex and treatment. Temperature in the laboratory was maintained at 22.2° - 1.1° C., whereas humidity was maintained at a constant 40%. Lighting in the laboratory was maintained by flourescent lights which remained on between the hours of 9 a.m. and 9 p.m.

## Experimental Design

The basic design used in this experiment was a 2 (taurine and saline) x 3 (strains) x 2 (sexes) x 2 (test order). An additional within subjects variable (trials) was included for some of

TABLE I

A REPRESENTATION OF THE STRAINS, SEXES, DRUGS AND TEST SITUATIONS ANIMALS WERE EXPOSED TO

| Age: In Days | | 8-----20 | | 100----------105----------110 | |
|---|---|---|---|---|---|
| Strain | Sex | Chemical Injected | No. | | |
| MNR/Har/Lu | Male | Taurine | n=2 | Open-Field | Avoidance Cond. |
| | | | n=2 | Avoidance Cond. | Open-Field |
| | | Saline | n=2 | Open-Field | Avoidance Cond. |
| | | | n=2 | Avoidance Cond. | Open-Field |
| | Female | Taurine | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| | | Saline | n=3 | Open-Field | Avoidance Cond. |
| | | | n=2 | Avoidance Cond. | Open-Field |
| MR/Har/Lu | Male | Taurine | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| | | Saline | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| | Female | Taurine | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| | | Saline | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| RCA/Lu | Male | Taurine | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| | | Saline | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| | Female | Taurine | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |
| | | Saline | n=3 | Open-Field | Avoidance Cond. |
| | | | n=3 | Avoidance Cond. | Open-Field |

the dependent measures. The taurine and saline injected rats were tested in a double blind manner.

The main measure recorded in this experiment was inhibitory response failure. This measure was used to examine the hypothesized inhibitory modulation effects of taurine. In addition, avoidance responses were recorded not because of any theoretical significance to this experiment but mainly because they were obvious aspects of the one-way active avoidance testing.

Open-field was included because this is the genetically selectively bred behaviour of these strains of rats (Broadhurst, 1960).

Apparatus

The open-field apparatus consisted of a box with dimensions of 90 cm x 90 cm, with 16 equal squares (Satinder & Hill, 1974). This arena was constructed of plywood and arborite. Walls were 45 cm high. The front of the arena was a transparent sliding door constructed of Plexiglas and was utilized as an observation screen. Illumination of 230 ftc. was maintained in the open-field with four, 90 cm flourescent lights suspended 90 cm above the floor level from a wooden frame. A white noise generator Model 1432, manufactured by the Lafayette Instrument Company was positioned in the experimental room and maintained at 65 dB (re .0002 µbar) from the centre of the open-field, to control for external noise.

A one-way active avoidance apparatus, Model A- 586 (85204) manufactured by the Lafayette Company and connected to a Neon Grid Shocker Scrambler unit with an adjustable level of shock

ranging from .47 mA (milliamperes) - 1.1 mA was also used.

The avoidance apparatus consisted of a chamber with dimensions 265 x 200 x 200 mm and was constructed from anodized aluminum, 6 mm thick. Sides of the chamber consisted of clear Plexiglas and the floor was constructed of steel bars 5 mm thick, spaced 10 mm apart. On one side of the chamber was a platform with dimensions 175 mm high, 200 mm wide and 137 mm deep. The platform was elevated 80 mm from the floor-level grid bars (Satinder & Petryshyn, 1974). A retracting door allowed the animal onto the platform and served as the conditioned stimulus (CS) to initiate the rat's movement from the grid bars to the platform.

A Plexiglas apparatus with dimensions 300 mm x 240 mm x 210 mm high, containing a steel grid floor with bars 5 mm thick and spaced 10 mm apart, was used to test foot shock sensitivity thresholds of all animals.

In addition, a Hunter Klockounter Model 220 C recorded the time, which in turn activated two Hunter digital timers, Model 127 S. (The first digital timer allowed for a 5-second time interval in which the rat could respond, thus allowing an avoidance from shock. A second digital unit connected to the shock unit timed the 5-second administration of shock to the grid bars of the shuttle system). Also present in the experimental room was a Universal Timer Model 168, manufactured by Dimco Gray Company, used to time a one-minute period for each of the 10 trials during each session. The Intertrial Interval (ITI) between each trial was

1 minute.

Procedure

Injection of Taurine. Following parturition the animals were divided into two groups using a split-litter technique. At eight days of age identification was established between the two groups of animals by marking the taurine injected group with red carbol fuchin on the right front leg and the physiological saline control animals on the left rear leg.

The experimental animals were injected with 62.5 µg/g body weight of 0.5 molar (M) taurine (1 µl of solution per gram of pup's body weight), whereas the control group of animals were injected with a similar amount of physiological saline of a comparable ionic strength to taurine. Pups were injected with solutions of taurine or physiological saline on postnatal days 8, 10, 12, 14, 16, 18, and 20 at approximately the same time of the day. The amount of drug injected each day was adjusted to animal body weight. After the animals were weaned on day 28, they were placed in housing cages and maintained according to sex, strain and treatment.

At 100 days of age subjects were removed from their cages and divided into two groups. One group of animals was tested in the open-field task. The remaining group of animals was tested in the one-way active avoidance task. The test order was reversed and the animals tested in the remaining task when either of the

tasks had been used to test each group.

Open-Field. Each animal was carried into a semi-darkened experimental room in a plastic cage. Animals were placed in the centre of the open-field arena on an individual basis under a Plexiglas container. All the rats were tested in exactly the same manner and position. As the Plexiglas container was lifted from the rat, a timer, lights and white noise generator were activated by the experimenter. Each session in the open-field arena lasted for two minutes, then was automatically deactivated by a pretimed clock.

The number of squares traversed, fecal boluses emitted and body weight was recorded for all animals tested in the open-field. All rats were tested for five consecutive days at approximately the same time of the day. A diluted solution of lysol was used to wash the open-field between testing of individual subjects to remove residual odors.

One-way Active Avoidance Task. One day prior to testing, all animals were carried into a fully lighted experimental room and tested for their foot shock sensitivity level. The Plexiglas apparatus as aforementioned in the apparatus section was connected to a shock scrambling unit. Animals were individually placed into the apparatus. Two minutes were allowed for adaptation in the unit, then electric shocks of increasing intensity were administered until the animal made a jump response which consisted of jumping from the grid bars. (Each animal was given

10 trials of the ascending series, using the methods of limits. The shock intensities were in steps of .47, .50, .54, .58, .62, .67, .73, .80, .97 and 1.05 and 1.10 mA. The mean level of shock which caused the rats to jump from the grid bars was chosen as the shock sensitivity level for testing inhibitory facilitatory behaviour and was termed the unconditioned escape response (UER) (Refer to Table 2).

The following day each animal was carried into the semi-dark experimental room in a plastic cage. The animal was placed in the one-way active avoidance conditioning unit and required to jump or climb onto the platform following a 5-second period when it was made available. If the animal attempted to climb onto the platform before the 5-second interval had expired it was forced to return to the grid bars. In the event that the animal did not ambulate from the grid bars to the platform within the allowed 5-second period succeeding presentation of the CS, a timer previously set by the experimenter and connected to the shock unit, delivered a shock to the grid bars of the active avoidance unit. The shock received by each subject was determined as mentioned earlier (i.e., UER). (The sliding door of the platform served as the CS to enable the rats to learn the 5 second delay response to allow for avoidance from the shock). At the end of each trial if the animal had not yet returned to the grid bars, it was forced to do so by retracting the sliding door. Each subject was tested for 10 trials each day, for four

consecutive days.

During avoidance training the following measures were recorded. Four of these were measures of acquisition of escape and avoidance responses and included: 1. number of avoidance responses: the number of avoidance responses for every animal over the daily 10 trials (designated as the animal's ability to move to the platform of the active avoidance conditioning unit to avoid onset of shock); 2. avoidance response latency: time taken to make an avoidance response; 3. number of escape responses: the animals were given a 5.0 second period to make an avoidance response after presentation of the CS. Shock was then applied to the grid bars. The responses made by the animals within the next 5.0 second period after presentation of shock were recorded as number of escape responses; 4. escape response latency: the time taken by the animals to escape after the onset of shock. The main measure; 5. inhibitory response failure: was obtained on the basis of an animal's ability to remain on the grid floor of the active avoidance conditioning unit for a maximum period of five seconds (after retrieval of the door to the platform in the conditioning unit by the experimenter) before eliciting an avoidance response. One other measure recorded included body weight.

At 113 days of age the rats were weighed and then sacrificed by placement into a glass container containing chloroform at 0.75% proof. Thyroids, adrenals and testes or ovaries were removed from each animal and placed in normal physiological saline 0.85%.

All glands extracted from each rat were then taken from saline solution, excess moisture removed and weighed (within seven minutes following death) on an Oretling balance scale.

# CHAPTER III

## RESULTS

The results were evaluated by analysis of variance. The minimal level of statistical significance accepted for the measures was $p < .01$. The significant differences from this experiment are reported in Table 3 (Refer to page 63).

The main effects for the between factors (strain, sex, drug and test-order and for the within factors (days and position effect noted in glandular analysis) were evaluated. Inhibition-facilitatory behaviour was chosen as the index which would specifically examine the hypothesized inhibitory effects of taurine. Inhibitory response failure examined an animal's ability to inhibit responding for five seconds after presentation of the CS. As previously mentioned, mean number of avoidances, avoidance response latency, mean number of escapes and escape response latency were not collected for any theoretical significance which could show taurine's effect but merely because they were obvious aspects of one-way active avoidance responding.

Glandular weight analysis was included for the thyroids, adrenals and gonads of the rats. It was possible that drug administration might have affected growth of the animal's endocrine glands. Additionally, the weights for the animals at 28 days (weaning period) and 100 days (first day of testing) were also analyzed.

Inhibitory Response Failures

There was significant differences in inhibitory response failures among the strains (MR/Har/Lu 6.29; MNR/Har 5.81 and RCA/Lu 2.00), $F$ (2,43) = 15.75 $p < .001$ (Refer to Figure 1). Analysis of the sex differences revealed that the female animals displayed an overall significantly greater number (5.88) of inhibitory response failures than the male rats (3.52), $F$ (1,43) = 11.91, $p < .005$ (Refer to Figure 2). There were no significant differences between taurine (4.94) and saline (4.46) injected rats on the inhibitory response failure measure (Refer to Figure 3).

No significant differences were noted between animals first tested in the open-field test (4.8) and those tested in the one-way active avoidance task (4.5).

Over a four day training period no systematic differences were found among strains, between sexes, drug groups and order of tests.

Mean Number of Avoidances

There were significant differences in mean number of avoidance responses among the strains (MR/Har/Lu 1.94, MNR/Har/Lu 1.57 and RCA/Lu 0.75), $F$ (2,43) = 8.77 $p < .001$. The female animals made more avoidance responses (1.63) than the male rats (1.32). This difference was not significant. There were no significant differences in avoidances between taurine (1.41) and saline (1.43)

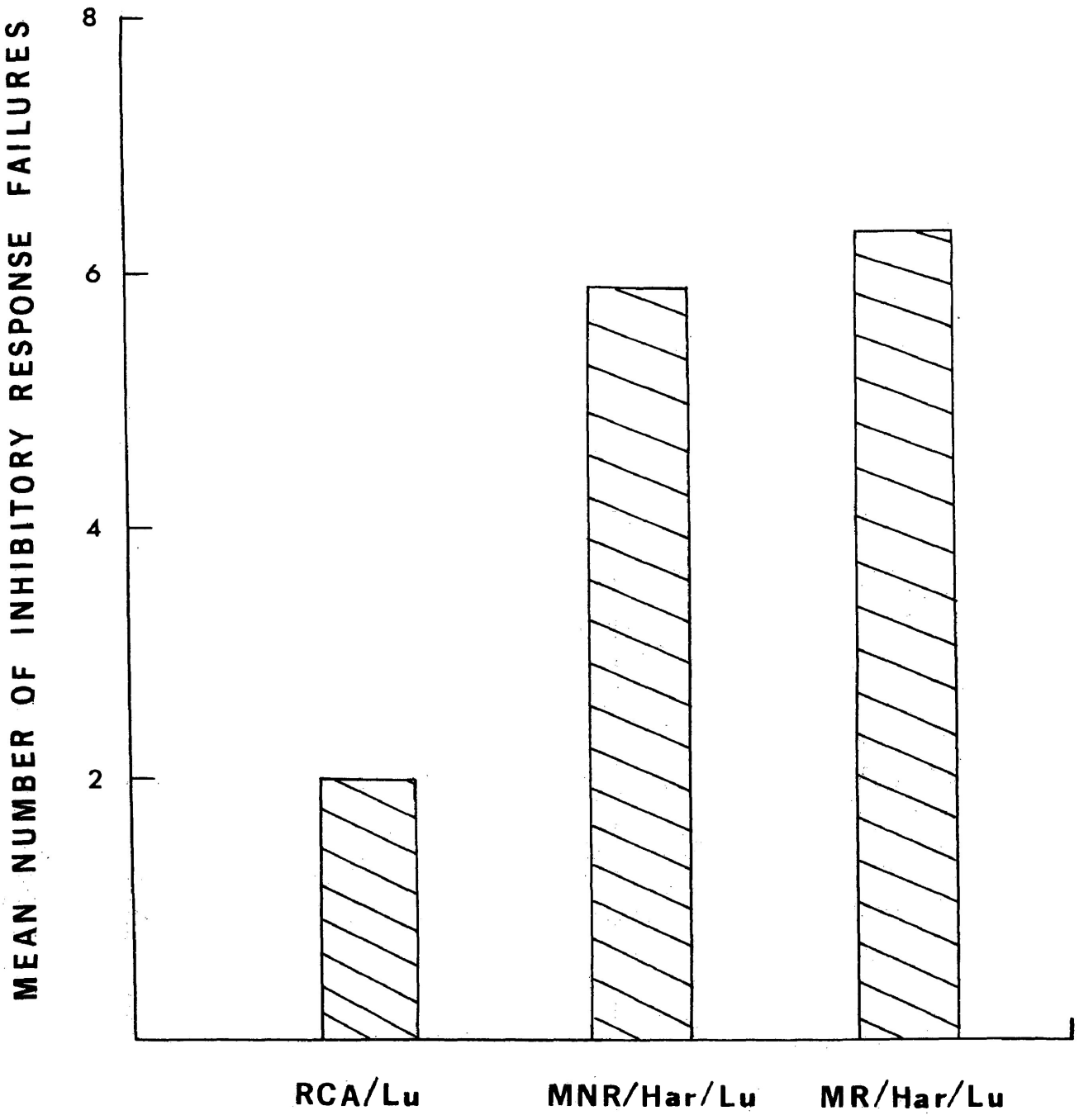



Figure 1: Mean number of inhibitory response failures among the strains of rats

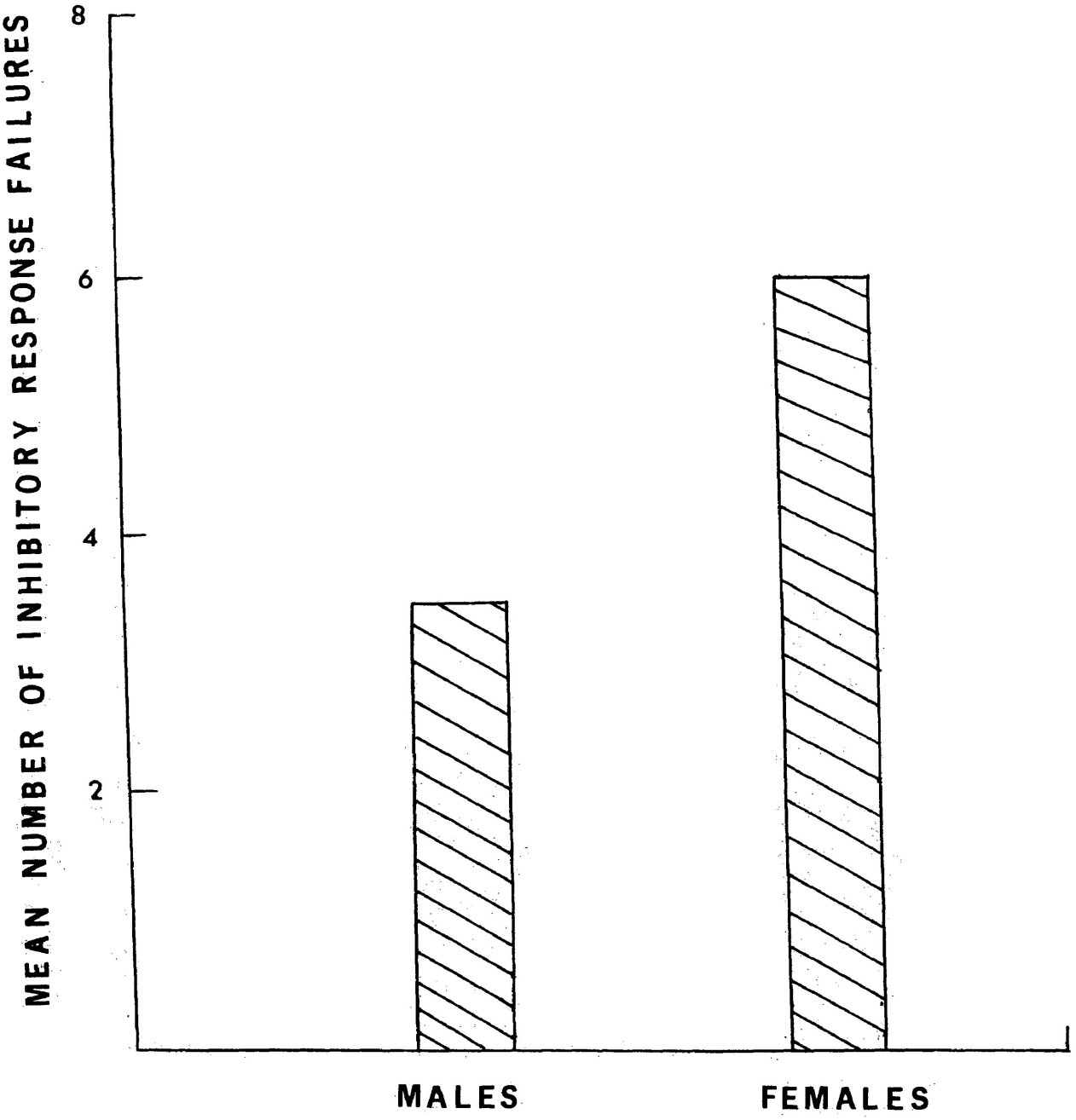



Figure 2: Mean number of inhibitory response failures between the sexes

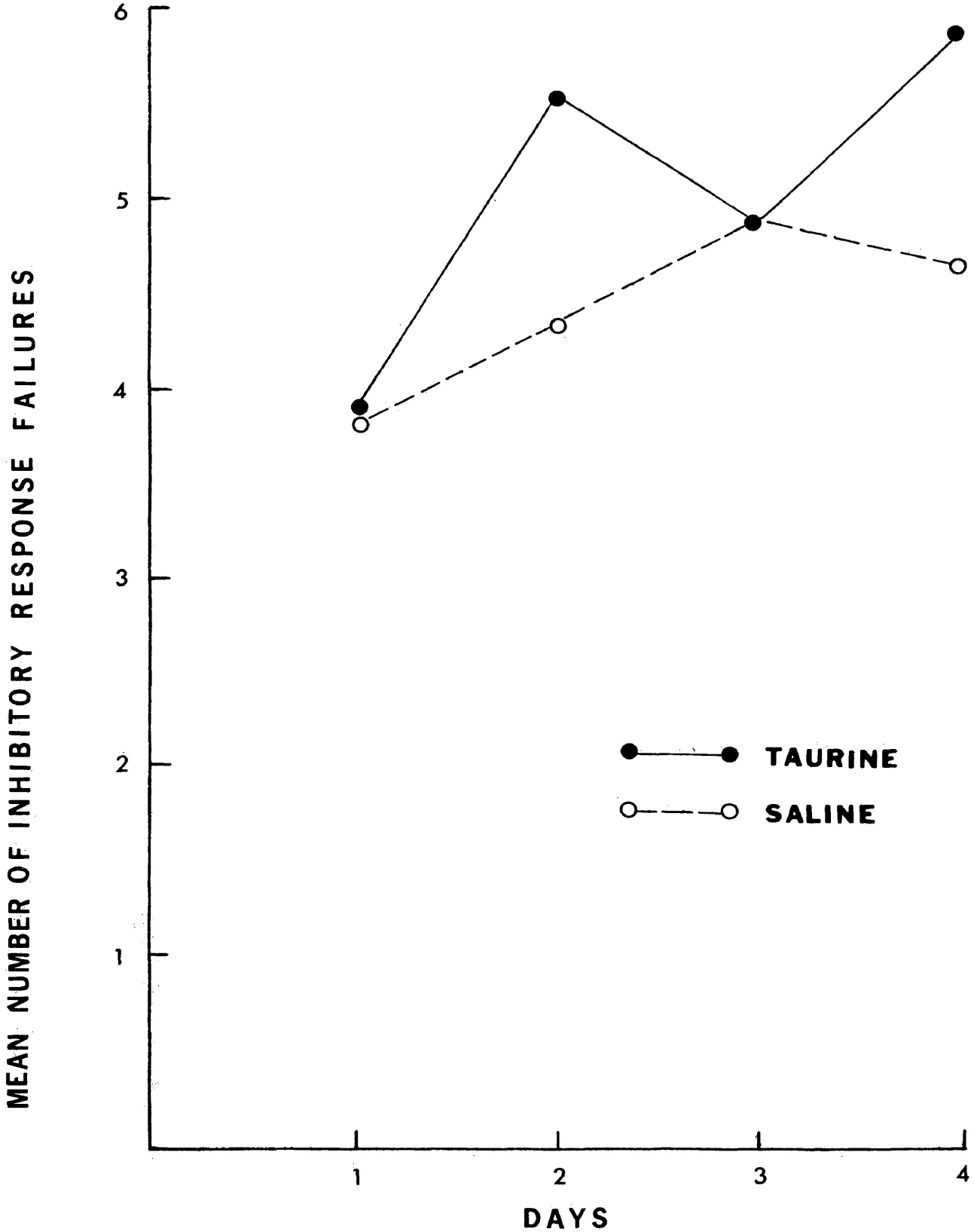



Figure 3: Mean number of inhibitory response failures for animals tested under the effects of taurine and physiological saline

injected rats.

There were no significant differences in avoidances between animals first tested in the open-field (1.50) and those tested in the one-way active avoidance task (1.34).

Over a four day training period no systematic differences were found among strains, between sexes, drug groups and order of tests.

Avoidance Response Latency

Avoidance response latency was negatively and significantly correlated with the mean number of avoidances over a four day test period: day 1 ($r = -.88$), day 2 ($r = -.95$), day 3 ($r = -.92$), day 4 ($r = -.96$) and therefore will not be discussed.

Mean Number of Escapes

Mean number of escapes were negatively and significantly correlated with mean number of avoidances over a four day test period: day 1 ($r = -.65$), day 2 ($r = -.86$), day 3 ($r = -.81$), day 4 ($r = -.96$) and therefore will not be discussed.

Escape Response Latency

There were no significant differences noted in escape response latencies among the strains (MNR/Har/Lu 1.38 sec., MR/Har/Lu 1.17 sec. and RCA/Lu 1.31 sec.).

There were no significant differences in escape response latencies between male (1.36 sec.) and female rats (1.21 sec.). There

were no significant differences in escape response latencies between taurine (1.32 sec.) and saline (1.25 sec.) injected animals. No significant differences were noted between animals first tested in the open-field task (1.22 sec.) and those animals tested in the one-way active avoidance task (1.35 sec.).

Over a four day training period no systematic differences were found among strains, between sexes, drug groups and order of testing. However, over four days of training there was a general decrease in escape response latency: day 1 (1.77 sec.), day 2 (1.20 sec.), day 3 (1.07), day 4 (1.10 sec.), $F$ (3,129) = 14.32, $p < .001$.

Defecation

There was a significant difference in number of defecations in the open-field for strains, (MNR/Har/Lu 0.03 boluses, MR/Har/Lu 3.40 boluses, RCA/Lu 1.21 boluses), $F$ (2,43) = 16.46, $p < .001$. That the MR/Har/Lu strain defecated more than the MNR/Har/Lu strain is in line with the findings of Broadhurst and Eysenck (1965), Rick et al. (1971) and Rick and Fulker (1972) who also noted higher defecatory behaviour in the reactive strain as compared to the non-reactive strain in the open-field test.

The male rats were noted to defecate significantly more (1.91 boluses) than the female rats (1.18) during open-field testing, $F$ (1,43) = 22.65, $p < .001$. There were no significant differences in defecation between taurine (1.63) and saline (1.47)

injected animals. Animals first tested in a one-way active avoidance task defecated significantly more (1.77) than animals first tested in an open-field task (1.33), $F$ (1,43) = 7.99, $p < .01$. These findings can be explained by the fact that animals first tested in the open-field test were not exposed to electric foot shock. Therefore animals tested in this situation tended to display little emotionality and traversed more sections in the open-field. Conversely the rats first tested in the one-way active avoidance task had been exposed to foot shock. Therefore when these animals were placed in the open-field they may have generalized being removed from their cages as a cue for being shocked. Consequently these rats would traverse less sections in the open-field and increase their defecatory behaviour.

There was a significant difference for defecatory behaviour over a five day test period among the strains, $F$ (4,172) = 5.47, $p < .001$. However, over the same five day training period no systematic differences were found between sexes, drug groups and order of testing.

Sections Crossed in the Open-Field

There were no significant differences in number of sections traversed in the open-field among the strains (MNR/Har/Lu 21.22, MR/Har/Lu 22.13, and RCA/Lu 21.42). Broadhurst (1960) has noted that the non-reactive animals generally show more ambulation in the open-field as opposed to reactive animals. However, on the

contrary the results of sections crossed by rats in this study do not show the same effects. Taurine administration did not have any effect on the rats' ambulatory behaviour, as shown by the data. Therefore drug administration can not be suggested as the main determinant of this effect. At this point it is not known why the strains of animals showed similar ambulatory behaviour in the open-field, and the reliability of these particular results are in question. The female rats traversed significantly more sections (29.94) than the male rats (18.06), $F$ (1,43) = 9.19, $p < .005$. There were no significant differences in sections crossed in the open-field between taurine (20.62) and saline (22.38) injected rats. Animals first tested in an open-field task traversed significantly more sections (25.13) than animals first tested in a one-way active avoidance task (17.88), $F$ (1.43) = 10.19, $p < .005$. That the rats crossed more sections when first tested in the open-field task as compared to fewer sections crossed by animals first tested in a one-way active avoidance task can be explained as a result of increased emotionality generated by UER shock application.

Over a five day training period no systematic differences were found in sections crossed among strains, between sexes, drug groups and order of testing.

Correlations were calculated between the following open-field measures: total sections crossed, defecatory behaviour and body weight of all animals tested over a five day period. Analysis of the data did not reveal any significant correlations between any

of the variables.

Correlations were also calculated for drug effects over a five day test period. No significant correlations emerged between any of the variables for saline or taurine injected animals.

Shock Sensitivity Thresholds

There were no significant differences in UER's for the strains, (MR/Har/Lu .55 mA, MNR/Har/Lu .50 mA, RCA/Lu .53 mA), (Refer to Table 2). These findings are similar to those of Satinder (1976) who found that the strains (MR/Har/Lu and MNR/Har/Lu) did not significantly differ in the amount of foot shock (in volts) required to elicit UER over a 10 trial period (MNR/Har/Lu: males 98 volts, females 82 volts; MR/Har/Lu: males 107 volts, females 84 volts). In fact Satinder (1976) has suggested a need for caution when interpreting relationships between shock sensitivity and body weight due to the fact that these measures are dependent upon the genotype and sex of the animals.

Male rats showed a significantly higher UER (.56) than the female rats (.50), $F$ (1,43) = 151.05, $p < .001$. This finding is in line with Satinder (1976) who also found that the male rats on the average required a higher level of shock (in volts) to elicit UER.

There were no significant differences in UER between taurine (.53 mA) and saline (.52 mA) injected rats. This might be a good indicator that taurine injections during infancy (post-natal days

8 - 20) did not cause any biological changes in the rats. Lastly, there were no significant order of testing effects for UER; open-field (.52 mA), active avoidance (.53 mA).

Glandular Weight Analysis

Weights of the thyroids, adrenals and gonads were analyzed according to absolute weight (mg weight). Additionally, the glands were analyzed according to a corrected weight (mg weight of the gland / one gram of animal body weight) to allow for the differences in gland weight due to body weight, since the thyroid does not grow isometrically with the body weight (Feuer, 1969).

Thyroid Glands

Analysis of the thyroid glands using absolute weight showed that there were significant differences among the strains, $F$ (2,43) = 8.62, $p < .001$ (Refer to Table 4). Thyroid glands were also analyzed according to a corrected weight measure for the strains. This difference was significant, $F$ (2,43) = 12,58, $p < .001$ (Refer to Table 4). The findings for the MNR/Har/Lu and MR/Har/Lu strains using both absolute and corrected weight measures are in line with those findings of Feuer and Broadhurst (1962c) who also noted that the non-reactive strain had a larger thyroid weight (in mg of tissue / 100 body weight) than the reactive strain.

The absolute weight measure revealed that there was a significatn sex difference. Male rats had larger mean thyroid

weights than female rats, $F$ (1,43) = 12.35, $p < .005$ (Refer to Table 4). However, using the corrected weight measure showed that female rats had significantly larger thyroid weights than the male rats, $F$ (1,43) = 67.51, $p < .001$ (Refer to Table 4). This is not surprising to find since the latter estimate allows for a better evaluation of the weight of the thyroid in relation to the animal's body weight. As Table 4 shows, females do have much larger thyroids than male rats.

There were no significant differences in thyroid weights between taurine and saline injected rats in absolute and corrected weight measures.

In addition, there were no significant differences in thyroid weight between animals first tested in open-field and those animals tested in a one-way active avoidance task in absolute and corrected weight measures.

There were no systematic differences found for right or left thyroid glands among strains, between sexes, drug groups and order of testing in either absolute or corrected body weight.

Adrenal Glands

Adrenal gland analysis in absolute weight showed a significant difference among strains, $F$ (2,43) = 218.59, $p < .001$ (Refer to Table 4). The findings for the MR/Har/Lu and MNR/Har/Lu strains are in line with the findings of Feuer and Broadhurst (1962c), Broadhurst and Eysenck (1965) and Feuer (1969) who analyzed the

endocrine glands and found the reactive animals to have larger adrenal gland weights than the non-reactive strain. Analysis of the adrenal glands in corrected weight was also significant for the strains, $\underline{F}$ (2,43) = 8.56, $\underline{p} < .01$ (Refer to Table 4) and showed similarly as absolute weight did that the reactive strain had larger adrenal glands than the non-reactive strain.

There were no significant differences in adrenal weight between female and male rats on the absolute weight measure. However, when the corrected measure for adrenal glands was analyzed there was a significant difference noted $\underline{F}$ (1,43) = 159.13, $\underline{p} < .001$ (Refer to Table 4). This difference proved highly significant since the female rats had much larger adrenal glands in proportion to their body weights. These findings are in line with the findings of Feuer and Broadhurst (1962a, c), Broadhurst and Eysenck (1965) and Feuer (1969) who showed female rats to have larger thyroid and adrenal gland weights than the male rats.

There were no significant differences in adrenal weight between taurine and saline injected rats for both the absolute and corrected weight measures.

There were no significant order of testing differences in absolute weight: open-field (32.70 mg); active avoidance (31.80 mg); and corrected weight: open-field (.1372 mg/g); active avoidance (.1346 mg/g) for adrenal glands.

Lastly, there were no systematic differences found for right or left adrenal glands among strains, between sexes, drug groups

and order of testing in either absolute or corrected weight measures.

Gonads

Absolute weight analysis showed a significant difference in gonads among the strains, $F$ (2,43) = 119.63, $p < .001$ (Refer to Table 4). Similarly analysis of gonads for corrected weights also revealed a significant strain difference, $F$ (2,43) = 64.77, $p < .001$ (Refer to Table 4). The findings for the MR/Har/Lu and MNR/Har/Lu strains are in agreement with the findings of Broadhurst and Eysenck (1965) and Feuer and Broadhurst (1962c) who also found the non-reactive strain to have larger gonads than the reactive strain. The obvious sex differences in ovaries and testes for the absolute and corrected weights need no explanation.

There were no significant differences in gonadal weight between taurine and saline injected rats for both absolute and corrected weight measures. That taurine injected rats had larger absolute weight measures for gonads may be a result of their larger body weight. However, when gonadal weight was analyzed in proportion to body weight saline rats were shown to have larger gonads in relation to body size.

Animals first tested in the open-field showed larger gonads for both absolute (702.25 mg) and corrected weights (2.486 mg/g) as compared to absolute (700.81 mg) and corrected weights (2.375 mg/g) for animals first tested in a one-way active avoidance task.

There were no systematic differences found for right or left gonads among strains, between sexes, drug groups and order of tests for either absolute or corrected weights.

Body Weight

The body weights of the rats were analyzed at both 28 and 100 days of age. There was a significant difference in body weight at 28 days of age among the strains RCA/Lu (69.25 g); MR/Har/Lu (55.42 g) and MNR/Har/Lu (52.71 g) $F$ (2.43) = 61.34, $p < .001$. There were no significant differences in body weight between sexes or drug groups. This seems to demonstrate that postnatal drug administration between days 8 and 20 did not affect an animal's body weight.

There was a significant difference in body weight among the strains at 100 days of age RCA/Lu (299.00 g); MR/Har/Lu (231.25 g) and MNR?Har/Lu (194.79 g) $F$ (2.43) = 407.05, $p < .001$. The male rats were significantly heavier (294.69 g) than the female rats (188.67 g), $F$ (1,43) = 122.78, $p < .001$. There were no significant differences in body weight at 100 days for taurine (243.16 g) or saline (240.19 g) injected rats.

# CHAPTER IV

## DISCUSSION

The results of this experiment indicate that taurine injections during a postnatal period produced no overall change in later adult behaviour. Taurine had no effect on inhibitory response failure and no effect on measures of acquisition of avoidance learning (mean number of avoidance responses and escape response latency). Taurine administration also had no significant effect on open-field measures (sections crossed and defecatory behaviour) and no significant effect on glandular weights (thyroids, adrenals and gonads).

Taurine was hypothesized to be similar to GABA, a known neurotransmitter inhibition substance. On this premise rats were injected with taurine with the intention that this chemical would cause similar inhibitory modulating effects in the CNS as GABA was proposed to have had. There was a specific interest in testing the MR/Har/Lu and MNR/Har/Lu animals because in bioassay measurement the reactive animals are known to display a greater concentration of GABA than the non-reactive strain (Rick et al., 1971).

Taurine injections during a postnatal period (Days 8 - 20) produced little overall effect on measures of inhibitory-facilitatory behaviour (inhibitory response failure, mean number of

avoidances and escape response latency). Taurine injections also had little effect on general reactivity measures (sections traversed in the open-field, defecatory behaviour and UER's). No evident effect of taurine administration was notable in animal body weight at 28 and 100 days of age. Taurine also had very little effect on thyroids, adrenals and gonads. At this point one should examine the experimental design of this experiment in an attempt to elucidate the failure of taurine to demonstrate any clear-cut effects on behavioural responses. It was earlier hypothesized that postnatal injections of taurine when the CNS is still plastic might permanently elevate taurine levels in the neuronal cells, allowing for greater adaptibility to inhibitory responses. However, the results of this experiment seem to imply that taurine did not facilitate any inhibitory modulating effects in neurons. If this chemical does have the ability to facilitate such a change in animal behavior, the behavioural tests used to reveal these properties were either not examined for a sufficient period of time or did not have the ability to allow for an adequate display of this behaviour.

Persinger et al., (1976) have questioned whether preweaning administration of taurine permanently elevates brain taurine levels or whether the elevation is transient but results in morphological changes in the developing brain. However, unpublished studies by Falter, Persinger and Lafreniere showed no significant differences between 30 day old taurine injected rats and their controls with respect to: 1) taurine levels in the cerebrum (4.4 μmole/g and

4.0 µmole/g, respectively) or the cerebellum (5.1 µmole/g and 3.6 µmole/g, respectively. Yet, Falter et al., point out that these measures may be too gross to reflect behaviourally relevant changes since extraordinary high concentrations of taurine have been reported by Crabai et al., (1974) in localized tissue such as the neurohypophysis. It must be remembered that the present experiment dealt with "normal" rats with presumable normal levels of taurine in their brains. Since taurine levels in the young rat brain are known to be already exceptionally high (Gaitonde, 1970), exogenous dosages of taurine might not be influential enough to over-ride built in metabolic controls. However, the unpublished work of Persinger, Valliant, Lafreniere and Falter suggest that the possibility of early taurine administration could bring about desirable changes in organisms with initial deficiencies in CNS taurine levels.

It is quite possible that taurine is not an effective inhibitory modulator substance as suggested by Gruener, Markovitz, Huxtable and Bressler (1975). Barbeau and Donaldson (1974) also question taurine's validity as a putative neurotransmitter inhibitory substance, due to the fact that it is metabolically broken down too slowly at the synaptic clefts in the neurons. Hence, future research should consider the fact that taurine may not be an inhibition modulator substance but may be only simulating such properties.

It is clear that taurine administration did not demonstrate any main effects on any of the behavioural or glandular measures.

The type of measures that taurine did influence did not clearly demonstrate its ability as a putative inhibition substance. Hence, it may be reasonable to assume that the locus of taurine's effect may not be at neuronal synaptic junctions. Therefore further research is needed in this specific area if a more complete understanding is to be acquired of such neurochemical-physiological interactions.

In glandular analysis (thyroids, adrenals and gonads) the three strains of rats (RCA/Lu, MNR/Har/Lu and MR/Har/Lu) differed significantly in both absolute and corrected body weight measures. Yet, as this experiment was mainly concerned with the reactive and non-reactive strains, the RCA/Lu strain will be omitted from this discussion. Since other investigations in glandular analysis have dealt with the corrected body weight measures of these two strains of rats this measure will be of prime concern (Feuer & Broadhurst, 1962b). As previously mentioned there is general disagreement among investigators about the relative weights of thyroid glands of the MR/Har/Lu and MNR/Har/Lu strains of rats. These strains have shown quite a variability in thyroid gland size. In addition, the females differed significantly from the males in respect to their corrected body weight measures. Rats from the MNR/Har/Lu had heavier thyroid glands on the average than the MR/Har/Lu strain. However, Feuer and Broadhurst (1962a) have suggested that it is not possible to state a causal relationship between differences in size and function of thyroids and the emotional activity of the animals.

The selective breeding processes for behavioural characteristics have definitely resulted in a selection of animals with different thyroid size and hormone content (Feuer & Broadhurst, 1962a). Harris (1955) has demonstrated that metabolic and secretory activity of the thyroid gland is affected by the functional processes of the hypothalamus and the pituitary and that direct stimulation of the hypothalamus can alter behavioural patterns. From this point of view it seems that this provides a sound physiological route in connecting thyroid activity and behaviour (Feuer & Broadhurst, 1962a). Indeed the differences in thyroid activity may have reflected changes in the pituitary function which could have triggered off different psychological reactions in the rats (Feuer & Broadhurst, 1962a).

This study also shows that the MR/Har/Lu strain had much larger adrenal gland weight than the MNR/Har/Lu strain. This finding was quite obvious in both corrected and absolute body weight measures. Feuer and Broadhurst (1962c) have stated that there is no concrete reason for this finding. There are conflicting ideas about the role of the adrenal medulla in emotionally arousing situations (Feuer & Broadhurst, 1962c). In this experiment animals were expected to learn a pattern of responding so as to avoid shock administration. The fear which arose in these strains could have caused the adrenal glands to produce more adrenalin. That the glands were larger in the MR/Har/Lu strain before the experiment was undertaken is not known. However, according to Feuer

and Broadhurst (1962c), Broadhurst and Eysenck (1965) and Feuer (1969) the reactive strain differs in adrenal gland size prior to emotionally arousing situations. The female rats were also found to have larger glands than the male rats. Although these findings were not significant they seem to suggest that the female rats have an increased adrenal gland size to allow for the increased adrenalin output into the vascular system which is probably a function of their hormonal systems.

The MNR/Har/Lu strain was shown to have larger gonads than the MR/Har/Lu strain both in absolute and corrected weight measures. At present the reason for the difference in gonads between these two groups is not known. However, there may be some connection between hormonal release by the pituitary and thyroid glands which directly causes the differences in gland size. That the MNR/Har/Lu has larger adrenals may be a result of hormonal release which would facilitate larger gonads in this strain. The differences in size of the gonads could be directly related to the fertility of rats. Feuer and Broadhurst (1962c) found that the non-reactive strain had marked fluctuations in their rates from generation to generation. In fact birth rates increased to approximately 20% after the sixth generation (Broadhurst, 1960).

## Suggestions for Future Investigation

The locus of taurine's effect in the brain is evidently still not clear (Persinger, 1974). Future investigation in this neuro-

physiological area might consider the attempt to inhibit taurine's circuitry. However, such an intervention is difficult and may involve undesirable side effects on other chemical circuits (Persinger, 1974).

It was originally mentioned that taurine had to be administered during postnatal development due to the plasticity of the CNS, because if administered during later development it would not pass through the blood-brain barrier as suggested by Chanda and Himwich (1970) and Jacobson and Smith (1968). However, recent investigation by Gaito (1976) and Baskin et al., (1974) have evidenced that taurine injection to adult rats does have the ability to facilitate change by interacting in the central and autonomic nervous system. For this reason, future behavioural testing of rats should adhere to administration of taurine prior to and during testing, not only in adolescent rats but also in adult rats, if an attempt is to be made to elucidate whether or not taurine has inhibition properties.

Indeed it would be useful to utilize the same procedure as aforementioned but inject animals with taurine immediately before testing in the one-way active avoidance task. It would also be helpful in this study to inject animals for a longer period of time either before or during testing since taurine is hypothesized to be a long term inhibition modulating substance and may require a longer period of time to display its effects.

In addition one might also attempt to change the type of task

requirement. Operant schedules of reinforcement would ideally test an animal's ability to make inhibition responses since they allow an animal to attend to learning a response. In order to differentiate taurine effects, a schedule of reinforcement which specifically tests, inhibition should be selected. Such a schedule is referred to as the DRL (differential reinforcement of low rates of responding). An animal placed on this schedule must learn to postpone consequent responses for some schedule-dependent interval. For example, an animal being tested on a DRL 6 second interval must wait for 6 seconds since his last response before responding again if he is to be reinforced with a pellet of food.

Long term adaptation to a static reinforcement schedule can be informative about long-term or gradually adjusting inhibition processes in the central nervous system. Halasz (1968) has introduced a new concept into the behavioural testing of neuropathological correlates that involve "response transients to demand changes". Essentially, Halasz (1968) considers the organism as a type of homeostatic response device to which systems theory can be applied. One of the outcomes of his work suggests that predictable response transients occur when the organism attempts to adapt to new demands in their reinforcement schedule environment. In fact the occurence of response transients to reinforcement schedule changes can be used to differentiate rats, which more static schedules do not distinguish. For example, earlier work by Halasz, Hughes, Humphreys and Persinger (1970) reported that short termed hyper-responding

occurred in neonatally irradiated rats but not control rats when they were subjected to schedule changes. Once the rats had adapted to the new schedules, differences in the groups were minimal. The utility of Halasz's technique can be anticipated as possible differentiation of short-termed neuronal mechanisms from longer term glial mechanisms.

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TABLE 2

STRAIN-SPECIFIC MEAN SHOCK THRESHOLDS (IN mA) FOR RATS PREVIOUSLY ADMINISTERED DRUGS AND EXPOSED TO TWO TASKS

| Strain | Sex | Drug | Test Order | Mean Shock Threshold (In mA) |
|---|---|---|---|---|
| MNR/Har/Lu | Female | Saline | Open-Field | .48 |
| | | | Avoidance | .47 |
| | | Taurine | Open-Field | .48 |
| | | | Avoidance | .48 |
| | Male | Saline | Open-Field | .50 |
| | | | Avoidance | .52 |
| | | Taurine | Open-Field | .54 |
| | | | Avoidance | .50 |
| MR/Har/Lu | Female | Saline | Open-Field | .53 |
| | | | Avoidance | .54 |
| | | Taurine | Open-Field | .51 |
| | | | Avoidance | .52 |
| | Male | Saline | Open-Field | .54 |
| | | | Avoidance | .59 |
| | | Taurine | Open-Field | .60 |
| | | | Avoidance | .58 |
| RCA/Lu | Female | Saline | Open-Field | .51 |
| | | | Avoidance | .50 |
| | | Taurine | Open-Field | .51 |
| | | | Avoidance | .50 |
| | Male | Saline | Open-Field | .55 |
| | | | Avoidance | .57 |
| | | Taurine | Open-Field | .54 |
| | | | Avoidance | .55 |

TABLE 3

THE SIGNIFICANT LEVELS FOR BETWEEN AND WITHIN FACTORS FOR ALL TESTED MEASURES

| | Measures | B1 | B2 | B12 | B3 | B13 | B4 | B14 | B23 | B123 | B24 | B124 | B34 | B134 | B234 | B1234 | W | W1B1 | W1B2 | W1B12 | W1B3 | W1B13 | W1B4 | W1B14 | W1B23 | W1B123 | W1B24 | W1B124 | W1B34 | W1B134 | W1B234 | W1B1234 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Avoidance Conditioning | Avoidance | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Escape Response Latency | | | | | | | | | | | | | | | | * | | | | | | | | | | | | | | | |
| | Inhibitory Response Failure | * | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | UER | * | * | | | | | | | | | | * | | * | | | | | | | | | | | | | | | | | |
| Open-Field | Sections Crossed (Total) | | * | | | * | | | | | | | | | | | * | | | | | | | | | | | | | | | |
| | Defecation | * | * | | | * | | | | | | | | | | | * | | | | | | | | | | | | | | | |
| Glandular Weight Analysis | Absolute Wt. Thyroids | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Adrenals | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Gonads | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Corrected Wt. Thyroids | * | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Adrenals | * | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | Gonads | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Body Weight | 28 Days | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 100 Days | * | * | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

* correlational significance at $p < .01$

B1 Strain, B2 Sex, B3 Drug, B4 Test Order, W Within Factor

TABLE 4

STRAIN AND SEX-SPECIFIC ABSOLUTE AND CORRECTED ENDOCRINE GLANDULAR WEIGHTS

| Strain | Sex | Measure in mg and mg/g | | | | | | Body Wt. |
|---|---|---|---|---|---|---|---|---|
| | | Thyroids | | Adrenals | | Gonads | | |
| | | mg | mg/g | mg | mg/g | mg | mg/g | (in g) |
| MNR/Har/Lu | Female | 5.49 | .0347 | 25.47 | .1610 | 58.25 | .367 | 158 |
| | Male | 6.22 | .0255 | 21.43 | .0878 | 1264.92 | 5.178 | 244 |
| MR/Har/Lu | Female | 5.92 | .0336 | 29.43 | .1668 | 55.50 | .315 | 177 |
| | Male | 7.35 | .0255 | 29.02 | .1001 | 1243.58 | 4.287 | 290 |
| RCA/Lu | Female | 6.87 | .0287 | 42.95 | .1789 | 66.67 | .278 | 240 |
| | Male | 7.21 | .0196 | 44.93 | .1220 | 1527.54 | 4.152 | 368 |