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Oral Taurine Effects on Inhibitory Behavior: Response Transients to Step-Like Schedule Changes

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Abstract. Rats habituated to DRL 6-s schedules that required response inhibition in order to obtain reward did not alter their total responses or efficiency ratios (response/reinforcement) when placed ad libitum (orally) on 0.9% taurine (1.1 ± 0.4 g/kg/24-h) relative to controls. In three separate experiments, taurine-administered rats did show significantly poorer adjustment profiles (higher response/reinforcement ratios) during the 15 min immediately following step-like increases in inhibition time demand to DRL 12 s. The effect was transient and was not significant in subsequent sessions. Taurine rats had been habituated to a DRL schedule intended to induce 'frustration' before the step-change did not differ from the taurine group maintained on the normal DRL schedule. No significant differences were noted between taurine and control groups, either before or after taurine administration or before or after the step-change in inhibition demand, with respect to defecation in the test chamber, daily fluid consumption, body weight or total responses. We concluded that oral taurine may inhibit learning during labile periods of adjustment following sudden changes of input demand but does not influence a well learned or established response pattern. These results imply taurine's role in the brain as a 'stabilizer' against short-term input fluctuations.

Key words: Response inhibition – Taurine – DRL schedule – Rat – Response transients – Defecation – Frustration – Temporal discrimination – Sudden reinforcement schedule changes.

Taurine has been suggested by several authors (e.g., Davidson and Kaczamarek, 1971) as an inhibitory transmitter or modulator candidate in the central nervous system. In general, taurine administration has been reported to inhibit behavioral (Baskin et al., 1974; Persinger et al., 1976) and neuroelectrical (Van Gelder, 1972; Mutani et al., 1974) processes. We decided to evaluate the effect of oral taurine (at a concentration that did not alter normal fluid intake) upon a complex behavior requiring response inhibition and learning. Although very high doses (21 mmole/kg) injected intraperitoneally (i.p.) have been associated with decreases in fixed-ratio responding (Thut et al., 1976), such behavioral changes may only reflect reactions to acute chemical concentrations since similar response patterns were produced by high concentrations of other substances.

If taurine is an inhibitor substance, then one might expect, simplistically, a facilitation of response inhibition. However, we suspected that the reported efficacy of taurine as an inhibitor of behavioral or neuroelectrical processes may be based on its propensity to retard labile CNS changes in the process of acquisition or consolidation. From this point of view, taurine would be a CNS 'stabilizer' against short-term input fluctuations. Newly acquired behaviors or recent deviations from neuroelectrical homeostasis would be significantly affected by taurine administration, older behaviors would not be influenced as much. The implication of this statement is most provocative with respect to taurine's therapeutic use: whereas recent CNS changes may be inhibited, undesirable and well established behaviors or congenital abnormalities may not be correspondingly inhibited by taurine treatments.

To test this hypothesis, we exposed rats to a behavioral situation that required well learned inhibitory response sequences as well as adjustment to new patterns of inhibition. The task selected was a DRL (differential reinforcement of low rate of responding) schedule, wherein a subject must postpone responding for a required interval of time in order to receive

a reward. Although steady-state response patterns typically are acquired over time for this schedule, transient response phenomena can be evoked when sudden changes in the inhibition time are instituted. Such short-term response patterns can differentiate subject populations that more static schedule procedures cannot (Halasz et al., 1970; Persinger et al., 1974). We suspected that taurine administration would not influence well learned responses to static schedules, but would exhibit short-term effects during transient periods of adjustment to new inhibitory demands.

However, if rats receiving taurine were to display less inhibitory responding only during the short period following a schedule change, then arguments could be posited that taurine facilitates 'frustration' or emotional responding to these extinction-like procedures. Such a possibility is not improbable in view of the extraordinarily high concentrations of taurine neurohypophysis and possibly ventral hypothalamus (Guidotti et al., 1972; Crabai et al., 1974). On the other hand, if taurine animals were exposed to a schedule that was similar to the schedule associated with the sudden change, they should show less failures of inhibition due to 'frustrational' factors during this period. This stimulus operation, in addition to the usual measurement of emotional behavior, i.e., defecation, was included in the present experimental design.

Oral administration of taurine was used since, unlike other modes, e.g., i.p. injections, less stress and handling artifacts confound the design. Passage of taurine into the adult mammalian brain has been described for this route (Urquhart et al., 1974), and most important, it would be the most likely route of administration for human treatment. In addition, unpublished data from our laboratory (Falter and Persinger, 1975) indicate significantly elevated forebrain and cerebellum taurine levels (+ 11% and + 18%, respectively) in rats maintained for 30 days on 0.9% taurine solutions during DRL training.

METHOD

In three separate experiments, 24 male Wistar strain rats (*Rattus norvegicus*), 100, 150, or 230 days of age when selected were used as subjects (8 rats/experiment). Experiments I, II, and III began in June, September, and December, 1974, respectively. Before testing, subjects had been maintained in single cages and gradually reduced to 80% free-feed body weight over a 21-day period. Subjects in Experiments I and III were maintained at this weight for the remainder of the study; weights of subjects in Experiment II were adjusted for growth. Following three days of continuous reinforcement training in single-lever Lafayette operant chambers (housed in ventilated masking noise boxes), the reinforcement schedule was changed to a DRL 6-s program. In this situation, the subject had to postpone lever responding at least 6 s in order to receive a 35 mg Noyes food pellet reward. If the time elapsed since the last reward was less than 6 s when the next lever press occurred, then the next reward availability was postponed another 6 s. This schedule was maintained by automatic programming equipment for the 2 test chambers used. However one of the chambers was so constructed that 1 out of every 3 pellets (an empirical average) did not fall into the delivery through but fell out of the subject's reach beneath the grid floor. This was called the 'frustration' DRL schedule. Four of the subjects for each experiment were tested in this chamber.

In all 3 experiments, subjects were maintained on the DRL 6-s schedule for 24 to 26 consecutive daily 30-min sessions until stable baselines were attained for daily total ratios of response (R)/total reinforcement (S^+), i.e., R/S^+ ratios. A stable baseline was defined as not more than 10% variation over a 5-day period for R/S^+ ratios between 2 and 3. Four of the animals in each experiment (2 for each test chamber) were then given 0.9% (0.07 M) taurine solutions in their graduated (ml) drinking cylinders. Pilot data indicated that this concentration did not significantly alter fluid consumption, a potentially important confounding variable in food reward operant studies. With this concentration of taurine, the average rat was expected to consume about 1g/kg/24 h of taurine. The other subjects received the vehicle (tap water). The amount of either taurine solution or water consumed every day was measured just before the daily test session. Taurine and water were changed daily.

After 7 days of taurine or water treatment, on what was called the 'step day', the schedule was suddenly changed half-way through the normal session from a DRL 6-s to a DRL 12-s schedule for the remaining 15 min, for each rat. The number of responses and reinforcements displayed before and after the 'step-change' in required inhibition time was recorded. During the later 10 to 14 daily sessions, the schedule remained at DRL 12 s. Subjects were always tested in the same chambers, in the same order and between 09:00 and 13:00. Post-sessional measurements of defecation in the chamber were taken for each rat. All analyses were completed by an IBM 360–40 computer and checked by hand calculations.

RESULTS

For analysis purposes, the subjects were divided into 4 groups (6 rats/group): taurine-normal DRL schedule (TN), taurine-'frustrational' DRL schedule (TF), control-normal DRL schedule (CN), and control-'frustrational' DRL schedule (CF). The mean R/S^+ ratios and their standard deviations for the TN, TF, CN, and CF groups for the 5 days before and 5 days after taurine (or water) administration are shown in Figure 1. A 2-way analysis of variance (ANOVA) indicated no statistically significant differences between schedules or treatments ($F < 1$, $df = 1/20$). The mean *changes in ratios* and their standard deviations, calculated by dividing the mean R/S^+ ratios for each subject after the taurine or water treatment by the mean R/S^+ ratios before the treatment for the TN, TF, CN, and CF groups, were 0.90 ± 0.09, 0.97 ± 0.16, 0.81 ± 0.25, 0.98 ± 0.12, respectively. However a 2-way analysis of variance (ANOVA) indicated no statistically significant differences between treatments ($F < 1$) nor schedules ($F = 3.02$;

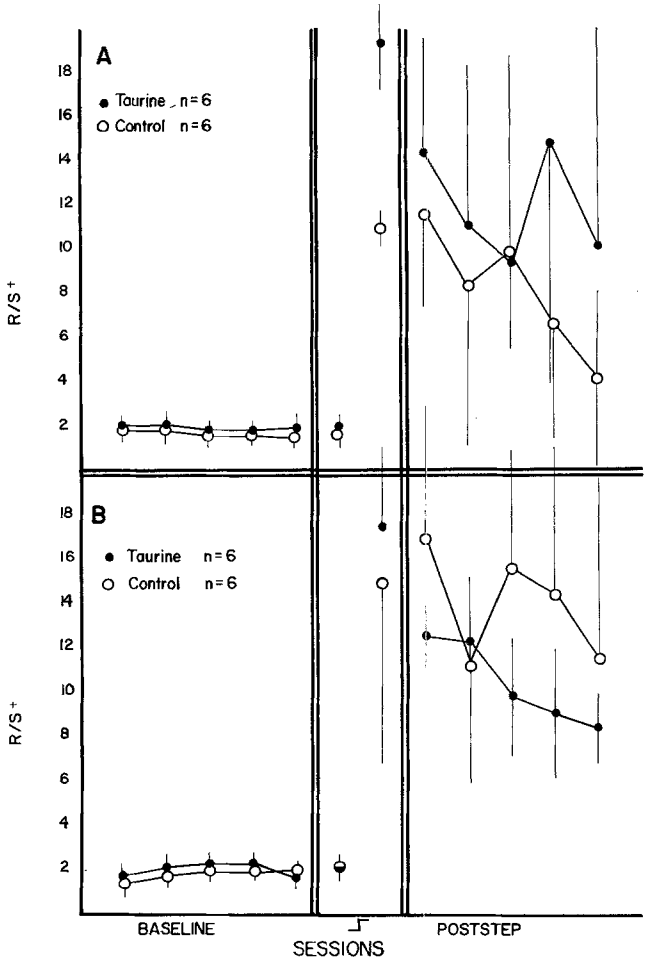

Fig. 1. Mean total response/total reinforcement ratios (R/S^+) from the separate experiments for rats that were maintained on taurine or water orally during: pre-step DRL 6 s baseline sessions, the sudden mid-session step (⌐) from DRL 6 s to DRL 12 s, and post-step (DRL 12 s) sessions. Animals in A (TN, CN) had been exposed to normal DRL 6-s schedules while those in B (TF, CF) had been exposed to DRL 6-s schedules intended to induce 'frustration'. Vertical bars indicate standard deviations

$df = 1/20$; $P < 0.10$). A 3-way ANOVA with one measure repeated for total responses emitted before and after treatment application showed no significant differences on any factor. Defecation in the chamber before and after ($\pm$ 5 days) taurine or water administration also was found by 3-way ANOVA not to be significant at any level of analysis. Ratios of daily water consumption for the 5 days before and after treatment for the TN, TF, CN, and CF groups were 1.09 ± 0.17, 1.13 ± 0.15, 1.12 ± 0.27, and 1.01 ± 0.05. These differences were not significant. Since the rats drank 25–50 ml of fluid/day, calculations demonstrated the taurine subjects were consuming 1.1 ± 0.4 g of taurine/kg of body weight/24 h.

The means and S.D.s for the R/S^+ ratios for different groups before and during the 15 min after the sudden schedule change (⌐) on the single step session and for post-step sessions are shown also in Figure 1. A 2-way ANOVA indicated only a significant treatment effect ($F = 7.23$; $df = 1/20$, $P < 0.01$; however, the homogeneity of variance test was significant ($P < 0.01$). Group variance tests indicated significant differences between the TN and TF groups ($F = 12.48$, $df = 6/6$, $P < 0.01$), and between the CN and CF groups ($F = 176.80$, $df = 6/6$, $P < 0.001$), but not between the TN and CN or TF and CF groups. The 12 frustration condition rats had significantly greater ($F = 35.48$, $df = 12/12$, $P < 0.001$) group variance than the 12 normal condition rats. When comparisons were made only between the control and taurine groups (with homogeneity of variance) tested in the normal DRL schedule, more significant differences were noted ($t = 11.05$; $df = 1/10$, $P < 0.01$). Nonparametric analysis also showed that the 12 taurine drinking rats were significantly different from the 12 control rats ($\chi^2 = 9.86$, $df = 1$, $P < 0.01$) on this measure. A 3-way ANOVA for experiments (3), conditions (2), and chambres (2) also indicated that *only* the taurine and control differences were statistically significant ($F = 5.98$, $df = 1/12$; $P < 0.05$). The mean post-step R/S^+ ratios between groups were not significant ($F < 1$). Means and S.D.s for the number of fecal boluses left in the chambers on the step day for the above groups were 1.7 ± 2.8, 0.0, 0.3 ± 0.5, and 1.0 ± 1.6, respectively ($F < 1$). Although there was a significant increase in defecation during the 5 days after the step relative to the 5-day baseline ($F = 30.35$; $df = 1/20$; $P < 0.001$), there were neither treatment or schedule differences ($F < 1$). There was a decrease in fluid consumption for all groups after the step change; the ratios of fluid consumed after with respect to before the step for the TN, TF, CN, and CF groups were 0.98 ± 0.11, 0.96 ± 0.22, 0.88 ± 0.25, and 0.97 ± 0.16 ($F < 1$). Pre/post-step ($\pm$ 5 days) body weight losses for the 4 groups were 0.97, 0.96, 0.98, and 0.96 of the 80% body weight.

DISCUSSION

The results of three replications indicated that well established or habituated response modes ostensibly involving inhibitory processes were not readily influenced by ingestion of 0.9% taurine for more than one week. The fact that improvement of inhibition was still possible was indicated by the decreasing response/reinforcement ratios for all groups during baseline sessions.

Instead, the major taurine effect occurred immediately following the change in response demand,

when the rats were attempting to adjust to the new learning schedule. Rats maintained on a normal DRL 6 s schedule while receiving taurine displayed significantly *poorer* adjustment immediately following the step-like change to DRL 12 s, relative to controls; however, this effect was transient and not evident in post-step sessions. Such an effect supports the thesis of taurine acting as a 'stabilizer' against short-term (relative to the response system) input fluctuations. This effect is interesting in light of taurine's likely affinity for calcium ions, which have a propensity to retard acquisition (John, 1967).

It is unlikely that the results were artifacts of water consumption, body weight, or total lever responding since the groups did not differ significantly on these measures. The confounding effects of 'emotional' or 'frustration' behavior following sudden decreases in reinforcement ratios do not seem likely since taurine subjects did not display greater chamber defecation, although any weak effect may have been masked by the highly significant post-step increases in this measure for all groups. Reinforcement histories intended to induce 'frustration' were associated with such large increases in group response variability that the role of this factor in the taurine effect is still not clear.

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